INVESTIGATION OF THE PRODUCTS OF THE REACTION OF EPICHLOROHYDRIN WITH AROMATIC AMINES

XV.* 4-OXO-1,2,3,4-TETRAHYDROBENZO[h]QUINOLINE AND 4-HYDROXY-6-CHLORO-1,2,3,4-TETRAHYDROBENZO[h]QUINOLINE

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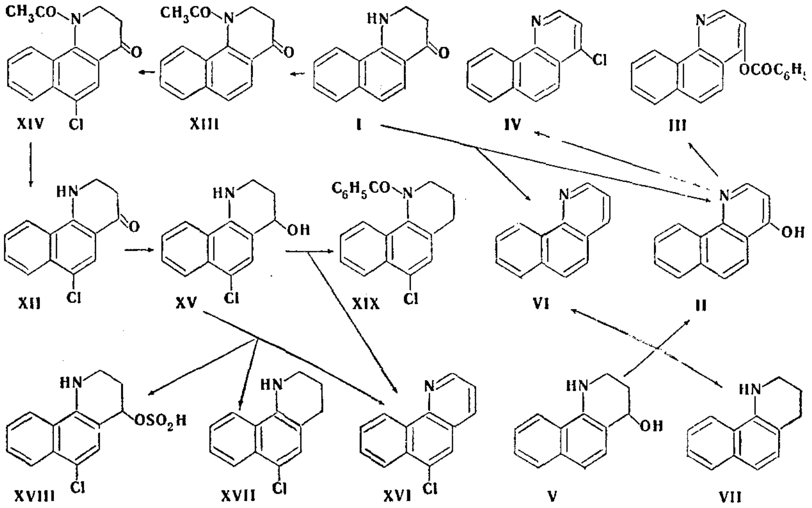
A relatively simple method is proposed for the preparation of 4-hydroxyquinoline derivatives from the corresponding 4-oxo-1,2,3,4-tetrahydroquinoline derivatives. 4-Hydroxy-6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline is readily converted to a mixture of 6-chlorobenzo[h]quinoline and 6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline.

Since the literature contains very little data on 4-oxo-1,2,3,4-tetrahydrobenzo[h]quinoline (I), we investigated several of its transformations. A base of the composition $C_{13}H_9NO$ was obtained in very low yield when I was heated with platinum black in a stream of nitrogen. The base was converted to the benzoyl and chloro derivatives by the action of benzoyl chloride and phosphorus oxychloride, respectively. On the basis of the data obtained and the information in the literature [3], it was established that the base is 4-hydroxybenzo[h]quinoline (II) and that the derivatives obtained are 4-benzoxy- (III) and 4-chlorobenzo[h]quinoline (IV). 4-Hydroxybenzo[h]quinoline was also obtained in low yield from 4-hydroxy-1,2,3,4-tetrahydrobenzo[h]quinoline (V) by heating the latter in phenol in the presence of Raney nickel. Benzo[h]quinoline (VI), 1,2,3,4-tetrahydrobenzo[h]quinoline (VII), and a "dimer" identical to that previously obtained in [2] were isolated along with II. It was found that II is formed in good yield (about 63%) along with a slight amount of VI when I is heated in phenol in the presence of Raney nickel.

The scheme of the formation of VI, VII, and the "dimer" when V is heated in phenol in the presence of Raney nickel can apparently be represented as follows. In addition to aromatization of V to II, V loses a



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*See [1] for communication XIV.

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molecule of water to give a dihydro derivative of benzo[h]quinoline, which is partially disproportionated to VI and VII and partially "dimerized" to give a compound of the $C_{26}H_{20}N_2$ composition.

Under the reaction conditions, I may be found in equilibrium with the enol form (4-hydroxy-1,2-dihydrobenzo[h]quinoline), which disproportionates to II and V. Hydroxy derivative V then reacts via the scheme examined above. The small amount of VII formed is dehydrogenated to VI under the reaction conditions.

Since the method for the preparation of II from I proved to be convenient, we made attempts to use it for the preparation of other 4-hydroxyquinoline derivatives, especially since the known methods for the preparation of hydroxyquinolines [3-6] have several disadvantages. Thus 4-hydroxyquinolines X and XI were obtained in good yields from 4-oxo-1,2,3,4-tetrahydroquinolines VIII and IX.

This relatively simple method is apparently a general method for the preparation of 4-hydroxyquinoline derivatives.

VIII, IX X, XI

VIII, X R = H; IX, XI R = OCH_3

We made an attempt to chlorinate I with thionyl chloride under the conditions of the preparation of 6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline [7]. However, the expected 4-oxo-6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline (XII) could not be obtained. It was synthesized by chlorination of 1-acetyl-4-oxo-1,2,3,4-tetrahydrobenzo[h]quinoline (XIII) with sodium chlorate in the presence of hydrochloric acid with subsequent saponification of the 1-acetyl-4-oxo-6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline (XIV). Reduction of XII with sodium amalgam in alcohol gave 4-hydroxy-6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline (XV). As should have been expected, XV is converted to 6-chlorobenzo[h]quinoline (XVI) on heating with thionyl chloride, while XVI and 6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline (XVII) are obtained at room temperature. In the latter case, the sulfurous acid ester of 4-hydroxy-6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline (XVIII) was also isolated.

The data obtained in the study of the reaction of XV with thionyl chloride demonstrate that in this case the formation of XVI and XVII proceeds through a step involving the dihydro derivative, which disproportionates to XVI and XVII. At higher temperatures, XVII is removed from the reaction mass as the product of the reaction with thionyl chloride.

The benzoylation of XV in ether with benzoyl chloride in the presence of pulverized potassium carbonate gave XVI and 1-benzoyl-6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline (XIX). The formation of the latter can apparently be explained by the fact that XV loses a molecule of water on refluxing in ether under the indicated conditions to give the dihydro derivative, which disproportionates to XVI and XVII. Compound XVII is then acylated to XIX.

Hydroxy derivative XV is dehydrated with subsequent disproportionation to a mixture of XVI and XVII not only in the presence of dehydrating agents but also without them, even when stored at room temperature.

EXPERIMENTAL

4-Hydroxybenzo[h]quinoline (II), Benzo[h]quinoline (VI), and 1,2,3,4-Tetrahydrobenzo[h]quinoline (VII). A. A mixture of 10.0 g (0.05 mole) of I and 0.15 g of platinum black was heated in vacuo at 310° in a stream of nitrogen for 3 h. The reaction mass was poured into a Petri dish and worked up to give 1.1 g (12%) of II with mp 245-247° (from methanol) (mp 242-243° [4]).

B. A mixture of 10.0 g (0.05 mole) of I, 2.0 g of Raney nickel, and 39 g of phenol was refluxed for 10-12 h. It was then cooled and diluted with ether. The crystalline precipitate and the catalyst were removed by filtration and washed thoroughly with ether. The 4-hydroxybenzo[h]quinoline was dissolved in 2.5% sodium hydroxide, and the catalyst was removed by filtration. The filtrate was acidified with sulfurous acid, and the resulting crystalline precipitate was removed by filtration to give 7.1 g (62%) of II with mp 245-247°. The phenol was washed out of the ether filtrate with sodium hydroxide solution, and the ether was removed by distillation to give 0.4 g (3.5%) of VI with mp 50-51° (mp 52° [8]).

C. A mixture of 2.0 g (0.01 mole) of V, 7.8 g of phenol, and 1.0 g of Raney nickel was refluxed for 6 h and then extracted with hot 25% sodium hydroxide solution. The solution was cooled to give 0.3 g (15%) of II with mp 245-247°. No melting-point depression was observed for a mixture of this product with an authentic sample of II. The residual oil yielded 0.36 g (18%) of VI with mp 50-51°, 0.26 g (14%) of VII with mp 45-46° (mp 46.5° [9]), and 0.2 g (5.5%) of a base with a molecular weight of 360 and mp 195-196.5° (see [2]).

4-Benzoxybenzo[h]quinoline (III). A 1.75-ml (0.015 mole) sample of benzoyl chloride was added to a solution of 1.0 g (0.005 mole) of II in 5 ml of pyridine, and the mixture was heated at 95° for 3 h. It was then treated with 10 ml of 25% sulfuric acid and water. The precipitate was removed by filtration and recrystallized from methanol to give 0.7 g (46%) of a product with mp 117-118°. Found: N 4.8, 4.8%. $C_{20}H_{13}NO_2$. Calculated: N 4.7%.

4-Hydroxyquinoline (X). A mixture of 2.0 g (0.014 mole) of 4-oxo-1,2,3,4-tetrahydroquinoline (VIII), 1.0 g of Raney nickel, and 7.8 g of phenol was refluxed for 1 h. It was then cooled, 100 ml of ether–petroleum ether (1 : 1) was added, and the mixture was held at 3-5° for 2-3 h. The crystalline precipitate and catalyst were removed by filtration, and the 4-hydroxyquinoline was dissolved in 24.5% sodium hydroxide solution. The catalyst was removed by filtration, and SO_2 was passed into the filtrate until the pH was 5-6. Recrystallization of the resulting precipitate from petroleum ether–ether (1 : 1) gave 1.5 g (74%) of colorless needles with mp 202-204° (mp 201° [5]).

4-Hydroxy-6-methoxyquinoline (XI). This compound was similarly obtained in 73% yield as colorless needles with mp 248.5-250° (from methanol) (mp 245-247° [6]).

1-Acetyl-4-oxo-1,2,3,4-tetrahydrobenzo[h]quinoline (XIII). A mixture of 20 g (0.1 mole) of I and 40 ml of acetic anhydride was refluxed for 4 h. It was then cooled, diluted with water, neutralized with sodium carbonate, and extracted with ether. The solvent was removed, and the residue was recrystallized from methanol to give 14.6 g (61%) of a product with mp 130.5-131.5°. Found: N 6.1, 5.9%. $C_{15}H_{13}NO_2$. Calculated: N 5.9%.

1-Acetyl-4-oxo-6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline (XIV). Concentrated hydrochloric acid (22 ml) was added to a solution of 11.95 g (0.05 mole) of XIII in 66 ml of glacial acetic acid, the mixture was cooled to −5 to −10°, and a solution of 5.3 g (0.05 mole) of sodium chlorate in 22 ml of water was added dropwise with stirring. The mixture was stirred at −5 to 0° for 3 h, and the resulting precipitate was removed by filtration and recrystallized from ethanol to give 6.8 g (48%) of a product with mp 212.5-214°. Found: Cl 12.9, 13.2; N 4.9, 4.8%. $C_{15}H_{12}ClNO_2$. Calculated: Cl 13.0; N 5.1%.

4-Oxo-6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline (XII). A 4.8-g (0.017 mole) sample of XIV was added to a solution of 0.7 g (0.017 mole) of sodium hydroxide in 50 ml of ethanol and 2 ml of water, and the mixture was refluxed for 2 h. It was then diluted with water and extracted with ether. The ether was removed, and the precipitated yellow needles were recrystallized from ethanol to give 2.6 g (65%) of a product with mp 159-160.5°. Found: Cl 14.9, 15.0; N 6.1, 6.3%. $C_{13}H_{10}ClNO$. Calculated: Cl 15.3; N 6.1%.

4-Hydroxy-6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline (XV). A solution of 1.55 g (0.006 mole) of XII in 15 ml of ethanol was added to sodium amalgam prepared from 0.6 g of sodium and 2 ml of mercury. The flask was sealed and shaken, with periodic opening, at room temperature for 1 h. The mercury was separated and washed with alcohol, and the alcohol solution was diluted with water and extracted with ether. The ether was removed, and the residual mass was treated with 0.5 ml of chlorobenzene. It began to crystallize in the course of an hour. The crystals were removed by filtration and recrystallized from chlorobenzene to give 0.9 g (63%) of XV with mp 61.5° (dec.). Found: Cl 15.1, 15.1; N 5.9, 5.9%. $C_{13}H_{12}ClNO$. Calculated: Cl 15.2; N 6.0%.

6-Chlorobenzo[h]quinoline (XVI), 6-Chloro-1,2,3,4-tetrahydrobenzo[h]quinoline (XVII), Sulfurous Acid Ester of 4-Hydroxy-6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline (XVIII), and 1-Benzoyl-1,2,3,4-tetrahydrobenzo[h]quinoline (XIX). A. A mixture of 1.1 g (0.005 mole) of XV and 4 ml of thionyl chloride was heated at 75° for 1 h, and the resulting precipitate was removed by filtration and washed with 2 ml of thionyl chloride. The 6-chlorobenzo[h]quinoline hydrochloride was dissolved in ethanol, treated with 20% sodium hydroxide solution, and diluted with water to give 0.49 g (46%) of XVI with mp 99.5-100.5° (mp 101° [10]).

B. A 1.1-g (0.005 mole) sample of XV was added to 4 ml of cooled (to −5°) thionyl chloride, and the mixture was held at 15-20° for 15 min. The mixture was then poured over crushed ice and treated with sodium hydroxide solution. The alkaline mixture was then extracted with ether. The ether was removed, and the residue was chromatographed on aluminum oxide with ether–petroleum ether (1 : 4) to give 0.1 g (9.1%) of XVI with mp 99.5-100.5°, 0.07 g (6%) of XVII with mp 66-67.5° (mp 67.5-68.5° [7]), and 0.8 g (52%) of ester XVIII with mp 188.0° (dec.) (mp 187.5° (dec.) [2]).

C. A 2.0-g (0.015 mole) sample of potassium carbonate was added to a solution of 3.0 g (0.012 mole) of XV in 30 ml of ether, and the mixture was refluxed for 15 min. A 2-ml (0.015 mole) sample of benzoyl chloride was added, and the mixture was refluxed for another 5 h. The crystalline precipitate was removed by filtration, and the potassium carbonate was washed away with water to give 1.0 g (26%) of XIX with mp 197-199° (from ethanol). Found: N 4.3, 4.2%. $C_{20}H_{16}ClNO$. Calculated: N 4.4%. The ether solution yielded 0.8 g (31%) of XVI with mp 99.5-100.5°.

D. A 1.1-g (0.005 mole) sample of XV was held at room temperature for 5 days in a sealed flask. The crystals of XV decomposed with the liberation of water (drops formed on the walls of the flask). Separation of the mass on aluminum oxide with ether–petroleum ether (1 : 4) gave 0.43 g (39%) of XVI with mp 99-100° and 0.35 g (31%) of XVII with mp 66.5-67.5°.

4-Oxo-1,2,3,4-tetrahydrobenzo[h]quinoline Phenylhydrazone. A 0.6-g (5.5 mmole) sample of phenylhydrazine was added to a solution of 1.0 g (5 mmole) of I in 10 ml of glacial acetic acid, and the mixture was held at 4° for 12 h. The precipitate was removed by filtration and washed with dilute acetic acid to give 1.0 g (70%) of a product with mp 178.5° (dec.). Found: N 14.5, 14.3%. $C_{19}H_{17}N_3$. Calculated: N 14.6%.

1-Nitroso-4-oxo-1,2,3,4-tetrahydrobenzo[h]quinoline. A solution of 4.0 g (0.021 mole) of I in 80 ml of glacial acetic acid was diluted with 20 ml of water and cooled to 0°. A solution of 1.38 g (0.021 mole) of sodium nitrite in 40 ml of water was then added with vigorous stirring. The precipitate was removed by filtration to give 4.2 g (91%) of yellow needles with mp 128° (dec.). Found: N 12.4, 12.3%. $C_{13}H_{10}N_2O_2$. Calculated: N 12.4%.

1-Nitroso-4-oxo-6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline. This compound was similarly obtained in 45% yield and had mp 134° (dec.). Found: Cl 13.4, 13.2; N 10.5, 10.6%. $C_{13}H_9ClN_2O_2$. Calculated: Cl 13.6; N 10.8%.

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