N-PHENYL-1-NAPHTHYLAMINE*

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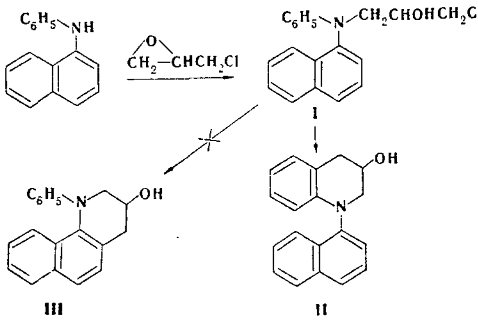
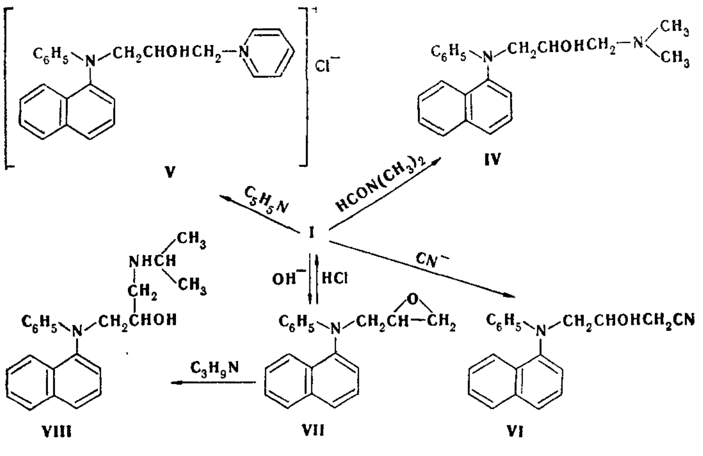
Heating N-phenyl-1-naphthylamine with epichlorohydrin gives N-phenyl-N-(3-chloro-2-hydroxypropyl)-1-naphthylamine, which cyclizes with the participation of the phenyl ring.

Heating diphenylamine with epichlorohydrin gives 1-phenyl-3-hydroxy-1,2,3,4-tetrahydroquinoline through a step involving N-(3-chloro-2-hydroxypropyl)diphenylamine [2], while the reaction of N-phenyl-2-naphthylamine with epichlorohydrin gives 1-phenyl-2-hydroxy-1,2,3,4-tetrahydrobenzo[f]quinoline [3]. N-Phenyl-N-(3-chloro-2-hydroxypropyl)-1-naphthylamine (I), which is formed in the case of N-phenyl-1-naphthylamine, can be cyclized to give both 1-(1-naphthyl)-3-hydroxy-1,2,3,4-tetrahydroquinoline (II) and 1-phenyl-3-hydroxy-1,2,3,4-tetrahydrobenzo[h]-quinoline (III).



The aim of the present study was to isolate the intermediately formed 3-chloro-2-hydroxypropyl derivative, to establish the direction of its cyclization, and to study the chemical properties of (I) and (II).

We have shown that primarily (I) is formed when N-phenyl-1-naphthylamine is heated to 65° with epichlorohydrin in the presence of acetic acid. The chlorine atom in (I) is readily replaced by the action of



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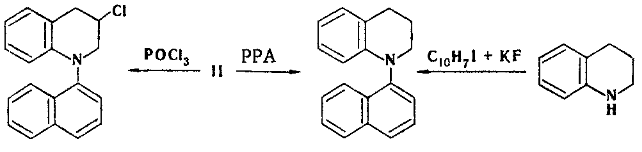
amine dimethylformamide (DMF) [4], potassium cyanide, etc. The transformations of (I) are presented in the scheme on the previous page.

When (I) is heated to 150°C it cyclizes to (II). To determine the direction of this cyclization, product (II) was heated with polyphosphoric acid (PPA). The free base, corresponding to 1-(1-naphthyl)-1,2,3,4-tetrahydroquinoline (IX), was isolated. The formation of (IX) can apparently be explained by disproportionation [5, 6] of the dihydro compound, which is formed by splitting out of a water molecule from (II). Base (IX) was synthesized independently by arylation of 1,2,3,4-tetrahydroquinoline with 1-iodonaphthalene in the presence of potassium fluoride [7].



X IX

Consequently, the hydrogen in the ortho position in the benzene ring in N-phenyl-N-(3-chloro-2-hydroxypropyl)-1-naphthylamine is more active than the hydrogen in the 2 position in the naphthalene ring, and the 1 position in the naphthalene ring in N-phenyl-N-(3-chloro-2-hydroxypropyl)-2-naphthylamine [3] is more active than the ortho position of the benzene ring.

The hydroxyl group is replaced by chlorine to give (X) during the action of phosphorus oxychloride on (II). The corresponding benzoyl (XI) and acetyl (XII) derivatives were obtained by benzoylation and acetylation of (II). The acetyl derivative (XII) was also obtained by the action of sodium acetate in alcohol of X. Acetyl derivative (XII) is converted to (II) by alkaline saponification.

EXPERIMENTAL

Chromatography was carried out by the thin-layer method and with a column using activity (II) aluminum oxide.

N-Phenyl-N-(3-chloro-2-hydroxypropyl)-1-naphthylamine (I). A) A mixture of 11.0 g (0.05 mole) of N-phenyl-1-naphthylamine, 9.2 g (0.1 mole) of epichlorohydrin, and 6.0 g (0.1 mole) of concentrated acetic acid was heated at 60-65° for 6 days, after which it was treated with water and extracted with ether. The solvent was removed, and the residue was chromatographed with a column with elution with ether–petroleum ether (2 : 1) to give an oily substance with R_f 0.5, which began to crystallize on prolonged standing in a desiccator to give 11.6 g (75%) of a product with mp 71-73° (from petroleum ether). Found %: Cl 10.9; N 4.5. $C_{19}H_{18}ClNO$. Calculated %: Cl 11.2; N 4.5.

B) Hydrogen chloride gas was passed into a solution of 13.8 g (0.05 mole) of VII in 50 ml of methanol for 20 min. After removal of the methanol, (I) was isolated as in method A. The yield of product with mp 71-73° (from petroleum ether) was 9.2 g (62%). No melting-point depression was observed for a mixture of this product with the product of method A.

1-(1-Naphthyl)-3-hydroxy-1,2,3,4-tetrahydroquinoline (II). A mixture of 15.5 g (0.05 mole) of (I), and 9.2 g (0.1 mole) of epichlorohydrin was heated at 150° for 5 days, after which it was diluted with water and extracted with ether. The solvent was removed, and the residue was subjected to column chromatography with elution by ether–petroleum ether (4 : 1) to give 10.3 g (75%) of a substance with mp 108-110° (from ether) and R_f 0.6. Found %: C 82.9; H 6.3; N 5.1. $C_{19}H_{17}NO$. Calculated %: C 82.9; H 6.2; N 5.1.

B) A mixture of 11.0 g (0.05 mole) of N-phenyl-1-naphthylamine and 9.2 g (0.1 mole) of epichlorohydrin was heated at 150-160° for 6 days, after which (II) was isolated as in method A to give 8.6 g (62%) of a product with mp 108-110° (from ether).

C) A mixture of 3.2 g (0.01 mole) of (XII), 1.7 g (0.03 mole) of potassium hydroxide, 25 ml of alcohol, and 5 ml of water was refluxed for 6 h, after which (II) was isolated as in method A to give 1.9 g (70%) of a product with mp 108-110° (from ether).

1-[(1-Naphthyl)anilino]-3-dimethylamino-2-propanol (IV) [4]. A mixture of 4.6 g (0.015 mole) of (I), 4 ml of DMF, and 2 g (0.05 mole) of ground sodium hydroxide was shaken for 15 min, after which 3 ml of water was added, and the mixture was heated at 60° for 2 h. Water was then added, and the mixture was extracted with petroleum ether. The resulting crystals were removed by filtration to give 1.2 g (25%) of a product with mp 89-90° (from petroleum ether). Found %: N 8.7. $C_{21}H_{24}N_2O$. Calculated %: N 8.8.

1-[3-(1-Naphthyl)anilino-2-hydroxypropyl]pyridinium Chloride (V). A mixture of 4.7 g (0.015 mole) of (I), 3.6 g (0.045 mole) of pyridine, and 6 ml of chlorobenzene was heated at 120° for 12 h. The resulting crystals were removed by filtration and washed with acetone to give 1.8 g (37%) of a product with mp 268-269° (from acetone). Found %: Cl 9.0; N 7.2. $C_{24}H_{23}ClN_2O$. Calculated %: Cl 9.0; N 7.2.

3-[(1-Naphthyl)anilino]-2-hydroxybutyronitrile (VI). A mixture of 15.5 g (0.05 mole) of (I), 20 ml of methanol, 6.5 g (0.1 mole) of potassium cyanide, and 20 ml of water was refluxed for 3 h. The methanol was removed by distillation, and the residue was treated with water and extracted with ether. The solvent was removed, and the residual crystals were removed by filtration to give 10.5 g (70%) of a product with mp 116-118° (from methanol). Found %: N 9.2. $C_{20}H_{18}N_2O$. Calculated %: N 9.2.

N-Phenyl-N-(2,3-epoxypropyl)-1-naphthylamine (VII). A) A mixture of 22.2 g (0.1 mole) of N-phenyl-1-naphthylamine, 18.4 g (0.2 mole) of epichlorohydrin, and 6 g (0.1 mole) of concentrated acetic acid was heated at 60-65° for 5 days, after which it was diluted with water and extracted with ether. The ether solution was refluxed for 3 h with 20 g (0.5 mole) of ground sodium hydroxide, after which it was washed with water. The ether was removed, and the residue was vacuum distilled in a stream of nitrogen. The fraction with bp 206-210° (1 mm) was collected. The yield was 16.5 g (60%). Found %: N 5.2. $C_{19}H_{17}NO$. Calculated %: N 5.1.

B) A 31.1-g (0.1 mole) sample of (I) was dissolved in 200 ml of ether, 20 g (0.5 mole) of ground sodium hydroxide was added, and the mixture was refluxed for 3 h and worked up as in method A to give 19.0 g (70%) of product.

1-[(1-Naphthyl)anilino]-3-isopropylamino-2-propanol (VIII). A mixture of 8.3 g (0.03 mole) of (VII) and 3.5 g (0.06 mole) of isopropylamine was maintained at room temperature for 6 days, after which it was dissolved in ether, and the resulting crystals were removed by filtration and washed with ether to give 4 g (40%) of a product with mp 102-103° (from ether). Found %: N 8.5. $C_{22}H_{26}N_2O$. Calculated %: N 8.4.

1-(1-Naphthyl)-1,2,3,4-tetrahydroquinoline (IX). A) A mixture of 5.5 g (0.02 mole) of (II) and 28 ml of polyphosphoric acid (PPA) was heated at 200° for 2 h, after which it was cooled and neutralized with 50% sodium hydroxide solution. The mixture was extracted with ether, the ether was removed, and the residue was chromatographed (elution with petroleum ether) to give 1.02 g (20%) of a product with mp 134-136° (from methanol) and R_f 0.5. Found %: C 87.9; H 6.7; N 5.4. $C_{19}H_{17}N$. Calculated %: C 88.0; H 6.6; N 5.4.

B) A mixture of 13.3 g (0.1 mole) of 1,2,3,4-tetrahydroquinoline, 25.4 g (0.1 mole) of iodonaphthalene, 18.03 g (0.31 mole) of anhydrous potassium fluoride, 2 g (0.014 mole) of cuprous oxide, and 1 g (0.016 g-atom) of copper powder was stirred at 220-230° for 30 h. It was then cooled, treated with water, and extracted with ether. The ether was removed, and the residue was chromatographed as in method A. Two recrystallizations from methanol gave 2.6 g (10%) of crystals with mp 134.5-136°.

1-(1-Naphthyl)-3-chloro-1,2,3,4-tetrahydroquinoline (X). A 13.8-g (0.05 mole) sample of (II) was dissolved in 15.2 g (0.1 mole) of phosphorus oxychloride, and the mixture was allowed to stand at room temperature for 2 days. It was then treated with ice, neutralized with 20% sodium hydroxide solution, and extracted with benzene. The solvent was removed, and the resulting crystals were separated by filtration to give 5.8 g (40%) of a product with mp 144.5-146° (from benzene). Found %: Cl 12.1; N 4.8. $C_{19}H_{16}ClN$. Calculated %: Cl 12.1; N 4.8.

1-(1-Naphthyl)-3-benzoxy-1,2,3,4-tetrahydroquinoline (XI). A mixture of 2.8 g (0.1 mole) of (II), 10 ml of pyridine, and 4.2 g (0.03 mole) of benzoyl chloride was heated at 85° for 3 h, after which it was cooled, treated with 20% sulfuric acid solution, and diluted with water. Recrystallization from ethanol–ether (5:1) gave 2.3 g (60%) of crystals of (XI) with mp 109.5-111°. Found %: N 3.8. $C_{26}H_{21}NO_2$. Calculated %: N 3.6.

1-(1-Naphthyl)-3-acetoxy-1,2,3,4-tetrahydroquinoline (XII). A) A mixture of 2.8 g (0.01 mole) of (II), 12 ml of pyridine, and 4 g (0.05 mole) of acetyl chloride was heated at 70° for 2 h, after which it was treated with 25% sulfuric acid and extracted with ether. The ether was then removed, and the resulting crystals were removed by filtration and washed with ether to give 1.6 g (50%) of a product with mp 130-132° (from ethanol). Found %: N 4.4. $C_{21}H_{19}NO_2$. Calculated %: N 4.4.

B) A 2.9-g (0.01 mole) sample of (X) was dissolved in 50 ml of ethanol, and an aqueous solution of sodium acetate (3.5 g of $CH_3COONa \cdot 3H_2O$ and 3 ml of water) was added. The mixture was heated on a boiling-water bath for 12 h, after which the alcohol was removed, and the residue was treated with water and extracted with ether. The resulting crystals were removed by filtration to give 1.3 g (40%) of a product with mp 130-132° (from ethanol). No melting-point depression was observed for a mixture of samples of (XII) obtained by methods A and B.

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