

process similar to that of Craig and Cass.⁵ The reaction mixture was made alkaline, and the crude bromoisquinoline separated as a dark colored oil. The oily layer was removed, and the solution was extracted with ether. The combined extracts and crude material were dried over solid potassium hydroxide and fractionated through a Vigreux column at a reflux ratio of 8 to 1. By careful fractionation, a yield of 56.5% of relatively pure 4-bromoisquinoline, m. p. 39–40°, was obtained without the necessity of recrystallization.

5-Bromocinchomeronic Acid.—Oxidation of 4-bromoisquinoline to 5-bromocinchomeronic acid was accomplished with alkaline permanganate by a method analogous to that of Edinger and Bossung.⁶ Purification by their method of precipitation of the lead salt afforded relatively pure samples, m. p. 236–237°; however, crude preparations contaminated with appreciable amounts of phthalic acid were more easily obtained by filtration of the oxidation mixture, acidification of the filtrate with hydrochloric acid, evaporation to dryness and removal of inorganic salts by leaching with cold water. For the preparation of 5-aminocinchomeronic acid, this crude product was satisfactory in that the phthalic acid was easily removed during the process.

Methyl 5-Bromocinchomerate.—A relatively pure sample of 5-bromocinchomeronic acid (1.4 g.) was dissolved in 20 cc. of methanol. Excess (10%) diazomethane in ether was added slowly to the solution. The mixture was allowed to stand for thirty minutes before the ether and methanol were evaporated. A viscous yellow oil was obtained which solidified when cooled. Recrystallization from petroleum ether gave 0.97 g. (62%) of colorless prisms, m. p. 75.5–76.5°.

Anal. Calcd. for $C_9H_8BrNO_4$: Br, 29.16. Found: Br, 29.22.

5-Aminocinchomeronic Acid.—A solution of 103 g. of crude 5-bromocinchomeronic acid and 24 g. of copper sulfate in 240 cc. of concentrated ammonium hydroxide was heated in sealed tubes at 200° for thirty hours. The reaction mixture was filtered, evaporated to dryness and dissolved in 400 cc. of water. Most of the material dissolved when the solution was heated. Concentrated hydrochloric acid was added until the solution reached a pH of 2. Upon cooling, the solution deposited fine crystals of phthalic acid which was filtered and washed with a small portion of dilute hydrochloric acid. The amount of phthalic acid, 31.8 g., indicated that the crude 5-bromocinchomeronic acid contained approximately 30.9% phthalic acid. Concentrated ammonium hydroxide was added to the filtrate until a green precipitate formed. The mixture was heated and saturated with hydrogen sulfide and at the same time agitated vigorously. The precipitate from this treatment was suspended in 250 cc. of water and again treated with hydrogen sulfide in an analogous manner. The filtrates from both sulfide treatments were combined and cooled in an ice-bath. Most of the 5-aminocinchomeronic acid, 26.7 g., crystallized from the cooled solution. The filtrate from this product was evaporated to dryness, and the residue was redissolved in hot water and treated with copper acetate. The green copper salt of the amino acid was removed and suspended in 250 cc. of hot water and treated with hydrogen sulfide. After removal of the copper sulfide, the filtrate was cooled in an ice-bath to obtain an additional amount, 8.4 g., of the amino acid. The total yield after accounting for phthalic acid as in impurity was 66.6% of the theoretical.

5-Aminocinchomeronic acid is insoluble in most organic solvents, including ethanol, methanol, acetone, chloroform, dioxane, benzene and carbon tetrachloride. It is sparingly soluble in hot water. After repeated recrystallizations from pyridine, the amino acid melted at 223–224°.

Anal. Calcd. for $C_7H_8N_2O_4$: N, 15.38. Found: N, 15.35.

(5) Craig and Cass, *ibid.*, **64**, 783 (1942); also Padbury and Lindwall, *ibid.*, **67**, 1268 (1945).

(6) Edinger and Bossung, *J. prakt. Chem.*, **43**, 190 (1891).

5-Hydroxycinchomeronic Acid.—A solution of nitrosylsulfuric acid was prepared by adding 0.9 g. of sodium nitrite slowly to 2 cc. of cold concentrated sulfuric acid. The nitrosylsulfuric acid was then diluted slowly at a low temperature with 1 cc. of cold water. A solution of 1.8 g. of 5-aminocinchomeronic acid in 4 cc. of concentrated sulfuric acid was added dropwise with vigorous agitation to the nitrosylsulfuric acid maintained at 2–4°. The reaction mixture was stirred for one hour at temperatures of 2–4° with gradual additions of small pieces of ice to liberate additional amounts of nitrous acid. The reaction mixture was then added slowly to 30 cc. of water maintained at 80°. After gas was no longer evolved, the solution was cooled and neutralized with a concentrated solution of 6.5 g. of sodium hydroxide and 2.9 g. of potassium hydroxide. The resulting solution, pH 3, deposited 0.75 g. of fine crystals of 5-hydroxycinchomeronic acid on cooling. An additional 0.15 g. of material was obtained by extracting with pyridine the residue from evaporation to dryness of the filtrate. The yield was 0.90 g. or 50% of the theoretical. Recrystallization from water and from methanol and drying under low pressure at 100° in the presence of phosphorus pentoxide gave colorless prisms, m. p. 243–244° with gas evolution.

Anal. Calcd. for $C_7H_8NO_5$: N, 7.65. Found: N, 7.86.

On standing in air the anhydrous form rapidly gained weight equivalent to one mole of water, and the melting point was lowered slightly, 237–238° with gas evolution.

Anal. Calcd. for $C_7H_8NO_5 \cdot H_2O$: N, 6.96. Found: N, 6.88.

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NEW ORLEANS, LOUISIANA RECEIVED AUGUST 5, 1946

The Action of Cuprous Cyanide on *p*-Methoxybenzyl Chloride

BY STANLEY WAWZONEK AND HSIEN-LIANG HSU¹

The action of sodium cyanide on *p*-methoxybenzyl chloride under the usual conditions gives a mixture of the benzyl alcohol and ethyl ether.² Modifications^{2,3} of this method give at best a 43% yield of *p*-methoxybenzyl cyanide.

In an attempt to increase the yield of the nitrile, the reaction of cuprous cyanide on *p*-methoxybenzyl chloride was investigated. The products obtained under various conditions were tars. These results indicate that in the presence of cuprous cyanide, *p*-methoxybenzyl chloride polymerizes in a similar fashion to that observed with benzyl chloride in the presence of certain metals and metallic chlorides.⁴ Benzyl chloride, however, behaved normally with cuprous cyanide under anhydrous conditions, giving a 71% yield of benzyl cyanide.

Experimental

Benzyl Cyanide.—Freshly distilled benzyl chloride (63.2 g.) and dry cuprous cyanide (45 g.) were heated with

(1) Abstracted from a thesis by Hsien-Liang Hsu presented to the Graduate College of the State University of Iowa, in partial fulfillment of the requirements for the M. S. degree, February, 1946.

(2) Lapine, *Bull. soc. chim.*, [5] **6**, 390 (1939).

(3) Shriner and Hull, *J. Org. Chem.*, **10**, 228 (1945).

(4) Shriner and Berger, *ibid.*, **6**, 305 (1941).

a trace of anhydrous copper sulfate and a drop of benzyl cyanide at 150° for six hours. After cooling, dry acetone (100 cc.) was added and the mixture filtered. Removal of the acetone followed by vacuum distillation gave 41.5 g. of benzyl cyanide, b. p. 119–122° (26 mm.).

No appreciable reaction was observed between benzyl chloride and cuprous cyanide at 100° after five hours.

The Action of Cuprous Cyanide on *p*-Methoxybenzyl Chloride.—The addition of *p*-methoxybenzyl chloride (44 g.) to cuprous cyanide (26 g.) at room temperature gave an instantaneous reaction accompanied by heat and gas evolution and the production of a tar. Carrying out the reaction in dry pyridine at –5° and then allowing the mixture to come to room temperature, likewise gave a tar. Treating *p*-methoxybenzyl chloride (26 g.) in acetone (30 cc.) with dry cuprous cyanide (15 g.) at –70° gave no reaction. When the mixture was allowed to reach room temperature, it reacted with an evolution of gas and the formation of a tar.

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The Solubility, Absorption Spectrum and Ionization Constant for Aloe-Emodin

BY K. G. STONE AND N. HOWELL FURMAN

In connection with some other work, it was necessary to know the apparent ionization constant of aloe-emodin. As part of the determination, the solubility and spectrum were required. The results of these measurements are reported here.

Experimental

The aloe-emodin used was prepared by the ferric chloride oxidation of Merck U. S. P. Aloin as described by Cahn and Simonsen.¹ The product after recrystallization from toluene melted at 218° (uncor.). The 0.1 *M* borax-sodium carbonate buffers described by Kolthoff and Vleschouwer² were prepared from c.p. materials which were analyzed where necessary.

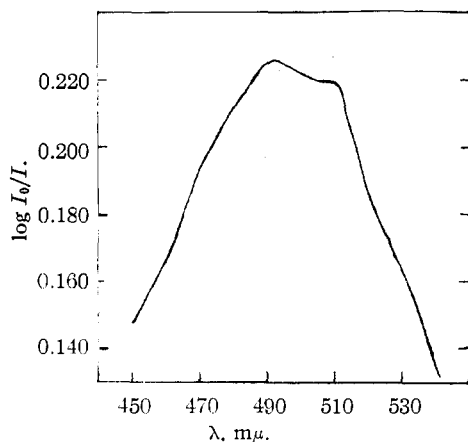


Fig. 1.—Aloe-emodin in pH 11 buffer; concentration, 0.20 mg. per ml.

Optical measurements were made with a Cenco-Sheard Spectrophotometer with an effective slit width of ten millimicrons and 1.0-cm. Corex cells. In all cases solutions containing all reagents except the aloe-emodin were used

(1) R. S. Cahn and J. L. Simonsen, *J. Chem. Soc.*, 2573 (1932).

(2) E. M. Kolthoff and J. J. Vleschouwer, *Biochem. Z.*, **189**, 191 (1927).

as blanks. All volumetric glassware was discarded if it did not meet the customary tolerances.

Saturated solutions of aloe-emodin in the buffer solutions were prepared by intermittent shaking of the buffer with solid aloe-emodin in a glass-stoppered flask in a water-bath at 25.0 ± 0.1°. Standard solutions for colorimetric calibration were prepared by dissolving weighed quantities of aloe-emodin in known volumes of buffer solutions.

Results

The spectrum of aloe-emodin in 0.1 *M* borax-sodium carbonate buffer of pH 11 is given in Fig. 1. The spectra in the buffers of other pH values were almost identical with the spectrum given. Beer's law was followed in all cases in the region from 480 to 510 millimicrons with concentrations up to 0.04 mg. per ml. where the measurements become uncertain.

The solubility measurements given in Table I were obtained by colorimetric analysis of the saturated solutions after dilution with pure buffer if necessary.

TABLE I

SOLUBILITY OF ALOE-EMODIN IN 0.1 *M* BORAX-SODIUM CARBONATE BUFFERS

pH	Moles/liter × 10 ⁵
9.8	7.60
10.0	9.63
10.4	14.8
10.8	28.7
11.0	43.3

The apparent ionization constant of aloe-emodin may be calculated graphically using the method of Davidson.³ By this method it was found that the intrinsic solubility of aloe-emodin is 5.5 × 10⁻⁵ mole per liter and that the apparent *K*_A is 6.8 × 10⁻¹¹.

(3) D. Davidson, *J. Chem. Ed.*, **19**, 221 (1942).

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The Acetylation of *o*-, *m*- and *p*-Nitroacetophenones by the Boron Trifluoride Method¹

BY HOWARD G. WALKER, JR., AND CHARLES R. HAUSER

Burgess² reported that the acylation of acetone with ethyl *p*-nitrobenzoate using sodium amide produced only a poor yield of the corresponding β-diketone. The acetylation of *m*-nitroacetophenone with ethyl acetate by this basic reagent method has also been unsatisfactory.³ On the other hand it seemed probable that the acetylation of nitroacetophenones with acetic anhydride by the boron trifluoride method⁴ would be satis-

(1) Paper XXXV on "Condensations"; paper XXXIV, THIS JOURNAL, **68**, 760 (1946).

(2) Burgess, *J. Chem. Soc.*, 2017 (1927).

(3) Mr. D. F. Thompson of this Laboratory obtained apparently none of the β-diketone using sodium amide.

(4) (a) Meerwein and Vossen, *J. prakt. Chem.*, **141**, 157 (1934); (b) Hauser and Adams, THIS JOURNAL, **66**, 345 (1944).