washed, dried, and evaporated to dryness, giving 7.3 g. of yellow crystals which were recrystallized from 10 volumes of ethanol plus 9.3 volumes of chloroform; m. p., 170–171°. Taylor and Woodhouse[2] give the same m. p.

Anal. Calcd. for $C_{17}H_{12}N_2O_2Br_2$: N, 6.43; Br, 36.67. Found: N, 6.61; Br, 36.85.

Bromination of *m*-Nitrophenylquinaldylcarbinol.—The carbinol (5 g.) in 325 cc. of chloroform was treated with bromine in chloroform as above, but no precipitate settled. After addition of the water and sodium bicarbonate solution, and drying with anhydrous sodium sulfate, an orange-colored precipitate formed on the sodium sulfate. The solid was filtered off, washed with water until free from sodium sulfate, and dried; wt., 0.8 g. It had an indefinite melting point, 137–185°, most of it melting at 153°.

Anal. Calcd. for $C_{17}H_{13}N_2O_2Br$: N, 7.84; Br, 22.37. Found: N, 8.29; Br, 16.00.

The dried chloroform solution was evaporated to dryness, giving a yellow-orange gum; wt., 5.2 g. This was treated with 15 cc. of chloroform, yielding 1 g. of white solid; m. p., above 200°.

Anal. Calcd. for $C_{17}H_{11}N_2O_2Br_3$: N, 5.44; Br, 46.55. Found: N, 6.24; Br, 45.46.

The mother liquor of this crop was evaporated to dryness and treated with ether and pentane, giving a further 0.6 g. of pale brown crystals; m. p., 110–120°. Its analysis indicated it to be slightly impure starting material.

Preparation of Monoaminophenylquinaldylcarbinols.—A mixture of the pure carbinol (5 g.) with 0.1 g. of Adams platinum catalyst was suspended in 100 cc. of methanol and shaken at room temperature with hydrogen in the Burgess–Parr apparatus. The initial pressure was approximately 39.5 lb. per sq. inch; as hydrogenation proceeded the sparingly soluble nitro derivative dissolved. After absorption of hydrogen was complete, or extremely slow, shaking was stopped, the catalyst filtered off and washed with methanol, and the filtrate plus washings evaporated to dryness. The product was recrystallized from boiling ethanol (see Table I), washed with dry ether and dried; yield, about 50%. All three amino derivatives were soluble in methanol, ethanol and chloroform; slightly soluble in ether or benzene; very sparingly soluble in carbon tetrachloride or heptane.

***p*-Aminophenylquinaldylcarbinol.**—The maximum yield was obtained when hydrogenation proceeded for three hours (but the pressure would continue to fall very slowly after the elapse of this period of time). The product was a sirup which was first obtained crystalline by adding a few cc. of dry ether. The pure substance was pale yellow-orange in color.

***o*-Aminophenylquinaldylcarbinol.**—Reduction was conducted for ninety minutes but there was no diminution in pressure during the last thirty minutes. The pure substance was colorless.

***m*-Aminophenylquinaldylcarbinol.**—Reduction was performed for three hours, the pressure remaining constant during the last thirty minutes. The pure substance was colorless.

Summary

1. The three mononitrophenylquinaldylcarbinols, and their corresponding styryl derivatives, have been prepared and some of their properties are described.

2. *m*-Nitrophenylquinaldylcarbinol has been successfully acetylated.

3. By catalytic hydrogenation of the nitro carbinols, the three monoaminophenylquinaldylcarbinols have been prepared.

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[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 304]

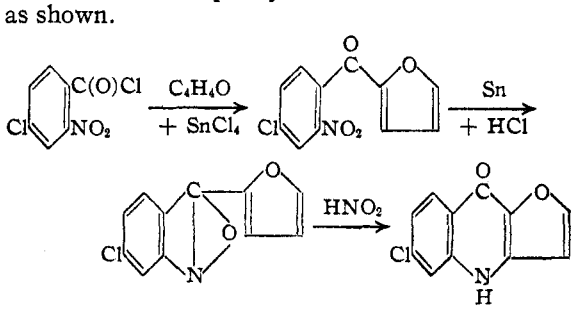
The Preparation of a Furo[3.2-b]quinolone

BY AVERY A. MORTON AND DOUGLAS BANNERMAN

Furo[3.2-b]quinolone is the furo analog of acridone. According to arguments presented in a previous paper[1] anisole and furan are comparable compounds and furan shows, to a greater degree than anisole, those reactions which are typical of aromatic compounds which contain methoxy groups. Hence furo[3.2-b]quinolone might also be regarded as the analog of 6-methoxyacridone.

Acridone and 6-methoxyacridone are important intermediates in the preparation of bacteriostatic and anti-malarial reagents. The object of this study is to prepare a compound which has the hitherto unknown furo[3.2-b]quinolone system for the ultimate purpose of comparing the physiological potency of derived compounds with those from the corresponding acridones and 6-methoxyacridones.

The compound selected for preparation was 6-chlorofuro[3.2-b]quinolone because it would be analogous to the intermediate now used in the preparation of atabrine. The steps employed utilize a furo nitrophenyl ketone and an anthranil as shown.



The anthranil was characterized by (a) a correct analysis, (b) its solubility in cold concentrated hydrochloric acid and precipitation on dilution, a behavior characteristic of all anthranils and (c) its conversion by means of a trace of nitrous acid to a higher melting isomer, the analog of acridone. The furoquinolone itself was characterized by its analysis, and by its possession of physical properties characteristic of acridones. The actual yield

(1) Morton and Patterson, THIS JOURNAL, **65**, 1346 (1943).

was only a few milligrams and the over-all yield from the technical 4-chloro-2-nitrotoluene used as the starting material was about 1%. Studies will be made to improve the yields so that sufficient quantities of this and other related products can be made available for physiological tests.

Experimental

4-Chloro-2-nitrobenzoyl Chloride.—This reagent was obtained from the corresponding acid[2] by treatment with phosphorus pentachloride.[3] It melted at 31 to 32°. The recorded values vary from 31 to 34°. A sufficiently pure grade of acid chloride can be obtained by extraction of the acid chloride and phosphorus oxychloride from the crude reaction product with thiophene-free benzene filtration, and distillation to remove the benzene and phosphorus oxychloride. The residue was then used in the preparation of the ketone.

4-Chloro-2-nitrophenyl 2-Furyl Ketone.—The procedure employed by Steinkopf[4] for the phenyl thiophenyl ketone was used with some modification. Fifty-two grams (0.2 mole) of anhydrous fuming stannic chloride was dissolved in 1.2 liters of anhydrous thiophene-free benzene in a three-necked flask fitted with a mercury-sealed stirrer, thermometer and dropping funnel. A mixture of 6.8 g. (0.1 mole) of furan and 22 g. (0.1 mole) of the acid chloride in 300 ml. of anhydrous thiophene-free benzene was added at 0 to 5° over a period of ninety minutes; the mixture was then stirred for two more hours and allowed to stand overnight. The reaction mixture was poured into water, the organic layer was steam distilled and the residue was filtered to separate some black solid which contained tin. The filtrate was extracted several times with ether, as was also the black solid, the combined ether layers were washed with sodium hydroxide to remove acid, and the ketone was recovered by evaporation of the ether. The oily product crystallized from 20% aqueous methanol solution. Recrystallization from benzene gave 6.2 g. of a pale yellow solid which melted at 93–94° (cor.).

Anal. Calcd. for $C_{11}H_8NO_4Cl$: C, 52.5; H, 2.38; N, 5.57. Found: C, 52.1; H, 2.10; N, 5.61.

After several weeks the black solid was pulverized in a ball mill and extracted in a Soxhlet apparatus with acetone. The extract was then evaporated and the residue purified as before mentioned for the ketones. The yield of the ketone was thus increased by 4.1 g. The total yield was 10.39 g. or 59%. Apparently the tin complex decomposes slowly when allowed to stand in the presence of air. The total weight of recovered acid was 6 g., which included 1 g. obtained from the black solid.

6-Chloro-3-(2-furyl)anthranil.—Concentrated hydrochloric acid, 65 ml., was cooled to −10° and added to 3.8 g. of the finely pulverized chloro-containing ketone and 45 g. of 20-mesh granulated tin in a 125-ml. Erlenmeyer flask. The mixture was set in the freezing compartment of a refrigerator where the temperature was −10°. It was allowed to remain there for thirty-five days, during which time the color changed from a dark-green to a red-violet to black. All of the tin had not dissolved by this time but the mixture was, nevertheless, poured in 300 ml. of water and the dark solid separated by filtration. The solid was dried overnight in the oven at 70° and then extracted in a Soxhlet apparatus with petroleum ether. The extract was next evaporated on a steam-bath and the yellow solid digested with petroleum ether. The extract was now evaporated on a steam-bath and the yellow solid treated with cold concentrated hydrochloric acid. The undissolved material, which was unchanged ketone, was separated by filtration through asbestos. The anthranil precipitated when the acid was diluted with three to four volumes of water. This crude product was then dissolved in 95% ethanol and treated with decolorizing carbon. After filtration the pure anthranil was precipitated by addition of three to four volumes of water. The pale yellow solid melted at 101.5 to 102° (cor.). The yield was 5.3 g. or 15%.

Anal. Calcd. for $C_{11}H_6NO_2Cl$: C, 60.1; H, 2.73; N, 6.38. Found: C, 60.1; H, 2.66; N, 6.38.

The residue from the petroleum ether extract formed a blood red solution in 95% alcohol or in acetone. It contained tin and was apparently a stable tin complex. When heated to 300° at 0.2 micron, no more of the anthranil could be obtained. Concentrated hydrochloric acid failed to extract more anthranil. However, after exposure to air for ten days, a small amount of additional anthranil could be recovered by solution in cold concentrated hydrochloric acid.

The method employed in the preparation of the anthranil follows the general procedure for these compounds outlined by Bamberger[5] and used by Steinkopf.[4] The separation of the anthranil seemed a little more difficult than anticipated of that class of compounds. Fractions which should contain the anthranil would at first show no trace of that compound and then, after several days, show considerable quantities when treated with the same reagents which had previously failed to have any action.

6-Chlorofuro[3.2-b]quinolone.—The general method of Bamberger[5] for the conversion of an anthranil to an acridone gave very good results. The anthranil, 0.2 g., was dissolved in 4 ml. of concentrated sulfuric acid cooled to −15°. Ten drops of a 10% aqueous solution of sodium nitrite were added over a period of two to three minutes, while the mixture was stirred. The agitation was continued until the solution became almost solid, presumably from sodium bisulfate. The color changed from light yellow to dark orange to greenish-black. The total reaction time required only fifteen minutes, after which the mixture was poured into ice water, and the gelatinous brown precipitate was recovered by filtration. After being washed and dried, the dark solid was digested three times with 30-ml. portions of petroleum ether in order to remove the unchanged anthranil. The crude residue melted at 270–280° and was insoluble in benzene, chloroform and ether. It was slightly soluble in cold alcohol or cold acetone and was moderately soluble in hot alcohol. The light brown powder obtained by recrystallization from ethanol began to soften at about 270° but did not melt until 370° (uncor.). Meanwhile, the solid underwent a considerable shrinkage in the capillary tube. All these behaviors are typical of the acridones. The yield was 0.086 g. or 43%.

Anal. Calcd. for $C_{11}H_6NO_2Cl$: N, 6.38. Found: N, 6.32.

Summary

6-Chlorofuro[3.2-b]quinolone has been prepared with the object of providing ultimately a compound in which the physiological equivalence of a 6-methoxyacridine and a similarly constituted furoquinoline system can be judged.

CAMBRIDGE, MASS. RECEIVED JULY 2, 1945

(2) Heller, *Ber.*, **49**, 546 (1916).

(3) Cohen and Armes, *J. Chem. Soc.*, **89**, 458 (1906).

(4) Steinkopf and Gunther, *Ann.*, **522**, 28 (1936).

(5) Bamberger, *Ber.*, **42**, 1707 (1909).