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

XVI.* 4-PHENYL-1,2,3,4-TETRAHYDROBENZO[*f*]QUINOLINE

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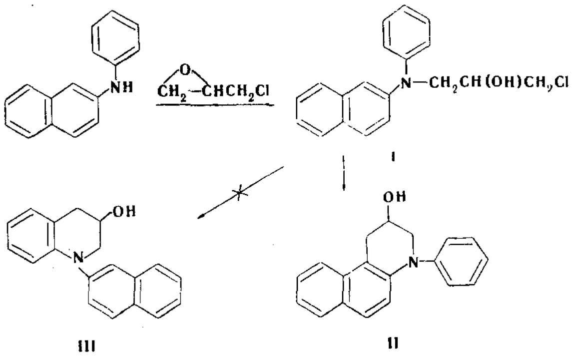
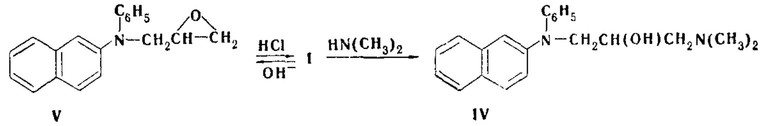
Heating N-phenyl-2-naphthylamine with epichlorohydrin gives N-phenyl-N-(3-chloro-2-hydroxypropyl)-2-naphthylamine, which is subsequently converted to 4-phenyl-2-hydroxy-1,2,3,4-tetrahydrobenzo[*f*]quinoline. The latter readily loses a molecule of water.

When diphenylamine is heated with epichlorohydrin, one obtains 1-phenyl-3-hydroxy-1,2,3,4-tetrahydroquinoline through a step involving N-(3-chloro-2-hydroxypropyl)diphenylamine [2]. In the case of N-phenyl-2-naphthylamine, the N-phenyl-N-(3-chloro-2-hydroxypropyl)-2-naphthylamine (I) formed can cyclize to form 4-phenyl-2-hydroxy-1,2,3,4-tetrahydrobenzo[*f*]quinoline (II) or 1-(2-naphthyl)-3-hydroxy-1,2,3,4-tetrahydroquinoline (III).



We have shown that primarily I is formed when N-phenyl-2-naphthylamine is heated with epichlorohydrin in the presence of concentrated acetic acid to 60°C. Compound I reacts with dimethylamine to give 1-[N-phenyl-N-(2-naphthyl)amino]-3-dimethylamino-2-propanol (IV) and with potassium hydroxide to give N-phenyl-N-(2,3-epoxypropyl)-2-naphthylamine (V). The latter is converted to the starting I by the action of hydrogen chloride. Cyclization to II occurs when I is heated to 130-135°.



If the reaction of N-phenyl-2-naphthylamine with epichlorohydrin in the presence of concentrated acetic acid is carried out at 100-105°, one isolates VII with composition $C_{21}H_{19}NO_2$, which has an acetate group. Alkaline saponification of VII gives hydroxy compound II. The formation of II and VII also proceeds at lower temperatures (70-80°), but a longer heating time is required. The formation of III or its derivatives is not observed. 4-Phenyl-1,2,3,4-tetrahydrobenzo[*f*]quinoline (VI) is obtained when II is heated with

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*See [1] for communication XV.

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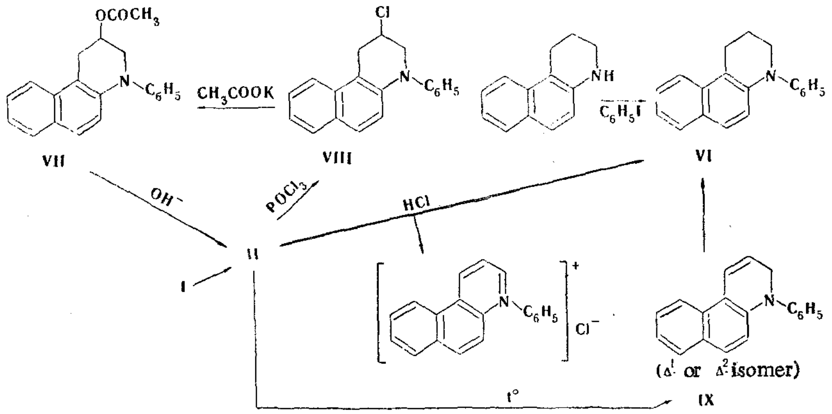

concentrated hydrochloric acid. The formation of VI can apparently be explained by disproportionation [3] of 4-phenyl-3,4 (or 1,4)-dihydrobenzo[*f*]quinoline, which is formed during cleavage of a molecule of water from II. Compound VI was synthesized by an independent route by phenylation of 1,2,3,4-tetrahydrobenzo[*f*]quinoline with iodobenzene in the presence of potassium fluoride [4].

When phosphorus oxychloride acts on II, a hydroxyl group is replaced by halogen to give 4-phenyl-2-chloro-1,2,3,4-tetrahydrobenzo[*f*]quinoline (VIII).

Compound II loses a molecule of water on vacuum distillation in the presence of sodium hydroxide and is converted to 4-phenyl-3,4 (or 1,4)-dihydrobenzo[*f*]quinoline (IX), which can be converted to VI by reduction. The splitting out of water from II is observed even during vacuum distillation.

EXPERIMENTAL

N-Phenyl-N-(3-chloro-2-hydroxypropyl)-2-naphthylamine (I). A. A mixture of 11.0 g (0.05 mole) of N-phenyl-2-naphthylamine, 9.2 g (0.1 mole) of epichlorohydrin, and 6.0 g (0.1 mole) of glacial acetic acid was heated at 60-65° for 5-6 days. The reaction mass was then diluted with water and extracted with ether. The ether was removed, and the residue was chromatographed (here and elsewhere, with a column filled with activity II Al_2O_3) with ether–petroleum ether (2 : 1) to give 10.2 g (65%) of a fraction with R_f 0.53. The light yellow oily product gradually darkened. Found: Cl 10.6, 10.5; N 4.6, 4.4%. $C_{19}H_{18}ClNO$. Calculated: Cl 11.2; N 4.5%.

B. Gaseous hydrogen chloride was bubbled into a solution of 13.8 g (0.05 mole) of V in 50 ml of methanol for 10-15 min. The methanol was removed, and 8.2 g (54%) of I was isolated as in method A.

4-Phenyl-2-hydroxy-1,2,3,4-tetrahydrobenzo[*f*]quinoline (II). A. A mixture of 3.2 g (0.01 mole) of VII, 2.0 g of potassium hydroxide, 50 ml of alcohol, and 10 ml of water was heated at 100-105° for 6 h. It was then diluted with water and extracted with ether. The solvent was removed, and the residue was recrystallized from benzene–hexane (1 : 2) to give 1.8 g (65%) of a product with mp 85-86°. Found: N 5.4, 5.2%. $C_{19}H_{17}NO$. Calculated: N 5.1%.

B. A mixture of 15.5 g (0.05 mole) of I and 9.2 g (0.1 mole) of epichlorohydrin was heated at 135-145° for 3-5 days. It was then chromatographed with ether–petroleum ether (4 : 1) to give 6.3 g (46%) of a fraction with R_f 0.6 and mp 85-86° [from benzene–hexane (1 : 2)].

C. A mixture of 11.0 g (0.05 mole) of N-phenyl-2-naphthylamine and 9.2 g (0.1 mole) of epichlorohydrin was heated at 140-150° for 5-6 days to give, after workup as in method B, 6.5 g (47%) of II with mp 85-86°. No melting-point depression was observed for mixtures of this product with the products of methods A and B.

1-[N-Phenyl-N-(2-naphthyl)amino]-3-dimethylamino-2-propanol (IV). A mixture of 11.0 g (0.05 mole) of N-phenyl-2-naphthylamine, 9.2 g (0.1 mole) of epichlorohydrin, and 40 ml of glacial acetic acid was heated at 60-65° for 70 h. It was then washed with water and extracted with 150 ml of ether. The ether was removed, and the residue was dissolved in 15 ml of dimethylformamide. Water (3 ml) and 4.0 g of sodium hydroxide were added to the solution, and the mixture was shaken at 40-45° for 2 h. It was then diluted with water and extracted with 300 ml of petroleum ether. The solvent was removed, and the residue was recrystallized from chlorobenzene to give 4.1 g (24%) of IV with mp 137-137.5°. Found: N 9.2, 9.1%. $C_{21}H_{24}N_2O$. Calculated: N 8.8%.

N-Phenyl-N-(2,3-epoxypropyl)-2-naphthylamine (V). A. A mixture of 11.0 g (0.05 mole) of N-phenyl-2-naphthylamine, 9.2 g (0.1 mole) of epichlorohydrin, and 40 ml of glacial acetic acid was heated at 60-65° for 70 h. The mixture was then washed with water and extracted with 150 ml of ether. The ether solution was dried, 10.0 g (0.25 mole) of ground sodium hydroxide was added, and the mixture was heated at 40-45° for 2 h. It was then washed with water, and the ether was removed. The residue was vacuum-distilled at 0.5 mm in a stream of nitrogen to give 2.2 g (16%) as a major fraction with bp 215-216°. The product was a transparent, viscous, light yellow mass. Found: N 5.1, 5.3%. $C_{19}H_{17}NO$. Calculated: N 5.1%.

B. A 15.5-g (0.05 mole) sample of I was dissolved in 50 ml of ether, 10.0 g (0.25 mole) of ground sodium hydroxide was added, and the mixture was heated on a water bath at 60° for 2 h. It was then washed with water and extracted with ether. The ether was removed, and the residue was chromatographed with ether–petroleum ether (1 : 2) to give 3.8 g (28%) of a fraction with R_f 0.5.

4-Phenyl-1,2,3,4-tetrahydrobenzo[*f*]quinoline (VI). A. Fifteen glass tubes were charged with 1.0 g of II and 25 ml of concentrated hydrochloric acid (sp. gr. 1.19) and heated at 195-200° for 9 h. The reaction mixtures were made alkaline with 25% sodium hydroxide solution and extracted with 200 ml of ether. The ether was removed, and the residue was vacuum-distilled in a stream of nitrogen to give 2.6 g (18%) of a major fraction with bp 184-186° (1.0-1.5 mm). Treatment with 10 ml of methanol gave colorless needles with mp 72.5-73.5°. Found: N 5.4, 5.4%. $C_{19}H_{17}N$. Calculated: N 5.4%. The picrate had mp 98.5-99° (from methanol). Found: N 11.7, 11.6%. $C_{19}H_{17}N \cdot C_6H_3N_3O_7$. Calculated: N 11.5%.

B. A mixture of 5.2 g (0.02 mole) of IX, 200 ml of concentrated hydrochloric acid (sp. gr. 1.19), and 80.0 g of tin metal was heated at 120-130° for 36 h. The reaction mixture was made alkaline and worked up as in method A to give 1.9 g (36%) of product.

C. A mixture of 18.3 g (0.1 mole) of 1,2,3,4-tetrahydrobenzo[*f*]quinoline, 20.4 g (0.1 mole) of iodobenzene, 18.0 g (0.31 mole) of anhydrous potassium fluoride, 2.0 g (0.014 mole) of cuprous oxide, and 1.0 g (0.016 g-atom) of copper powder was stirred at 215-225° for 40 h. The mixture was then treated with water and extracted with 200 ml of ether. The ether solution was washed with 80 ml of 6% hydrochloric acid, the 1,2,3,4-tetrahydrobenzo[*f*]quinoline hydrochloride was separated, and 3.5 g (13%) of VI was isolated as in method A. No melting-point depression was observed for a mixture of this product with the product obtained by methods A and B.

4-Phenyl-2-acetoxy-1,2,3,4-tetrahydrobenzo[*f*]quinoline (VII). A. A mixture of 22.0 g (0.01 mole) of N-phenyl-2-naphthylamine, 18.5 g (0.2 mole) of epichlorohydrin, and 8 ml of glacial acetic acid was heated at 100-105° for 23 h. The mixture was then washed with water and extracted with 300 ml of ether. The ether was removed, and the residue was recrystallized from alcohol to give 9.0 g (28%) of colorless crystals of VII with mp 123-124.5°. Found: N 4.5, 4.5%. $C_{21}H_{19}NO_2$. Calculated: N 4.4%.

B. A mixture of 5.5 g (0.02 mole) of II, 6 ml of acetic anhydride, and five to ten drops of concentrated sulfuric acid was heated on a boiling-water bath for 10 min. It was then diluted with water and extracted with ether. The ether was removed, and the residue was recrystallized from methanol to give 2.1 g (33%) of a product with mp 123-124.5°.

C. A mixture of 2.9 g (0.01 mole) of VIII, 3.9 g (0.03 mole) of potassium acetate, 20 ml of alcohol, and 20 ml of water was heated at 115-120°. It was then cooled to −5°, and the resulting crystals were recrystallized from alcohol to give 2.3 g (74%) of product. No melting-point depression was observed for a mixture of this product with the products obtained by methods A and B.

4-Phenyl-2-chloro-1,2,3,4-tetrahydrobenzo[*f*]quinoline (VIII). A 5.5-g (0.02 mole) sample of II was dissolved in 5 ml of phosphorus oxychloride, and the crystals that formed in the course of 23 h were removed by filtration and dissolved in 35 ml of water. The solution was made alkaline with 25% potassium hydroxide solution and extracted with ether. The solvent was removed, and the residue was recrystallized from alcohol to give 3.2 g (51%) of colorless crystals of VIII with mp 70.5-71°. Found: Cl 12.3, 12.4; N 4.8, 4.7%. $C_{19}H_{16}ClN$. Calculated: Cl 12.1; N 4.8%.

4-Phenyl-3,4 (or 1,4)-dihydrobenzo[*f*]quinoline (IX). A 5.5-g (0.02 mole) sample of II was vacuum-distilled (0.5-1.0 mm) in a stream of nitrogen in the presence of 2.0 g of ground sodium hydroxide. The fraction collected at 210-219° began to crystallize to give 3.5 g (66%) of a product with mp 83.5-84.5°. A mixture of this product with II had mp 71-76°. Found: N 5.5, 5.4%; mol. wt. 257 (by mass spectrometry). $C_{19}H_{15}N$. Calculated: N 5.5%; mol. wt. 257. The picrate had mp 137-138° (from methanol). Found: N 11.7, 11.6%. $C_{19}H_{15}N \cdot C_6H_3N_3O_7$. Calculated: N 11.4%.

Compound IX was also obtained by vacuum distillation of II in a stream of nitrogen.

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