[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA
AND THE NATIONAL INSTITUTE OF HEALTH]

STUDIES IN THE PHENANTHRENE SERIES. XXV. DIBENZO-[f,h] QUINOLINE AND 7-METHOXYDIBENZO-[f,h] QUINOLINE[1]

JOHN KRUEGER AND ERICH MOSETTIG

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In continuation of previous investigations in the naphthoquinoline series (1), we describe in this communication the synthesis of dibenzo-[f,h]quinoline (I) and 7-hydroxydibenzo[f,h]quinoline (IV) and some of their derivatives. The quinoline bases I and IV were prepared in satisfactory yields by applying the Skraup synthesis to 9-aminophenanthrene[2] and to 3-methoxy-9-aminophenanthrene. The quinoline bases were reduced catalytically to the "py-tetrahydro" derivatives II and V. When we attempted to convert II into the methiodide of III by the previously (1b) successful procedure with potassium hydroxide and methyl iodide, only the tertiary base (III) was obtained. The fact that under these conditions no addition of methyl iodide to base III could be achieved, points to a sterically hindering effect for which the nearness of carbon atom 12 to the N-methyl group in position 1 may be responsible. Difficulties were also experienced in preparing the methiodide VIa, either from base V or base VI. In the latter reaction the yield of methiodide was low. The salt could be readily decomposed into methyl iodide and tertiary base. These observations being of qualitative nature only do not justify speculations on the influence of the hydroxyl or methoxyl group in position 7 on the quaternary salt formation.

EXPERIMENTAL

All melting points are corrected unless otherwise designated.

9-Aminophenanthrene. A mixture of 24 g. of pure 9-acetylphenanthrene[3], 19 g. of

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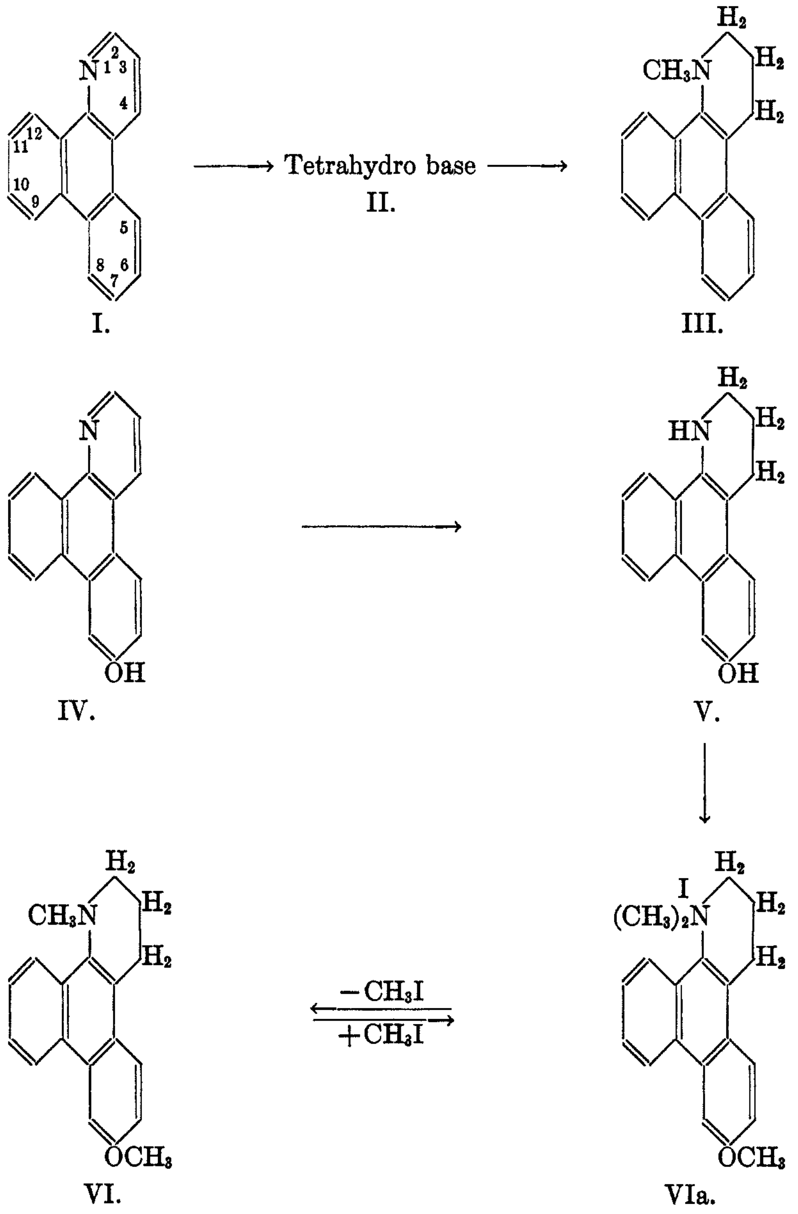
[1] The work reported in this paper is part of a unification of effort by a number of agencies having responsibility for the solution of the problem of drug addiction. The organizations taking part are: The Rockefeller Foundation, the National Research Council, the U. S. Public Health Service, the U. S. Bureau of Narcotics, the University of Virginia, and the University of Michigan. Publication authorized by the Surgeon General, U. S. P. H. S.

[2] The synthesis of I ("phenanthroquinoline") has been reported previously by Herschmann (2).

[3] 9-Acetylphenanthrene was conveniently prepared by the method of Bachmann and Boatner [*J. Am. Chem. Soc.*, **58**, 2097 (1936)].

hydroxylamine hydrochloride, 34 cc. of pyridine, and 90 cc. of absolute ethanol was boiled for three and one-half hours. The solution was poured into water and a white oil precipitated, which gradually became crystalline. The crystalline material weighed 26 g. and melted unsharply at 120–130°. It was dissolved in a mixture of 90



cc. of acetic acid and 60 cc. of acetic anhydride. Hydrogen chloride gas was passed rapidly through the mixture for thirty-five minutes. The flask was stoppered and allowed to stand overnight. The heavy crystalline precipitate was filtered off, and the compound was hydrolyzed by boiling in a mixture of 200 cc. of glacial acetic acid and 200 cc. of 18% hydrochloric acid. The amine hydrochloride was filtered off, suspended in hot water, and decomposed with ammonia. The base melted at 128–130°; yield 60% (calculated from the acetylphenanthrene).

Dibenzo[f,h]quinoline (I). Eighteen grams of the crude 9-aminophenanthrene, 8 cc. of nitrobenzene, and 45 cc. of glycerine were well mixed in an Erlenmeyer flask, and 18 cc. of C. P. sulfuric acid was added with thorough stirring. The mixture was heated at 145° for four hours, and was allowed to stand overnight. It was poured into water and extracted three times with ether. On addition of ammonia to the aqueous solution, a dark brown solid precipitated, which was filtered off and dried at 100°. It was sublimed at 150° in an oil-pump vacuum. The yellow base obtained crystallized from benzene in long, fine, felted yellow needles; 10 g., m.p. 167–169°. Herschmann (2) gives the m.p. 174°.

The *hydrochloride* crystallized from alcohol in white needles.

Anal. Calc'd for $C_{17}H_{12}ClN$: Cl, 13.35. Found: Cl, 13.63.

1,2,3,4-Tetrahydrodibenzo[f,h]quinoline (II). Six and one-half grams of dibenzo[f,h] quinoline in 200 cc. of glacial acetic acid absorbed the calculated amount (2 moles) of hydrogen (0.4 g. of platinum oxide as catalyst) within thirty hours. The catalyst was filtered off, and a concentrated aqueous sodium chloride solution was added to the filtrate, whereby the hydrochloride was precipitated. It was decomposed with ammonia, and the base was extracted into ether. The yield was 5.4 g. of the tetrahydro compound melting at 115–116°. The base crystallized from a benzene-petroleum ether mixture in pale yellow prisms, m.p. 117–118°.

Anal. Calc'd for $C_{17}H_{15}N$: C, 87.51; H, 6.49.
Found: C, 87.49; H, 6.45.

The *hydrochloride*, white, shiny leaflets, melted after recrystallization from aqueous hydrochloric acid at 245–247° (softening at 230°, uncorr., evac. tube).

Anal. Calc'd for $C_{17}H_{16}ClN$: Cl, 13.15. Found: Cl, 13.00.

1-Methyl-1,2,3,4-tetrahydrodibenzo[f,h]quinoline (III). To a mixture of 5.4 g. of the tetrahydroquinoline derivative and 8.5 cc. of methyl iodide was added a mixture of 9 g. of potassium hydroxide in 10 cc. of water and 50 cc. of acetone. No precipitation was observed when the mixture was allowed to stand at room temperature for three hours. On evaporation of the acetone, an oil precipitated. This was brought into solution again with acetone, 4 cc. of methyl iodide and 4.5 g. of potassium hydroxide in 5 cc. of water were added, and the mixture was heated in a Lintner bottle at 100° for one and one-half hours. The acetone was distilled off, and the oil that precipitated was extracted with ether. The residue left on evaporation of the ethereal solution became gradually crystalline and melted at 65–67° (5.2 g.). The base was most conveniently purified, practically without losses, by very slow distillation in an oil-pump vacuum at 110°. The distillate consisted of nearly colorless, broad, elongated prisms, which melted at 81–83°. The base is easily soluble in alcohol, ether, and petroleum ether.

Anal. Calc'd for $C_{18}H_{17}N$: C, 87.41; H, 6.93.
Found: C, 87.28; H, 6.97.

The *hydrochloride* was prepared in the usual manner with alcoholic hydrogen chloride. It crystallizes from an alcohol-ether mixture in balls of fine needles which gradually change to stout prisms. The melting point is rather indefinite. In a vacuum the substance begins to melt at about 200° and gradually decomposes between 230° and 275°.

Anal. Calc'd for $C_{18}H_{18}ClN$: C, 76.16; H, 6.40.
Found: C, 76.71; H, 6.42.

No methiodide was formed when a mixture of base and methyl iodide in a small amount of acetone was allowed to stand for two days.

7-Hydroxydibenzo[f,h]quinoline (IV). The starting material for the synthesis of this compound, 3-hydroxy-9-aminophenanthrene, was prepared according to Burger and Mosettig (3), with the modification, however, that the saponification of the acetoxy compound and the reduction of 3-hydroxy-9-nitrophenanthrene were carried out in one procedure. A suspension of 18.5 g. of finely divided 3-acetoxy-9-nitrophenanthrene in 200 cc. of 50% sodium hydroxide was heated at 90° until a dark red solution was formed. A solution of 55 g. of sodium hydrosulfite was added, the temperature not being allowed to rise above 110°. After five minutes, 200 cc. of water was added, and heating at 90–95° was continued for ten minutes. The solution was diluted with water to a volume of two liters, and carbon dioxide was passed through. The heavy, yellowish precipitate was washed first with water containing some sodium hydrosulfite, and then successively with water and alcohol. The dry reduction-product weighed 13.5 g. and was used without further purification in the Skraup synthesis.

Thirteen and five-tenths grams of the above product, 15 cc. of nitrobenzene, 3.0 g. of ferrous sulfate, and 32 g. of glycerine were well mixed. Fifteen cubic centimeters of C. P. sulfuric acid was added with thorough stirring, and the mixture was heated to 145° until the reaction set in. Then the reaction was allowed to proceed without application of heat. After the reaction had subsided, the mixture was heated at 145° for thirty minutes. The dark reaction-mixture was diluted with water and extracted with ether. To the aqueous layer concentrated sodium chloride solution was added, which precipitated a brown hydrochloride. From this the base was liberated with ammonia as a gray crystalline mass. It was purified by sublimation in an oil-pump vacuum, and subsequent recrystallization from dioxane; pale yellow needles, m.p. 270–273° (evac. tube), yield 9 g. The base is sparingly soluble in alcohol, chloroform, acetone, and ether.

Anal. Calc'd for $C_{17}H_{11}NO$: C, 83.25; H, 4.51; N, 5.70.
Found: C, 83.47; H, 4.89; N, 6.06.

Hydrochloride. Two-tenths gram of the base was treated with hot dilute hydrochloric acid, some insoluble material was filtered off, and concentrated hydrochloric acid was added to the filtrate. The hydrochloride precipitated in tiny, bright yellow, felted needles (0.15 g.) that showed an indefinite melting point. The salt hydrolyzes strongly.

Anal. Calc'd for $C_{17}H_{12}ClNO$: Cl, 12.59. Found: Cl, 12.68.

7-Hydroxy-1,2,3,4-tetrahydrodibenzo[f,h]quinoline (V). Twelve grams of the above quinoline base and 1.5 g. of Chromite catalyst in 75 cc. of absolute ethanol were heated in an Adkins high-pressure hydrogenation apparatus to 150° in about one hour. Shaking at this temperature and at a pressure of 140 atm. was continued for forty minutes. From the reduction-mixture, a fraction of 8 g., melting at 228–230°, and a less pure fraction of 2.5 g., melting at 210–220°, were obtained. The tetrahydro base crystallized from absolute ethanol in pale green, hexagon-shaped crystals, which melted at 230–232°. The base may be purified also by sublimation at 180° in an oil-pump vacuum.

Anal. Calc'd for $C_{17}H_{15}NO$: C, 81.89; H, 6.07; N, 5.62.
Found: C, 81.97; H, 5.99; N, 5.73.

The *hydrochloride* was prepared in the usual manner with alcoholic hydrogen chloride. It melted, after recrystallization from aqueous hydrochloric acid, unsharply at 279–286° (uncorr.). The salt hydrolyzed readily.

Anal. Calc'd for $C_{17}H_{16}ClNO$: Cl, 12.41. Found: Cl, 12.55.

7-Methoxy-1-methyl-1,2,3,4-tetrahydrodibenzo[f,h]quinoline (VI). A mixture of 3.2 g. of base V, 8 g. of methyl iodide, 5.1 g. of potassium hydroxide, 5 cc. of water, and 30 cc. of acetone in a Lintner bottle was heated at 100° for one hour. The following day, 4 g. of methyl iodide and 2.5 g. of potassium hydroxide were added, and the mixture was heated again for one hour. The solvent was allowed to evaporate until the methiodide precipitated in brownish crystals. These were filtered off and decomposed in a water-pump vacuum at 150–170°. The tertiary base was then distilled over at 200°. The partly oily and partly crystalline distillate was dissolved in alcohol, from which the base crystallized on cooling in colorless rectangular crystals; m.p. 131.5–133°, yield 2.2 g.

Anal. Calc'd for $C_{19}H_{19}NO$: C, 82.26; H, 6.91; N, 5.05.
Found: C, 81.91; H, 6.65; N, 5.21.

The *hydrochloride* prepared in the usual manner melted at 204–206° with gas evolution. It hydrolyzes readily.

Anal. Calc'd for $C_{19}H_{20}ClNO$: Cl, 11.31. Found: Cl, 11.39.

The *methiodide* (VIa) was prepared by dissolving 0.2 g. of the N-methyltetrahydro base (VI) in a mixture of 3 cc. of acetone and 1 cc. of methyl iodide. The crystalline precipitate (0.1 g.) was collected after two days. The substance has an indefinite melting point; softening began at 145°, gas evolution took place at 175°, and the melt became clear at 200°. It resolidified on cooling and remelted at 128–130°. Apparently the methiodide is converted into the tertiary base by melting.

Anal. Calc'd for $C_{20}H_{22}INO$: I, 30.29. Found: I, 30.00.

SUMMARY

The preparation of dibenzo[f,h]quinoline and 7-methoxydibenzo[f,h]quinoline and some of their derivatives is described.

WASHINGTON, D. C.

REFERENCES

(1) (a) MOSETTIG AND KRUEGER, *J. Am. Chem. Soc.*, **58**, 1311 (1936).
(b) MOSETTIG AND KRUEGER, *J. Org. Chem.*, **3**, 317 (1938).
(2) HERSCHMANN, *Ber.*, **41**, 1998 (1908).
(3) BURGER AND MOSETTIG, *J. Am. Chem. Soc.*, **56**, 1745 (1935).