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

XI.* 4-HYDROXY-1,2,3,4-TETRAHYDROBENZO[h]QUINOLINE

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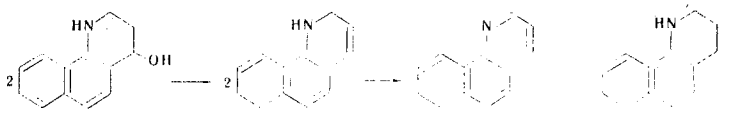
4-Hydroxy- and 4-oxo-1,2,3,4-tetrahydrobenzo[h]quinolines were synthesized. Benzo[h]-quinoline, 1,2,3,4-tetrahydrobenzo[h]quinoline, and a "dimeric" compound are formed when the 4-hydroxy derivative is heated with hydrochloric acid or without it. The reaction of 4-hydroxy-1,2,3,4-tetrahydrobenzo[h]quinoline with thionyl chloride was carried out.

Benzo[h]quinoline and its 1,2,3,4-tetrahydro derivatives are formed when 3-hydroxy-1,2,3,4-tetrahydrobenzo[h]quinoline is heated with hydrochloric, phosphoric, or polyphosphoric acids [2,3]. In developing this research, we investigated similar transformations of 4-hydroxy-1,2,3,4-tetrahydrobenzo[h]quinoline (I). The starting 4-oxo-1,2,3,4-tetrahydrobenzo[h]quinoline (II) could not be obtained by the method in [4] (the yield of II did not exceed 5%). Compound II was obtained in good yield by heating 3-(1-naphthylamino)propionitrile with anhydrous aluminum chloride in chlorobenzene. We were unable to isolate I from the reaction mixture on reduction with lithium aluminum hydride [5]. The reduction of II with sodium amalgam in 95% ethanol gave I in almost quantitative yield.

Benzo[h]quinoline (III), 1,2,3,4-tetrahydrobenzo[h]quinoline (IV), and a base with molecular weight 360, which is capable of forming azo dyes as azo components, were obtained when I was heated with concentrated hydrochloric acid in sealed glass tubes. Since the formation of III and IV proceeds through a step involving 1,2-dihydro derivatives, 1,2-dihydrobenzo[h]quinoline in this case, the dihydro compound not only disproportionates to III and IV but is apparently also converted to "dimeric" compound $C_{26}H_{20}N_2$.



I III IV

The formation of III, IV, and the "dimer" occurs on heating or during vacuum distillation of I and also on refluxing the latter in chlorobenzene. Consequently, I is more readily dehydrated than 3-hydroxy-1,2,3,4-tetrahydrobenzo[h]quinoline, and the disproportionation of the dihydro derivative proceeds not only in acid [2] and alkaline [3] media but also in neutral media at comparatively low temperatures.

As noted in [6,7], 3-hydroxy-6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline is initially formed in the reaction of thionyl chloride with 3-hydroxy-1,2,3,4-tetrahydrobenzo[h]quinoline at room temperature, while 6-chlorobenzo[h]quinoline is initially formed on heating [2], i.e., in the latter case, chlorination at the 6 position and aromatization of the tetrahydropyridine ring occur. It seemed of interest to us to establish how 6-chlorobenzo[h]quinoline forms. On repeating the indicated investigations with 3-hydroxy-1,2,3,4-tetrahydrobenzo[h]quinoline, we were unable to isolate any intermediate compounds. Subsequent investigations of the reaction with thionyl chloride were therefore carried out in the case of 4-hydroxy-1,2,3,4-tetrahydrobenzo[h]quinoline. When I was refluxed with thionyl chloride for 15-20 min, only 6-chlorobenzo-[h]quinoline (V) was isolated. The latter is also obtained from the reaction of I with thionyl chloride at

*See [1] for communication X.

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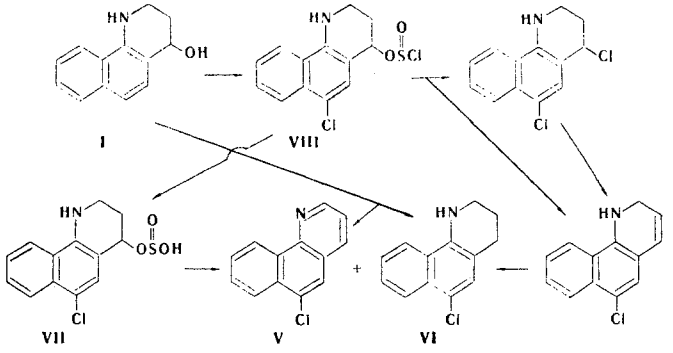
room temperature for 4-5 days. Compound V and 6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline (VI) were isolated from the reaction of I with thionyl chloride for 5 h. The formation of VI is apparently possible only through a step involving the formation of 6-chlorodihydrobenzo[h]quinoline, which disproportionates to V and VI. When the reaction time of I with thionyl chloride was shortened to 15-30 min with subsequent treatment of the mass with a mixture of water and ice, the major reaction product was a crystalline substance with the composition $C_{13}H_{12}ClNO_3S$, which is quite soluble in dilute alkali solution. Compounds V, VI, and sulfur dioxide are formed when it is refluxed in o-dichlorobenzene. Only V is isolated when it is refluxed in thionyl chloride. On the basis of the above, it is apparent that the compound obtained in the reaction of I with thionyl chloride with subsequent treatment of the mass with a mixture of water and ice is an ester of sulfuric acid and 4-hydroxy-6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline (VII), which is apparently formed from the intermediate chlorosulfite derivative of 4-hydroxy-6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline (VIII).



The formation of chlorosulfites during the action of thionyl chloride on secondary aliphatic alcohols was also noted previously [8] in a study of the chlorinating action of thionyl chloride. The intermediate chlorosulfite loses sulfur dioxide to form a carbon–halogen bond.

On the basis of literature data [7, 9-11] and our investigations, the formation of 6-chlorobenzo[h]-quinolines during the action of thionyl chloride on I can apparently be represented as follows. As in the case of 3-hydroxy-1,2,3,4-tetrahydrobenzo[h]quinoline [7], I is initially chlorinated in the 6 position followed by esterification of the hydroxyl group, which is apparently replaced by chlorine. The dihydro compound, which disproportionates to 6-chlorobenzo[h]quinoline and its 1,2,3,4-tetrahydro derivative, is subsequently formed from the 4-chloro derivative or the ester. The low yield of the 1,2,3,4-tetrahydro derivatives as compared with the yield of V can be explained by the fact that 6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline reacts with thionyl chloride even at room temperature, and its derivatives cannot be isolated. At higher temperatures, or when the reaction mass is held at room temperature for a longer time, all of the VI formed reacts with thionyl chloride, and only 6-chlorobenzo[h]quinoline is isolated from the reaction mass. The fact that the yield of V from I and the yield of its derivatives do not exceed 50% is also evidence in favor of the formation of 6-chlorobenzo[h]quinoline through a step involving disproportionation of the dihydro derivatives.

It must be assumed that the formation of V from 3-hydroxy-1,2,3,4-tetrahydrobenzo[h]quinoline on reaction with thionyl chloride proceeds similarly, i.e., through a step involving disproportionation of the dihydro derivative.

EXPERIMENTAL

4-Oxo-1,2,3,4-tetrahydrobenzo[h]quinoline (II). A solution of 39.2 g (0.2 mole) of 3-(1-naphthylamino)-propionitrile in 80 ml of chlorobenzene was heated to 70-80°, and 106.7 g (0.8 mole) of anhydrous aluminum chloride was added gradually with stirring. The mixture was then heated at 115-120° for 2 h, 3 ml of concentrated hydrochloric acid was added, and the mixture was heated for another hour. The reaction mass was poured carefully over ice. The chlorobenzene was removed by steam distillation, and the residue was extracted with benzene. Removal of the solvent gave 16.1 g (41%) of small yellow needles with mp 160.5-162.0° (from ethanol) (mp 157.6-158.6° [4]). Found: N 7.2, 7.2%. $C_{13}H_{11}NO$. Calculated: N 7.1%.

4-Hydroxy-1,2,3,4-tetrahydrobenzo[h]quinoline (I). A solution of 54 g (0.27 mole) of 4-oxo derivative II in 380 ml of ethanol was added to sodium amalgam prepared from 18.6 g (0.82 g-atom) of sodium and 1550 g of mercury. The flask was immediately sealed and shaken vigorously, with removal of the stopper

from time to time for pressure equalization. The temperature rose rapidly to 40-50°. After shaking for 1 h and 20 min, the mercury was separated and washed with alcohol, and the alcohol solution was diluted with 2 liters of cold water. The mixture was extracted with ether, the ether was removed, and the resulting oil began to crystallize on standing over calcium chloride to give 39.5 g (73%) of colorless needles with mp 78.5-80.5° (from chlorobenzene). Found: N 7.1, 6.9%; M 198. $C_{13}H_{13}NO$. Calculated: N 7.0%; M 199.

Benzo[h]quinoline (III) and 1,2,3,4-Tetrahydrobenzo[h]quinoline (IV). A) Seven glass tubes were each charged with 1.0 g of I and 25 ml of concentrated hydrochloric acid. The sealed tubes were heated on an oil bath (bath temperature 195-205°) for 8 h. The contents of the tubes were made alkaline with 25% sodium hydroxide solution and extracted with ether–benzene (1 : 1). A portion of the mass began to crystallize after removal of the solvent. The crystals were removed by filtration and washed with ether to give 1.25 g (10%) of a base with mp 195-196.5° (from ethanol). Found: C 86.2, 86.4; H 5.4, 5,5; N 8.0, 7.8%; M 360 (by mass spectrometry). $C_{26}H_{20}N_2$. Calculated: C 86.6; H 5.6; N 7.8%. The oil obtained after removal of the crystals was dissolved in 30 ml of 10% hydrochloric acid. The resulting hydrochloride of IV was removed by filtration to give 1.55 g (20%) of a product with mp 261° (dec.) [12]. Alkalinization of the filtrate gave 2.0 g (32%) of III with mp 51.0-52.0° [13].

B) A Claisen flask with a rod and disk fractionating column was charged with 10 g (0.05 mole) of I and immersed in a bath heated to 130-140°. After the substance melted, a stream of nitrogen was bubbled in, and the vacuum pump was switched on. The bath temperature was raised to 200° (10-15 mm), and the mixture was heated for 20 min. The major portion of the mass was then distilled at 160-170° (5 mm). The residue was recrystallized from ethanol to give 0.8 g (4.5%) of a substance with mp 195-196.5°. The distillate was dissolved in 20 ml of 10% hydrochloric acid, and the resulting hydrochloride of IV was removed by filtration to give 3.2 g (29%) of a product with mp 260° (dec.). The filtrate was made alkaline to give 2.1 g (23%) of III with mp 51-52°.

C) A 10-g (0.05 mole) sample of I was heated at 150° for 1 h and at 300° for 1.5 h under nitrogen. The reaction mass was dissolved in ethanol and allowed to stand at 0-5° for 10 h. The resulting crystalline precipitate was removed by filtration to give 1.85 g (10%) of a substance with mp 195-196.5°. The ethanol was removed, and the residual oil was dissolved in 10% of hydrochloric acid. The resulting hydrochloride of IV was removed by filtration to give 2.75 g (25%) of a product with mp 261° (dec.). Alkalinization of the filtrate gave 2.9 g (32%) of III with mp 50.5-51.0°.

D) A mixture of 7 g (0.035 mole) of I and 125 ml of chlorobenzene was refluxed for 4 h. The solution was treated with activated charcoal, and the chlorobenzene was removed by distillation. The resulting mass began to partially crystallize on standing. The crystals were removed by filtration to give 0.5 g (4%) of a substance with mp 194-196° (from ethanol). The solvent was removed by distillation, and the resulting oil was dissolved in 10% of hydrochloric acid to give 0.7 g (9%) of the hydrochloride of IV with mp 260° (dec.) and 0.83 g (9%) of the hydrochloride of III with mp 212° (mp 213° [14]).

6-Chlorobenzo[h]quinoline (V), 6-Chloro-1,2,3,4-tetrahydrobenzo[h]quinoline (VI), and 4-Hydroxy-6-chloro-1,2,3,4-tetrahydrobenzo[h]quinoline Sulfite (VII). A) A 2-g (0.01 mole) sample of I was added gradually to 7 ml of thionyl chloride cooled to −7°. After I had dissolved, the reaction mixture was held at 75° for 15 min. The resulting hydrochloride of V was removed by filtration and dissolved in ethanol. The ethanol solution was treated with 5% aqueous potassium carbonate solution to give 1.06 g (50%) of V with mp 99.5-100.5° (from ethanol) (mp 101° [15]).

B) A mixture of 2 g (0.01 mole) of I and 7 ml of thionyl chloride was held at room temperature for 4-5 days. The resulting hydrochloride of V was removed by filtration and dissolved in alcohol. The alcohol solution was treated with aqueous potassium carbonate solution to give 1.0 g (48%) of V with mp 99.7-100.5°.

C) A 2-g (0.01 mole) sample of I was added gradually to 7 ml of thionyl chloride cooled to −7°. The reaction mass was held at room temperature for 5 h and then poured over ice. The mixture was made alkaline and extracted with ether. The solvent was removed, and the resulting mass was separated by chromatography on aluminum oxide with elution by petroleum ether–ether (9 : 1) to give 0.3 g (15%) of V with mp 100-101° and 0.09 g (4%) of VI with mp 67-68.5° [7].

D) A 3-g (0.015 mole) sample of I was added gradually to 10 ml of thionyl chloride cooled to −7°, and the mixture was held at 15-20° for 15 min. The reaction mass was poured over ice, and the mixture was made alkaline and extracted with ether. The ether was removed, and the residue (0.8 g) was separated by

chromatography on aluminum oxide with elution by petroleum ether–ether (9:1) to give 0.3 g (9%) of V with mp 100-101° and 0.1 g (3%) of VI with mp 65.5-67.5°. The alkaline solution remaining after removal of V and VI was acidified with concentrated hydrochloric acid and allowed to stand at 3-5° for several hours to give 3.05 g (68%) of sulfite VII with mp 178.5° (dec., from concentrated hydrochloric acid). Found: Cl 12.4, 12.5; N 4.7, 4.9; S 9.9, 10.3%. $C_{13}H_{12}ClNO_3S$. Calculated: Cl 11.9; N 4.7; S 10.7%.

E) A mixture of 2.9 g (0.01 mole) of VII and 10 ml of thionyl chloride was heated at 75° for 2 h. The resulting precipitate was removed by filtration, washed with 2 ml of thionyl chloride, and dissolved in ethanol. The ethanol solution was treated with 20% sodium hydroxide solution and diluted with water to give 0.9 g (42%) of V with mp 100-101°.

F) A 1-g (0.003 mole) sample of VII was refluxed with 35 ml of 21% hydrochloric acid for 8 h. The mixture was cooled, diluted with water, made alkaline with 20% sodium hydroxide solution, and extracted with ether. The ether was removed, and the reaction mass was separated by chromatography with elution with hexane–ether (7:3) to give 0.3 g (47%) of V with mp 99.5-100.5° and a very small amount of VI with mp 65.5-66.5°.

G) A 3-g (0.01 mole) sample of VI was refluxed with 12 ml of o-dichlorobenzene under nitrogen for 1.5 h. The cleaved sulfur dioxide was absorbed with 120 ml of water. The o-dichlorobenzene was removed by vacuum distillation, and the residue began to crystallize to give 0.8 g (37%) of V with mp 99-100° (from ethanol). A very small amount of VI with mp 66-67.0° was obtained from the mother liquor after removal of V.

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