SYNTHESIS OF BENZO[g]QUINOLINE DERIVATIVES

III. The Reaction of 1, 2, 3, 4-Tetrahydro-4-oxobenzo[g]quinoline with Ammonia*

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In the condensation of 1,2,3,4-tetrahydro-4-oxobenzo[g]quinoline with ammonia, which leads to the formation of 4-aminobenzo[g]quinoline, the by-products are benzo[g]quinoline (V) and 1, 2, 3, 4-tetrahydrobenzo[g]quinoline (VI), which are also obtained from 1,2,3,4-tetrahydro-4-hydroxybenzo[g]quinoline by its dehydration and the subsequent disproportionation of the dihydrobenzo[g]quinoline formed.

We have previously found [1] that in the condensation of 1,2,3,4-tetrahydro-4-oxobenzo[g]quinoline (VII) with ammonia, in addition to the main reaction product 4-aminobenzo[g]quinoline (IX) a crystalline substance with mp 117–118° C is formed as a by-product which, according to the nitrogen analysis, corresponds to benzo[g]quinoline (V). Its hydrochloride has mp 198–199° C, and its picrate mp 256–257° C being identical with the corresponding salts of benzo[g]quinoline described by Braun and Gruber [2].

Melting Points of Mixtures of Benzo[g]quinoline and 1, 2, 3, 4-Tetrahydrobenzo[g]quinoline

Ratio of V and VI	Mp, °C
Mixture with V predominating	119—120
Mixture of equal amounts of V and VI	136—137
Mixture with VI predominating	142—143

However, when the base with mp 117–118° C was chromatographed, it gave two spots with R_f 0.538 and 0.757. After recrystallization from aqueous ethanol, the base melted at 132° C, the nitrogen content remained the same, and on chromatography the same two spots with the R_f values given were found.

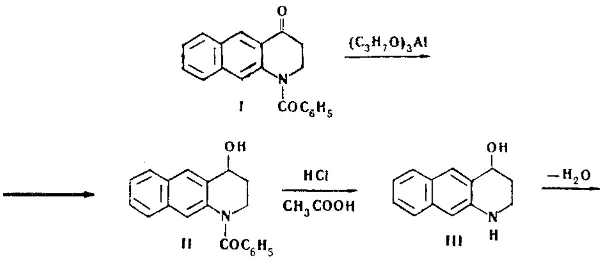
To explain these results and to refine the characteristics of the substance, the information given in the literature was checked.

Benzo[g]quinoline (V) was first obtained in 1922 by the oxidation of 6,7,8,9-tetrahydrobenzo[g]quinoline by heating it to 700° C with lead oxide [2]. In 1946, two other methods of obtaining V were proposed: by the dehalogenation of 10-chlorobenzo[g]quinoline and by the reduction of azanthraquinone (benzo[g]quinoline-5, 10-dione) [3]. The formation of V in the decarboxylation of benzo[g]quinoline-2,4-dicarboxylic acid has been reported [4, 5]. In these papers the following characteristics for V and its salts were given: mp of the base 113–114° C [2–5], 116–117° C, and 117–118° C [2, 3]; mp of the hydrochloride 197–198° C [2] and 142–143° C [3]; and mp of the picrate 258° C [2] and 247–248° C [2].

To identify the V isolated and to study the impurity accompanying it, we repeated the investigations of Etienne referred to above [3] and obtained the following results: the dehalogenation of 10-chlorobenzo[g]quinoline by heating with zinc dust and zinc chloride gave a very low yield of V, which was identified in the form of the picrate with mp 255–256° C; the reduction of azanthraquinone with zinc dust in a melt of zinc chloride and sodium chloride gave V with mp 118° C, with a hydrochloride having mp 197–198° C, in contrast to the mp 142–143° C given by Etienne [3].

To obtain V we also subjected 10-chlorobenzo[g]quinoline to reductive dehalogenation with Raney alloy in an alkaline medium. It was found that under these conditions not only was halogen removed but the pyridine ring of V was reduced with the formation of 1, 2, 3, 4-tetrahydrobenzo[g]quinoline (VI). Moreover, under milder conditions the product with mp 131–132° C was obtained which gave two spots on a chromatogram with R_f 0.538 and 0.757. A mixture of this substance with the product of mp 132° C that we had isolated gave no depression. These products consisted of mixtures of V and VI, since on chromatographing the pure substances, benzo[g]quinoline gave R_f 0.538 and 1,2,3,4-tetrahydrobenzo[g]quinoline gave R_f 0.757. Furthermore, the melting points of mixtures of V and VI containing the components in the various ratios given in the table were determined.

A comparison of the melting points given in the table with those of the products isolated from the reaction, 117–118° C and 131–132° C shows that the latter consist of mixtures of V and VI in different proportions. Finally, to obtain V, we reduced compound VII, in the form of its N-benzoyl derivative (I), to the 4-hydroxy derivative (II), by the Meerwein-Ponndorf-Verley method. The latter, on being heated in an acid medium, underwent dehydration to form 1,2-dihydrobenzo[g]quinoline (IV), which disproportionated and was converted into V and VI. This process can be represented in the following way:



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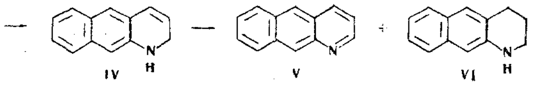
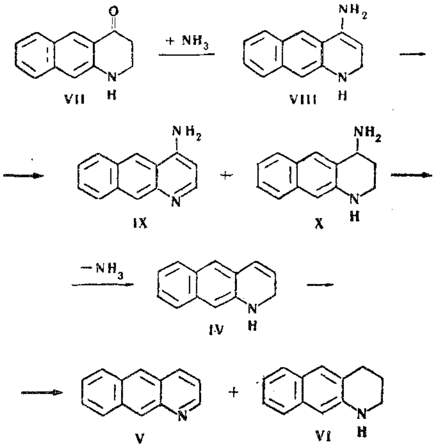
*For communication II, see [1].



Compound V was isolated from the mixture of V and VI after its benzoylation by extraction with dilute hydrochloric acid from a benzene solution, followed by neutralization. Mp of V 119.5–120° C, mp of the hydrochloride 197–198° C, mp of the picrate 258–259° C. The melting points of mixtures of the base and corresponding salts of V obtained by other methods gave no depression; only one spot, with R_f 0.538, was obtained on a chromatogram. The UV spectra was identical with the spectra given in the literature [6, 7].

The 1,2,3,4-tetrahydrobenzo[g]quinoline isolated from its benzoyl derivative was identical with a sample of VI obtained by the method described above. Its IR spectrum showed the band of the stretching vibrations of the secondary amino group; R_f 0.757.

From the facts given it follows that in the condensation of VII with ammonia, besides the main reaction product IX, benzo[g]quinoline and 1, 2, 3, 4-tetrahydrobenzo[g]quinoline, without substituents in position 4, are also formed. The appearance of V and VI in this reaction takes place as a result of the following processes:



The 4-amino-1,2-dihydrobenzo[g]quinoline (VIII) formed disproportionates under the reaction conditions, being converted into IX and 4-amino-1,2,3,4-tetrahydrobenzo[g]quinoline (X). On heating, the latter loses ammonia and forms IV which, in addition to oxidation and conversion into V, undergoes disproportionation giving V and VI. These transformations of the partially hydrogenated heterocyclic systems of benzo[g]quinoline are connected with its instability and its tendency to form the more stable aromatic system.

EXPERIMENTAL

The chromatographic data given relate to a thin nonfixed layer of alumina (benzene). The UV spectrum was taken in 96% ethanol on an SF-4 instrument and the IR spectrum on a UR-10 instrument in the crystalline state (tablets with KBr).

Dehalogenation of 10-chlorobenzo[g]quinoline. The initial 10-chlorobenzo[g]quinoline was obtained by the Skraup reaction from α-chloronaphthylamine and glycerol in 70% sulfuric acid with the addition of arsenic acid as oxidizing agent. Yield 25.7%. Mp 140.5–141° C (from heptane). Literature data [8]: mp 141° C.

a) A mixture of 0.5 g of 10-chlorobenzo[g]quinoline, 0.5 g of zinc dust, and 0.5 g of zinc chloride was heated according to Etienne's method [3]. The V was purified and isolated in the form of the picrate. Yellow crystalline powder with mp 252–253° C. The melting point of a mixture with the picrate of benzo[g]quinoline (256–257° C) showed no depression.

b) A solution of 0.5 g of 10-chlorobenzo[g]quinoline in 10 ml of methanol was mixed with a solution of potassium hydroxide (1.2 g of potassium hydroxide in 6 ml of water) and heated to 80° C, and, with stirring, 0.5 g of nickel-aluminum alloy was added. The mixture was stirred at the given temperature for 1 hr. After cooling, the catalyst was filtered off and heated with ethanol. The addition of water to the combined filtrates gave 0.1 g cream-colored precipitate. Mp 132–133° C. Found, %: N 8.12. Calculated for $C_{13}H_9N$, %: N 7.82.

c) A solution of 1.2 g of 10-chlorobenzo[g]quinoline in 30 ml of ethanol was mixed with a solution of potassium hydroxide (2.9 g of potassium hydroxide in 15 ml of water) and heated to 80° C, and, with stirring, 2.7 g of nickel-aluminum alloy was added. The mixture was stirred at the given temperature for 2 hr and was treated as described in (b). Compound VI was isolated with a yield of 0.6 g (58.2%). Mp 148.5–149° C (from heptane). According to the literature [2], mp 149° C. Found, %: N 7.66, 7.70. Calculated for $C_{13}H_{13}N$, %: N 7.64.

The hydrochloride of VI was obtained by dissolving the base in ether and adding ethanolic hydrochloric acid; light cream-colored crystalline powder with mp 228.5–229° C. According to the literature [2], mp 229° C.

Reduction of azanthraquinone. The initial azanthraquinone was obtained by the oxidation of 10-chlorobenzo[g]quinoline with chromic anhydride in acetic acid. The yield of azanthraquinone was 75.8%. Mp 275–276° C. Literature data [8]: mp 276° C.

0.3 g of azanthraquinone was heated in a melt of 0.3 g of sodium chloride, 0.3 g of zinc dust, and 1.5 g of fused zinc chloride by Etienne's method [3]. The yield of benzo[g]quinoline was 0.1 g (38.9%). Light gray lustrous crystals with mp 118–118.5° C. The **hydrochloride** of V was obtained by dissolving the base in ethanolic hydrochloric acid with subsequent precipitation by ether; yellow crystalline powder with mp 197–198° C, soluble in water and ethanol, insoluble in ether, unstable on storage in the air.

Disproportionation of N-benzoyl-4-hydroxy-1,2,3,4-tetrahydrobenzo[g]quinoline (II). A solution of 6.0 g of N-benzoyl-4-oxo-1,2,3,4-tetrahydrobenzo[g]quinoline in isopropanol (120 ml) was reduced with a solution of aluminum isopropoxide (6.0 g) in 80 ml of isopropanol, the mixture being heated to the boil and the acetone formed being distilled off. After the excess of isopropanol had been distilled off, the residue was treated with 50 g of ice and 7 ml of hydrochloric acid. The yield of II was 3.7 g (61.3%). Mp 176.5–177° C (from aqueous ethanol). Cream-colored crystalline powder, readily soluble in ethanol, acetone, and benzene, sparingly soluble in heptane, insoluble in water. Found, %: N 4.48, 4.57. Calculated for $C_{20}H_{17}NO_2$, %: N 4.62.

A mixture of 3.7 g of II, 55 ml of concentrated hydrochloric acid, and 40 ml of acetic acid was boiled for 1 hr and then the mixture of acids was distilled off in vacuum and the residue was made alkaline and extracted with benzene. The extract was dried with sodium sulfate. To the dry benzene extract were added 15 ml of pyridine and 6 ml of benzoyl chloride and the mixture was heated to the boil for 2 hr. Then 6 ml of absolute ethanol was added and the mixture was heated for another 30 min. After the pyridine hydrochloride that had deposited had been filtered off, the filtrate was treated with dilute hydrochloric acid. The aqueous acid layer was separated off, treated with activated carbon, filtered, and made alkaline; benzo[g]quinoline separated in the form of light-colored crystals. Yield 0.5 g (45%). Mp 118–118.5° C. After recrystallization from aqueous ethanol, colorless lustrous crystals, mp 119.5–120° C; the melting point of a mixture with the benzo[g]quinoline obtained by Etienne's method showed no depression. UV spectrum: λ_{max} nm (log ε) 228 (4.66), 253 (5.17), 326 (3.39), 340 (3.56), 357 (3.74), 367 (3.58), 385 (3.47).

Hydrochloride of V—yellow crystals with mp 197–198° C. Found, %: Cl 16.50. Calculated for $C_{13}H_9N \cdot HCl$, %: Cl 16.44.

Picrate—yellow crystals, mp 258–259° C.

The benzene extract mentioned above was dried with sodium sulfate and, after the benzene had been distilled off, the residual oily product was treated with 30 ml of concentrated hydrochloric acid and 30 ml of acetic acid. The mixture was heated to the boil for 1 hr and worked up in the usual way to give 1.0 g (90.9%) of VI in the form of a cream-colored crystalline powder with mp 148–149° C (from aqueous ethanol); IR spectrum: 3360 cm^{-1}.

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