Reduction[12] of the dye and oxidation[13] of the diamine so formed gave 1,4-naphthoquinone, identified by melting point and mixed melting point.

2. Other diazonium salts: Coupling under the same conditions with diazonium salts from *m*-aminobenzoic acid, anthranilic acid and benzidine gave dyes which were found not to contain boron and were not investigated further.

4-Methoxy-1-naphthaleneboronic Acid.—To the Grignard solution (concentration about 0.8 *M*) from 4-methoxy-1-bromonaphthalene[14] was added dropwise an equimolar amount of *n*-butyl borate as an ether solution of concentration about 1.1 *M* while the temperature was maintained at −60°. The reaction mixture was allowed to remain in the cooling bath overnight. It was treated with water, and the product was recovered by several extractions of the ether solution with 2% aqueous sodium hydroxide. The crude boronic acid was obtained in 53% yield by acidification of the alkaline extracts. It was purified by reprecipitation from dilute alkali by acidification, followed by precipitation from ethanol by dilution with water. Samples dried *in vacuo* at room temperature underwent visible decomposition at about 150–155°, in an ordinary melting point determination, but the decomposition product (presumably the anhydride) did not melt completely at temperatures up to 250°. A reproducible melting point of 195° could be determined by the instant immersion method.[15] The boronic acid was titrated in 20% ethanol solution containing mannitol with 0.05 *N* sodium hydroxide solution to a phenolphthalein end-point; the neutralization equivalent was found to be within the limits of 199–203 (calcd. 201.8).

Reactions of 4-Methoxy-1-naphthaleneboronic Acid. (a) **With Nitric Acid.**—To a well-stirred suspension of one gram of the boronic acid in 10 ml. of glacial acetic acid at room temperature was added 1 ml. of a solution of equal volumes of concentrated nitric acid and water. Thirty minutes later the mixture was diluted with 50 ml. of cold water, and the solid which separated was recrystallized from 95% ethanol. The yellow solid melted at 138–139°, and the melting point was not changed by the addition of authentic 2,4-dinitro-1-naphthol.

When the experiment was repeated with the temperature of the reaction mixture maintained at about 2° the 4-methoxy-1-naphthaleneboronic acid was recovered.

(b) **With Nitrous Acid.**—To a vigorously stirred suspension of 1 g. of the acid in 10 ml. of glacial acetic acid at room temperature was added 1.5 ml. of 20% aqueous sodium nitrite solution. Thirty minutes later the mixture was filtered and the filtrate was diluted with 75 ml. of water. The diluted solution was extracted with ether and the oil which remained after evaporation of the ether was dissolved in ethanol, decolorized and treated with 1,3,5-trinitrobenzene. The crystals which formed melted at 138–139° (lit.[16] 138°) alone or mixed with the trinitrobenzene derivative of 1-methoxynaphthalene.

No reaction occurred when the experiment was carried out at 0°.

(c) **With Dilute Acetic Acid.**—A mixture of 1 g. of the boronic acid and 15 ml. of glacial acetic acid was refluxed for thirty minutes. Examination of the cooled solution revealed no evidence of reaction, so 10 ml. of water was added and the refluxing was continued for an additional half-hour. The cooled solution was diluted with 50 ml. of water and the oil which separated was extracted with ether. The ether extracts were washed with dilute alkali, dried and evaporated to give an oil which was identified as 1-methoxynaphthalene by conversion to the trinitrobenzene derivative as described in the preceding section.

(d) **With Aqueous Sodium Hydroxide.**—A solution of 1 g. of the boronic acid in 25 ml. of 10% aqueous sodium hydroxide was boiled gently for half an hour with occasional additions of water to keep the volume approximately constant. The cooled mixture was extracted with ether and the dried extracts were evaporated to give a small amount of an oil which was identified as 1-methoxynaphthalene by the melting point and mixed melting point of the trinitrobenzene derivative. Acidification of the alkaline solution caused the separation of 0.6 g. of the unchanged boronic acid (II).

Summary

4-Dimethylamino-1-naphthaleneboronic acid and 4-methoxy-1-naphthaleneboronic acid have been prepared and subjected to the action of various reagents. The boronic acid group of either substance is removed readily by mild hydrolysis or by replacement under the influence of reagents such as dilute acids, dilute bases, nitric acid, nitrous acid and certain diazonium salts. The boronic acid group is more highly labilized by the 4-dimethylamino group than by the 4-methoxyl group.

(12) Conant, Lutz and Corson, "Org. Syn.," Coll. Vol. I, ed. 2, p. 49.

(13) Fieser, *ibid.*, p. 383.

(14) Tourneau and Trefouel, *Bull. soc. chim.*, **45**, 121 (1929).

(15) Branch, Yabroff and Bettmann, THIS JOURNAL, **56**, 937 (1934).

(16) See p. 141 of the work cited in ref. 11.

URBANA, ILLINOIS RECEIVED JULY 24, 1947

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Synthesis of β-Carbolines. IV. 3-Aminoharman and Some of its Derivatives[1]

BY H. R. SNYDER, STANLEY M. PARMERTER[2] AND HOWARD G. WALKER[3]

In the preceding paper the synthesis of 6-aminoharman by the reduction of the nitro compound was reported. It is to be expected that the isomeric 3-aminoharman may be prepared from harman-3-carboxylic acid by application of the Hofmann[4] or Curtius[5] reaction. This paper reports the synthesis of 3-aminoharman from the acid azide and its conversion to the sulfanilyl derivative (III) and the 3-diethylaminopropyl derivative (IV), isolated as the dipicrate.

Preliminary tests indicated that the ester (I) could be converted to the hydrazide much more

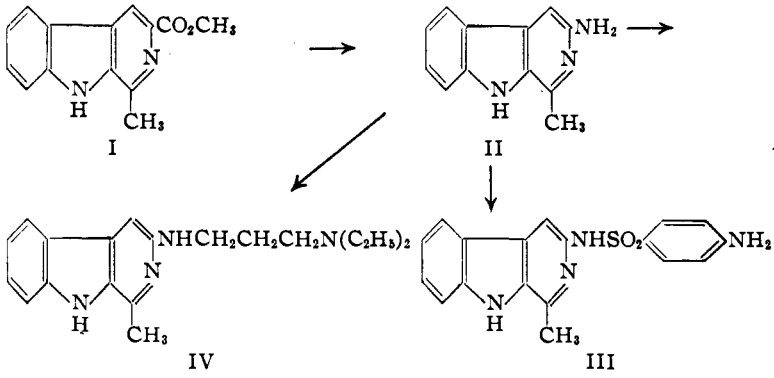
(1) For the preceding paper see Snyder, Parmerter and Katz, THIS JOURNAL, **69**, 222 (1947).

(2) Wm. S. Merrell Post-Doctorate Fellow, 1944–1945. Present address: Eastman Kodak Co., Rochester, N. Y.

(3) Wm. S. Merrell Post-Doctorate Fellow, 1946–1947. Present address: University of California at Los Angeles.

(4) See Wallis and Lane, *The Hofmann Reaction*, "Organic Reactions," Vol. III, John Wiley and Sons, New York, N. Y. 1946, p. 267.

(5) See Smith, *The Curtius Reaction*, "Organic Reactions," Vol. III, John Wiley and Sons, New York, N. Y., 1946, p. 337.



readily than to the amide, so that the Curtius reaction was chosen for the preparation of the amine (II). The azide, obtained by treatment of the hydrazide with cold aqueous nitrous acid, proved to be quite stable. It could be converted directly to the amine by refluxing with fifty per cent. acetic acid, but better yields of a more readily purified product resulted from the preparation and hydrolysis of the benzyl carbamate. The sulfanilyl derivative (III) was prepared by the reaction of the amine with acetylsulfanilyl chloride in the presence of pyridine[6] and hydrolysis of the acetyl group in the usual fashion. The 3-diethylaminopropyl derivative of the amine was prepared by refluxing an ethanol solution of the amine and 3-diethylaminopropyl chloride containing a trace of potassium iodide. The resulting triamine has been purified as the dipicrate; the free base and its salts with various mineral acids and carboxylic acids have resisted all attempts to induce crystallization.

Experimental

Harman-3-carbonyl Hydrazide.—A mixture of 10 g. of methyl 3-harmancarboxylate,[7] 50 ml. of 85% hydrazine hydrate, 100 ml. of *n*-amyl alcohol and 28 ml. of absolute ethanol was refluxed four hours. The solution was cooled overnight in the refrigerator (5°) before the tan needles were collected and washed with cold water and ether. The crude material melting at 295° (dec.) weighed 9.0 g. (yield, 90%). Concentration of the mother liquor gave 0.7 g. of less pure material. A sample recrystallized from ethanol (95%) melted at 288°.

Anal. Calcd. for $C_{13}H_{12}N_4O$: C, 64.99; H, 5.04. Found: C, 65.04; H, 5.31.

Harman-3-carbonyl azide was prepared by dissolving 4.16 g. of the hydrazide in 200 ml. of water containing 2.5 ml. of concentrated hydrochloric acid. The solution was cooled to below 5°, and a solution of 1.38 g. of sodium nitrite in 5 ml. of water was added. The resulting mixture was allowed to stand in the cold with occasional stirring for fifteen minutes, and was then neutralized by the addition of excess saturated sodium bicarbonate solution. The pasty suspension thus formed was rather difficult to filter, but this method was found most satisfactory for the isolation of the solid azide. The crude azide was washed with cold water and then with ether before being dried to constant weight *in vacuo*. An approximately quantitative yield of azide was obtained. The crude product was used without purification. The compound appeared to be completely stable at room temperature.

Benzyl 3-Harmylcarbamate.—The preparation of the benzyl carbamate was carried out in a 100-ml. flask with a reflux condenser provided with a drying tube. A mixture of 4.27 g. of the azide, 40 ml. of dry xylene and 4.0 ml. of redistilled benzyl alcohol was placed in the flask and the temperature raised to 110–120° by means of an oil-bath. The evolution of nitrogen proceeded smoothly at this temperature. The heating was maintained for one-half hour and the reaction mixture was allowed to stand in the refrigerator overnight. The product was filtered, washed with cold xylene followed by low-boiling petroleum ether and dried; yield 4.48 g. (81%); m. p. 188–190°. No appreciable amount of material could be obtained by the addition of low-boiling petroleum ether to the mother liquor. A sample was recrystallized twice from *n*-butyl alcohol, m. p. 186–186.5°.

Anal. Calcd. for $C_{20}H_{17}O_2N_3$: C, 72.48; H, 5.19; N, 12.68. Found: C, 72.07; H, 5.50; N, 12.96.

3-Aminoharman from the Benzyl Carbamate.—A mixture of 9.75 g. of the carbamate, 50 ml. of diethylene glycol, 8.35 ml. of water and 8.35 g. of potassium hydroxide was stirred for one-half hour in a 200-ml. round-bottom flask equipped with an air condenser and immersed in an oil-bath at 150–160°. The cooled contents of the flask were poured into 325 ml. of ice and water and allowed to stand in an ice-bath for one and one-half hours before the solid product was filtered. The crude product (m. p., 223–226°) was recrystallized from dilute aqueous ethanol, yielding 4.80 g. (83%) of dried product, m. p. 226–227°. A sample of the 3-aminoharman which had been recrystallized several times from dilute ethanol melted at 228–229°.

Anal. Calcd. for $C_{12}H_{11}N_3$: C, 73.09; H, 5.62. Found: C, 72.97; H, 5.58.

3-Sulfanilamidoharman.—In a 100-ml., two-necked flask equipped with a sealed stirrer and a reflux condenser protected by a drying tube was placed 3.72 g. of 3-aminoharman, 48 ml. of dry pyridine and 4.55 g. of acetylsulfanilyl chloride (commercial grade recrystallized once from chloroform). The mixture was heated on the steam-bath with stirring for three hours and then poured into 700 ml. of cold water. A crystalline product formed slowly and was allowed to stand in an ice-bath for one hour before it was filtered and washed well with cold water. A sample of this product was dried, m. p. 287–289° (dec.). The wet product (7.24 g.) was suspended in 207 ml. of 12% hydrochloric acid and heated on the steam-bath for thirty-five minutes with stirring. Since most of the solid had gone into solution at the end of this time, the solution was filtered. The residue remaining on the filter was heated for fifteen minutes with an additional 30-ml. portion of the dilute acid, and after filtration of this mixture the acid filtrates were combined, cooled and made alkaline with concentrated ammonium hydroxide. The mixture was allowed to stand in an ice-bath for one hour, and the slightly yellow crystals were filtered and recrystallized from a pyridine–water mixture. There was obtained 3.70 g. of recrystallized 3-sulfanilamidoharman (57%), m. p. 301–302° (dec.).

Anal. Calcd. for $C_{18}H_{16}O_2N_4S$: C, 61.35; H, 4.58. Found: C, 61.46; H, 4.41.

3-(3′-Diethylaminopropylamino)-harman.—A mixture of 0.85 g. of 3-aminoharman, 0.79 g. of γ-diethylaminopropyl chloride and 8.5 ml. of ethanol (95%) containing a crystal of potassium iodide was refluxed on the steam-bath for about thirty hours.[8] At the end of this time, the alcohol was removed by distillation, water was added

(6) Winterbottom, THIS JOURNAL, **62**, 160 (1940).

(7) Snyder, Hansch, Katz, Parmerter and Spaeth, *ibid.*, **70**, 219 (1948).

(8) Method of Easton and Snyder, *ibid.*, **68**, 1550 (1946.)

to the reaction product and the resulting solution made basic with excess ammonium hydroxide. The organic material was taken up in chloroform, washed with water and dried over sodium sulfate. The product was converted to a picrate by removing the chloroform at reduced pressure, dissolving the residue in a minimum of absolute ethanol and adding an excess of a chilled, saturated solution of picric acid in absolute ethanol. After standing overnight in the refrigerator the crude picrate was filtered and placed in a Soxhlet extraction cup. The material was extracted with methanol until no further crystallization from the hot solvent occurred. There was obtained 1.35 g. of orange solid, m. p. 210–212° (dec.), which evidently was the dipicrate of 3-(3′-diethylaminopropylamino)-harman. After two more recrystallizations from methanol it melted at 213.5–215° (dec.).

Anal. Calcd. for $C_{31}H_{32}N_{10}O_{14}$: C, 48.44; H, 4.20. Found: C, 48.33; H, 4.20.

Summary

3-Aminoharman is prepared from methyl harman-3-carboxylate by means of the Curtius reaction. 3-Sulfanilamidoharman and 3-(3′-diethylaminopropylamino)-harman (as the dipicrate) are prepared from 3-aminoharman.

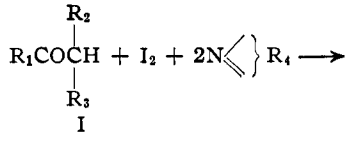
URBANA, ILLINOIS RECEIVED AUGUST 7, 1947

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NORTHWESTERN UNIVERSITY]

The Reaction of Ketones with Iodine and Pyridine

BY L. CARROLL KING, MARGARET MCWHIRTER AND R. L. ROWLAND

Previous papers from this Laboratory,[1] and from the National Cancer Institute,[2] have reported the preparation of quaternary salts of type (II) by means of the following reaction.



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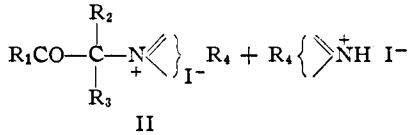


II

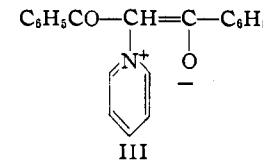
where $R_3 = R_2 = H$

Salts have been reported where R_1 was aryl[1a,1b,2] or a cyclopentanophenanthrene derivative[1a] and where $N\langle\rangle R_4$ was any of a number of heterocyclic nitrogeneous bases.[1c,2] In the present paper this reaction has been extended to include variation in R_2 and R_3 and additional variation in R_1.

The quaternary salts obtained when R_1 was 2- or 3-phenanthryl, thienyl or any of a variety of substituted phenyl groups are listed in Table I. When R_2 was an alkyl or aryl side chain the reaction gave the expected quaternary salt in each case but with increasing length of the alkyl side chain the salts became more difficult to purify and crystallize. A pure quaternary salt was not obtained from isobutyrophenone ($R_2 = R_3 = CH_3$). Data for these materials are also reported in Table I.

In addition to the substances reported in the tables, quaternary salts were prepared from dibenzoylmethane (R_2 = benzoyl), and from α-tetralone.

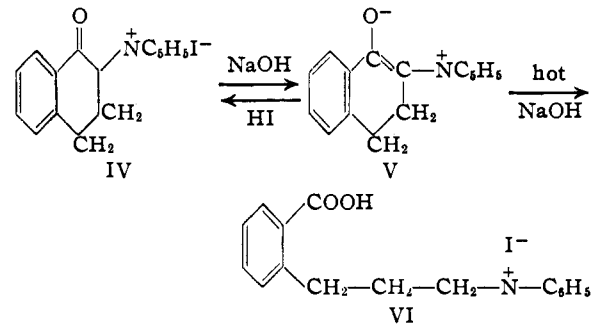
From the reaction of dibenzoylmethane with iodine and pyridine, 1-phenacylpyridinium iodide was isolated. The betaine (III) reported to be produced in 40% yield from the reaction of bro-



III

modibenzoylmethane with pyridine[3] was not observed.

From the reaction of α-tetralone with pyridine and iodine, 1-keto-2-tetrahydronaphthylpyridinium iodide (IV) was obtained. When (IV) was treated with cold alkali an orange betaine (V) separated. This substance could be reconverted to the salt (IV) and on prolonged alkaline hydrolysis in the presence of potassium iodide (IV) was converted to (VI). This behavior is analogous to



IV V VI

that reported by Krollpfeiffer and Müller[4] for the corresponding pyridinium bromide.

Each of the quaternary salts reported was subjected to alkaline hydrolysis. The acids produced in these experiments are listed in Table II. No isodurylic acid was obtained from 1-(2,4,6-tri-

(1a) King, THIS JOURNAL, **66**, 894, 1612 (1944).
(1b) King, McWhirter and Barton, *ibid.*, **67**, 2089 (1945).
(1c) King and McWhirter, *ibid.*, **68**, 717 (1946).
(2) Hartwell and Kornberg, *ibid.*, **68**, 868, 1131 (1946).
(3) Kröhnke, *Ber.*, **68**, 1177 (1935). However, this betaine was obtained when Kröhnke's procedure was used.
(4) Krollpfeiffer and Müller, *ibid.*, **68**, 1169 (1935)