SYNTHESIS OF BENZO[g]QUINOLINE DERIVATIVES. XII.* 1,2,3,4-TETRAHYDRO-4-OXO-10-CHLOROBENZO[g]QUINOLINE

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1,2,3,4-tetrahydro-4-oxobenzo[g]quinoline was halogenated with elementary chloride. The structure of the product — 1,2,3,4-tetrahydro-4-oxo-10-chlorobenzo[g]quinoline — was established by alternative synthesis.

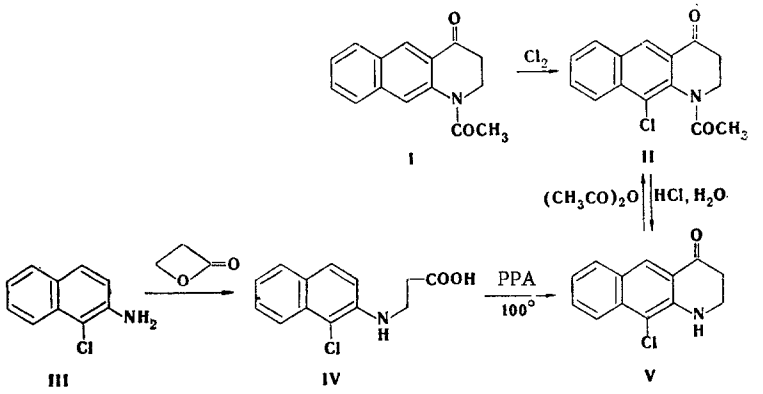
An extremely limited amount of study has been devoted to electrophilic substitution in the benzo[g]quinoline series, and this problem has not even been touched upon at all in partially hydrogenated systems such as 1,2,3,4-tetrahydro-4-oxobenzo[g]quinoline.

We have found that the chlorination of n-acetyl-1,2,3,4-tetrahydro-4-oxobenzo[g]quinoline (I) in acetic acid at room temperature gives a monochloro derivative (II) of 1,2,3,4-tetrahydro-4-oxobenzo[g]quinoline.

In order to establish the location of the halogen we investigated other possible methods for the synthesis of II.

We attempted to use 4-chloro-3-amino-2-naphthoic acid, which we obtained by chlorination of 3-acetamido-2-naphthoic acid, as the starting compound. Its physical constants correspond to those of the product obtained by oxidative decomposition of 1-chloro-2,3-naphthisatin [2]. In addition, the acid that we isolated was converted by the Sandmeyer reaction to the known 4-chloro-2-naphthoic acid [3]. However, attempts to achieve the cyanoethylation and carboxyethylation of 4-chloro-3-amino-2-naphthoic acid did not give positive results.

We therefore investigated the possibility of the use of 1-chloro-2-naphthylamine (III) as the starting material. It was found that the latter does not undergo cyanoethylation under various conditions, including reaction in the presence of Triton B, which catalyzes the cyanoethylation of o-chloroaniline [4].



We were able to obtain the necessary N-(1-chloro-2-naphthyl)-β-alanine (IV) in 20% yield by reaction of III with β-propiolactone in acetonitrile. In an investigation of the condi-

*See [1] for communication XI.

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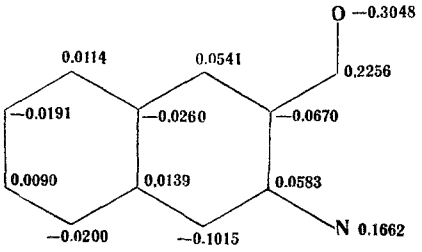
tions for the cyclization of IV in polyphosphoric acid (PPA) we varied the component ratios, the reaction temperature, and the heating time. The optimum variant involved heating IV in PPA at 100° for 4 h. The yield of 1,2,3,4-tetrahydro-4-oxo-10-chlorobenzo[g]quinoline(V) in this case was 61%, and 28% of unchanged IV was recovered.

The physical constants and properties of V are identical to those of the product isolated from the deacetylation of II. Acetylation of V with acetic anhydride gives II.

Thus in the halogenation of 1,2,3,4-tetrahydro-4-oxobenzo[g]quinoline the halogen atom enters the position with the maximum electron density, i.e., the 10 position, which is apparent from the molecular diagram of 1,2,3,4-tetrahydro-4-oxobenzo[g]quinoline, calculated by the Hückel MO method.*



1,2,3,4-Tetrahydro-4-oxo-10-chlorobenzo[g]quinoline (V) was characterized as the 2,4-dinitrophenylhydrazone (VI). The hydrochloride of V is unstable even in air and decomposes with liberation of the base.

Bands of stretching vibrations at 1677 cm^{-1} (ν_{CO}) and 3387 cm^{-1} (ν_{NH}) are observed in the IR spectrum of V. The UV spectrum of V is similar to the spectrum of 1,2,3,4-tetrahydro-4-oxobenzo[g]quinoline [5], and six characteristic maxima (log ε) are observed at 240 (4.28), 256 (4.47), 270 (4.62), ∿ 303 (3.77), ∿ 320 (3.50), and 420 nm (3.32); the long-wave maximum of V is shifted hypsochromically as compared with the nonhalogenated analog.

EXPERIMENTAL METHOD

The IR spectrum of a mineral-oil suspension of V was recorded with a UR-20 spectrometer. The UV spectrum of an alcohol solution of V was recorded with an SF-4 spectrophotometer.

4-Chloro-3-acetamido-2-naphthoic Acid. A stream of dry chlorine was bubbled into a suspension of 5.7 g (0.025 mole) of 3-acetamido-2-naphthoic acid in 50 ml of glacial acetic acid at 40-50° for 30 min, after which the resulting precipitate was removed by filtration and washed with dilute acetic acid to give 4.5 g (69%) of 4-chloro-3-acetamido-2-naphthoic acid as a cream-colored powder with mp 231-232° (dec., from alcohol). Found %:Cl 13.3; N 5.2. $C_{13}H_{10}ClNO_3$. Calculated %: Cl 13.4; N 5.3.

4-Chloro-3-amino-2-naphthoic Acid. A mixture of 1 g of 4-chloro-3-acetamido-2-naphthoic acid in 5 ml of concentrated H_2SO_4 was heated at 100-110° for 20 min, after which it was cooled and poured over ice. The resulting precipitate was removed by filtration and washed with water to give 0.6 g of 4-chloro-3-amino-2-naphthoic acid as a yellow powder with mp 255-256° (dec., from alcohol) (mp 254° [3]). Found %: Cl 16.0 N 6.4. $C_{11}H_8ClNO_2$. Calculated %: Cl 16.0; N 6.3.

4-Chloro-2-naphthoic Acid. A saturated solution of 0.2 g of sodium nitrite in water was added with stirring at 0° to a mixture of 0.55 g of 4-chloro-3-amino-2-naphthoic acid in 2 ml of alcohol and 0.35 ml of concentrated H_2SO_4, after which the mixture was heated slowly to the boiling point. It was then cooled, and the resulting precipitate was removed by filtration and washed with water to give 0.3 g of 4-chloro-2-naphthoic acid as a cream-colored powder with mp 251-252° (from alcohol) (mp 248-250° [4]). Found %: Cl 16.7. $C_{11}H_7ClNO_2$. Calculated %: Cl 17.2.

N-(1-Chloro-2-naphthyl)-β-alanine (IV). A mixture of 5.3 g (0.03 mole) of 1-chloro-2-

*The calculation was made by I. E. Shumakovich in the E. I. Martsinovskii Institute of Medicinal Parasitology and Tropical Medicine, for which the authors express their thanks.

naphthylamine in 10 ml of acetonitrile and 3 ml of β-propiolactone was refluxed for 13 h, after which it was cooled, and the resulting precipitate was removed by filtration to give 1.5 g (20%) of IV as a cream-colored powder with mp 169-170° (from ether). Found %: Cl 13.8; N 5.9. $C_{13}H_{12}ClNO_2$. Calculated %: Cl 14.2; N 5.6.

1,2,3,4-Tetrahydro-4-oxo-10-chlorobenzo[g]quinoline (V). A) A 3-g (0.012 mole) sample of IV was added to 175 g of PPA (75 g of orthophosphoric acid and 100 g of P_2O_5) at 100°, and the mixture was heated at 100° with stirring for 4 h, after which it was poured into 400 ml of ice water. The resulting precipitate was removed by filtration, treated with sodium carbonate solution, and washed with water to give 1.7 g (61%) of V as bright-yellow crystals with mp 141-142° (from heptane). Found %: C 67.3; H 4.2; Cl 15.1 N 6.1. $C_{13}H_{10}ClNO$. Calculated %: C 67.4; H 4.4; Cl 15.3; N 6.0. The 2,4-dinitrophenylhydrazone (VI) of V had mp 320-322° [dec., from dimethylformamide (DMFA)]. Found %: Cl 8.6; N 17.0. $C_{19}H_{14}ClN_5O_4$. Calculated %: Cl 8.6; N 17.0. Acidification of the sodium carbonate solution gave 0.7 g (28%) of starting IV.

B) A mixture of 1.35 g (0.005 mole) of V, 5 ml of concentrated HCl, 1 ml of acetic acid, and 0.5 ml of water was heated with stirring at 85° for 30 min, after which the mixture of acids was removed from the reaction mixture by distillation, the residue was treated with 5% NaOH solution, and the resulting precipitate was removed by filtration to give 1.1 g (96%) of V with mp 141-142° (from heptane). No melting-point depression was observed for a mixture of this product with V obtained by method A.

N-Acetyl-1,2,3,4-tetrahydro-4-oxo-10-chlorobenzo[g]quinoline (II). A) A mixture of 0.58 g (0.0025 mole) of V, 0.12 g of potassium acetate, and 12 ml of acetic anhydride was refluxed for 5 h, after which the acetic anhydride was removed by distillation, and the residue was crystallized from ether to give 0.6 g (88%) of II as a cream-colored powder with mp 168-169° (from heptane). Found %: Cl 13.1; N 4.7. $C_{15}H_{12}ClNO_2$. Calculated %: Cl 13.0; N 5.1.

B) A stream of dry chlorine was bubbled into a solution of 2.4 g (0.01 mole) of I in 15 ml of glacial acetic acid and 5 ml of water at room temperature for 30 min, after which the mixture was poured into 100 ml of water, and the resulting precipitate was removed by filtration to give 2.2 g (81%) of II with mp 168-169° (from heptane). No melting-point depression was observed for a mixture of this product with II obtained by method A.

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