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A STUDY OF THE REACTION PRODUCTS FROM EPICHLOROHYDRIN AND AROMATIC AMINES

I. N-Phenyl-3-Hydroxy-1,2,3,4-Tetrahydroquinoline And Its Transformation Products

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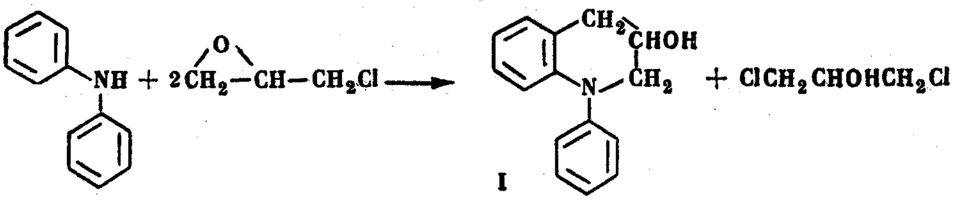
A method of preparing N-phenyl-3-hydroxy-1,2,3,4-tetrahydroquinoline is developed, and some of its conversion products are obtained. The structures of N-phenyl-3-chloro-1,2,3,4-tetrahydroquinoline and N-phenyl-1,2,3,4-tetrahydroquinoline are proved, the latter being formed by heating N-phenyl-3-hydroxy-1,2,3,4-tetrahydroquinoline with concentrated hydrochloric acid.

N-phenyl-3-hydroxy-1,2,3,4-tetrahydroquinoline I has previously been prepared from diphenylamine by the action of epichlorohydrin under pressure, or without pressure and at high temperatures in the presence of sodium iodide [2.3]. It was considered [3] impossible to prepare I at atmospheric pressure without using a catalyst.

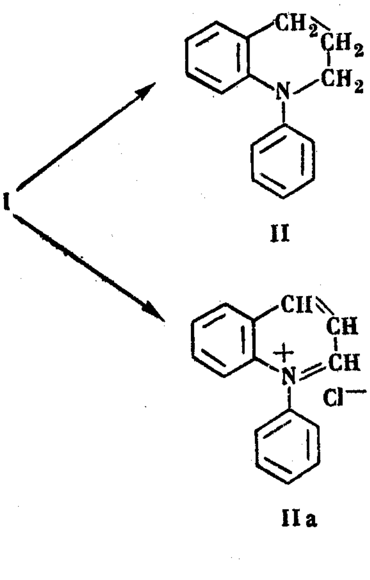
Notwithstanding the literature results, I has now been obtained by heating diphenylamine with excess epichlorohydrin (molar ratio 1:2.2) at atmospheric pressure, without using a catalyst. The yield is 63-68% of the theoretical, twice that stated in the literature [3].

The products obtained by heating diphenylamine with epichlorohydrin are neutral, and dichlorohydrin can be separated from them, showing that the hydrogen chloride evolved when I is formed reacts with the epichlorohydrin, converting it to dichlorohydrin.



In a further study of I, it was of interest to replace its hydroxyl group by a chlorine atom.

An attempt was made to achieve this by treating I with hydrogen chloride. However, not only was the expected chloro-substituted I obtained, but there was also a reaction in another direction [4]. The main product isolated was a pale yellow liquid, whose composition corresponded to $C_{15}H_{15}N$, a weak base which dissolves in concentrated hydrochloric acid, and couples with a 4-nitrobenzenediazonium salt, to give a dark red crystalline monoazo-dye. From these properties of the compound, and analogy with disproportionation reactions of 3-hydroxy-1,2,3,4-tetrahydrobenzoquinolines [5], it could be assumed that what had been isolated was N-phenyl-1,2,3,4-tetrahydroquinoline II, hitherto undescribed in the literature. A second product formed must be the N-phenylquinoline salt IIa, which it has so far not been possible to isolate.

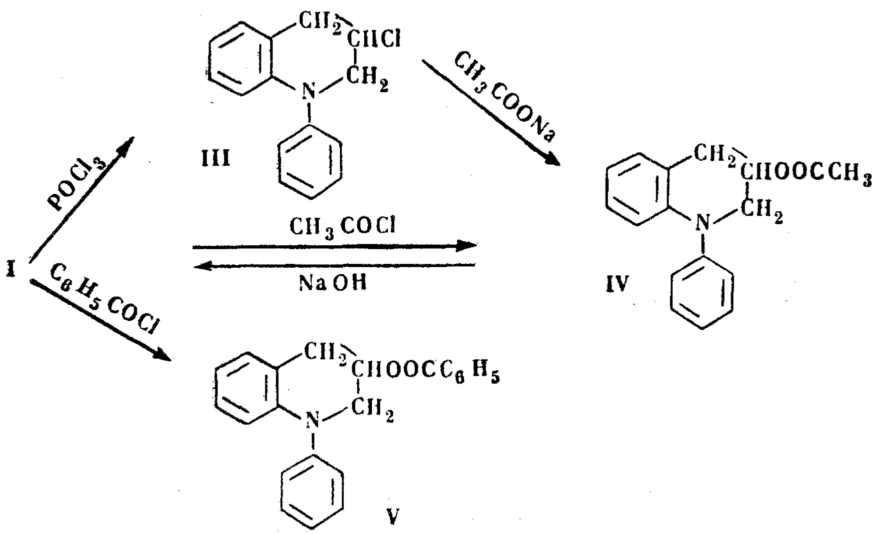


To prove the structure of this compound, it has been synthesized from 1,2,3,4-tetrahydroquinoline by dephenylating it in the presence of potassium fluoride [6]. The identities of the compounds obtained were proved by the properties of their perchlorates and hydriodides, and by their IR and UV spectra

According to a recently published paper [7], the properties of II prepared by other methods, agree basically with those found here. However, there is a difference of extinction coefficient: $\varepsilon = 12\ 500$; $\lg \varepsilon = 4100$; $\lambda = 296$ mμ, while the German authors give $\varepsilon = 4110$.

An attempt was made to obtain 3-chloro-1, 2, 3, 4-tetrahydroquinoline by treating I with phosphorus oxychloride. After heating I with phosphorus oxychloride in chloroform for 3 hr, a crystalline colorless compound having the formula $C_{15}N_{14}NCl$ could be isolated as the main product from the reaction mixture. When this was treated in alcohol with sodium acetate, the chlorine atom was replaced by an acetyl group. The ester from acetic acid and N-phenyl-3-hydroxy-1, 2, 3, 4-tetrahydroquinoline IV, was identical with the ester made by acetylating I.

The ester prepared from the chloro-derivative was saponified with aqueous-alcoholic potassium hydroxide. The crystalline substance then isolated proved to be identical with I. Hence the compound obtained by treating I with phosphorus oxychloride is N-phenyl-3-chloro-1, 2, 3, 4-tetrahydroquinoline (III).



Heating I with phosphorus oxychloride gives an 18% yield of III, but if the reaction effecting replacement of the hydroxyl group by a chlorine atom is carried out without a solvent and at low temperatures (from −1° to −2°), the yield of III is raised to 60%. Evidently this is because a molecule of water is split out at high temperatures, to give dihydroderivatives of N-phenylquinoline, and the yield of III is lowered. 3- or 4- hydroxy derivatives of 1, 2, 3, 4-tetrahydroquinolines are known to be prone to lose water [5, 8].

Experimental

N-phenyl-3-hydroxy-1, 2, 3, 4-tetrahydroquinoline (I). 16.9 g (0.1 mole) diphenylamine and 20.4 g (0.22 mole) epichlorohydrin were heated together for 36 hr* at 155-160° under reflux. The reaction products were vacuum-distilled in a current of nitrogen; the cut boiling below 60°(2.5 mm) (11.8 g) and containing excess epichlorohydrin and glycerol dichlorohydrin (bp 173.0-174.3°, $n_D^{16.9}$ 1.4808), while diphenylamine (0.6 g) was identified in that boiling up to 175° (2.5 mm) (3.1 g). The main fraction, coming over at 175-195° (2.5 mm) was taken up in 12 ml ether, and the precipitate which separated after standing for 6 hr was filtered off, washed with 8 ml ether, and recrystallized from alcohol. Yield of I 13.5 g (60%), mp 78.5-79.0°. Found: C 80.2, 80.3; H 6.8, 6.8; N 6.2, 6.2%. Calculated for $C_{15}H_{15}ON$: C 80.0; H 6.7; N 6.2%.

I was also isolated by another method. After taking the cut boiling below 60° (2.5 mm), what remained was diluted with ether, when the yield of pure reaction product was 14.2-15.3 g (63-68%).

I was also synthesized using large quantities of starting materials, 169 g (1 mole), 338 g (2 mole) diphenylamine and 203.5 g (2.2 mole), 407 (4.4 mole) epichlorohydrin, when the yield of pure reaction product corresponded to that previously stated.

N-phenyl-1, 2, 3, 4-tetrahydroquinoline (II).

a) 1.0 g I and 25 ml concentrated hydrochloric acid (d 1.19) were placed in each of 120 glass tubes, which were then sealed and heated at 205-215° for 18 hr in an oil bath. The contents of the tubes (3 *l*) were diluted with 9 *l* water, cooled, extracted with petrol ether (600 ml), and the bulked extracts dried over sodium sulfate. The petrol ether was distilled off and the residue distilled in a current of nitrogen, when the main fraction distilled at 142.5-145° (2-3 mm), Yield 23.6 g (21%). On repeated distillation the main part of the product (18 g) distilled over at 144-144.5° (2.5-3 mm), forming a pale yellow oil. It was readily soluble in organic solvents and concentrated hydrochloric acid, poorly soluble in dilute acid. Found: N 6.7, 6.9%. Calculated for $C_{15}H_{15}N$: N 6.7%.

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*Reaction was almost complete in 26-30 hr, a longer time only slightly raised the yield of I.

b) The same experiment was run in a nitrogen atmosphere. 65 g I give 14.5 g (24% yield) II, bp 142.5-145° (2-3 mm).

N-phenyl-1,2,3,4-tetrahydroquinoline hydriodide. 1.2 g II, 7 ml ether, and 2.5 ml HI (d 1.7) were shaken together, and the resultant precipitate filtered off and washed with dry ether. Weight 1.8 g. Recrystallized from absolute alcohol-ether (1:2) (dissolved in alcohol, diluted with ether), to give pale yellow crystals mp 149.0° (decomp). Found: N 4.4; 4.3%. Calculated for $C_{15}H_{15}N \cdot HI$: N 4.2%

N-phenyl-1,2,3,4-tetrahydroquinoline perchlorate. 1.2 g II, 6 ml methanol, and 7 ml 40% perchloric acid were shaken together to give 1.5 g perchlorate, which, after recrystallizing from methanol (7 ml) formed colorless crystals mp 175.5° (decomp.) Found: N 4.6, 4.7; Cl 11.3, 11.4%. Calculated for $C_{15}H_{15}N \cdot HClO_4$: N 4.5; Cl 11.5%.

Reverse synthesis of N-phenyl-1,2,3,4-tetrahydroquinoline (II). 40.0 g (0.33) mole 1,2,3,4-tetrahydroquinoline, 68 g (0.33 mole) iodobenzene, 58 g (1 mole) anhydrous potassium fluoride, 2 g (0.014 mole) cuprous oxide, and 1 g (0.016 mole) copper powder were stirred and heated together for 40 hr at 215-225°. The products were then treated with water (200 ml), and extracted with ether (400 ml). After distilling off the ether, the unreacted 1,2,3,4-tetrahydroquinoline was extracted with 200 ml 6% hydrochloric acid, and the residue (a mixture of iodobenzene and reaction product), extracted with ether, and the ethereal solution dried over potash. After distilling off the ether the residue was vacuum-distilled in a stream of nitrogen. The reaction product distilled at 143-146° (2.3 mm), yield 12.4 g (18%). Repeated distillation gave a main cut of product (8 g) distilling at 144-145° (2.5-3 mm). Found: N 6.7; 6.8%. Calculated for $C_{15}H_{15}N$: N 6.7%.

The iodide and perchlorate gave undepressed mixed mp with the iodide and perchlorate of 1,2,3,4-tetrahydroquinoline.

N-phenyl-3-chloro-1,2,3,4-tetrahydroquinoline (III).

a) 22.5 g (0.1 mole) powdered I was dissolved in 38.3 g (0.25 mole) phosphorus oxychloride, and kept for 3 days at −1° to −2°, then for 1 day at 15-20°. The reaction products were then treated with 200 ml petrol ether (or ethyl ether) and 300 g ice, and slowly neutralized, while being stirred, with a 20% sodium hydroxide solution. It was repeatedly extracted with petrol ether (75 ml), the extracts bulked, washed a few times with water (300 ml), dried over sodium sulfate, and then, after distilling off the petrol ether, the residue was vacuum dried at 50-60° (2 mm), dissolved in dry ether (23 ml), and diluted with absolute alcohol (58 ml). The solution was left for 3 days at about −5°, and the crystals formed filtered off and washed with ether-alcohol (1:3). Yield 14.6 g (60%), mp 46.0-46.7°. The product was readily soluble in ether, petrol ether, benzene, and acetone, slightly soluble in alcohol. Recrystallization from dry ether-alcohol (1:2.5), using active carbon, gave colorless crystals of III, mp 47.6-48.0° Found: N 6.0, 6.0; Cl 14.7, 14.6%. Calculated for $C_{15}H_{14}NCl$: N 5.8; Cl 14.6%.

b) Heating a mixture of 9.0 g I in 50 ml $CHCl_3$ and 7.2 g $POCl_3$ for 3 hr at 80-90° gave 1.9 g III (yield 18%).

N-phenyl-3-hydroxy-1,2,3,4-tetrahydroquinoline acetate (IV).

a) 2.3 g (0.01 mole) I was dissolved in 12 ml pyridine, and 4.0 g (0.05 mole) acetyl chloride added with cooling, after which the whole was heated for 2 hr 30 min on a steam bath. After cooling the reaction products were diluted, with stirring, with 35 ml 25% sulfuric acid, followed by 100 ml water. The viscous oil which separated was extracted with ether (75 ml) and the extract dried over sodium sulfate. The ether was distilled off, and the crystalline residue transferred to a filter, and washed with 2 ml ether. Yield 1.5 g mp 64.1-64.7°; repeated recrystallization from absolute alcohol, using active carbon, gave colorless plates of IV, mp 65.1-65.5°. Found: N 5.4, 5.3%. Calculated for $C_{17}H_{17}O_2N$: N 5.2%.

b) 1.2 g III was dissolved in 45 ml alcohol, an aqueous solution of sodium acetate (3.5 g $CH_3COONa \cdot 3H_2O$ in 3 ml water) added, and the mixture heated on a steam bath for 2 hr. After cooling the products were diluted till the solution became turbid, left for a day, and the crystals formed were filtered off. Yield 1.0 g; recrystallization from absolute alcohol, using active carbon, gave colorless plates of IV mp 65.1-65.5°. Mixed mp with the product of acetylating I undepressed.

0.4 g IV, prepared from III, was dissolved in 10 ml alcohol, 10 ml 3% potassium hydroxide solution added, and the whole heated for 9 hr on a steam bath. The crystals formed on cooling to about −3° were filtered off; yield 0.3 g, mp 78.0-78.6°, recrystallized from alcohol, mp 78.6-79.0°. Mixed mp with I undepressed.

N-phenyl-3-hydroxy-1,2,3,4-tetrahydroquinoline benzoate (ester) (V). 2.3 g (0.01 mole) I was dissolved in 10 ml pyridine, and 4.2 g (0.03 mole) benzoyl chloride added with stirring. Then the reaction mixture was heated on a steam bath for 3 hr, the products cooled, and diluted with 50 ml 20% sulfuric acid, followed by 75 ml water. The supernatant aqueous layer was poured off, and the viscous product remaining dissolved in 30 ml methanol, then this solution was made alkaline with 10% sodium hydroxide solution, and diluted with 200 ml water. The supernatant aqueous layer was again decanted, and the viscous oil washed a few times with water, in its own container after which it was dissolved in 30 ml methanol. The crystals formed after standing for 3 days over calcium chloride were filtered off and washed with methanol (5 ml). Yield 2.1 g, mp 73.4-74.6°. Recrystallization from acetone, using activated carbon, gives colorless plates of V, mp 76.6-77.5°. Mixed mp with I 58.0-63.5°. Found: C 80.0, 80.1; H 6.0, 5.9%. Calculated for $C_{22}H_{19}O_2N$: C 80.2; H 5.8%.

REFERENCES

1. N. N. Vorozhtsov, Jr. and S. I. Kutkevichus, ZhOKh, 27, 2152, 1957.
2. German Patent 284291 (Fr., XII, 152).
3. W. Davies and W. Savige, J. Chem. Soc., 890, 1950.
4. N. N. Vorozhtsov, Jr. and S. I. Kutkevichus, Transactions of the Conference on the Chemistry, Technology, and Applications of Pyridine and Quinoline Derivatives [in Russian], Riga, October 1957.
5. N. N. Vorozhtsov, Jr. and S. I. Kutkevichus, ZhOKh, 28, 2682, 1958.
6. N. N. Vorozhtsov, Jr., G. G. Yakobson, and A. E. Ioffe, Author's Certificate No. 106585.
7. H. König and R. Huisgen, Berlin, 92, 429, 1959.
8. H. O. Jones and P. E. Evans, J. Chem. Soc., 99, 334, 1911; M. G. Edwards, R. E. Garrod, and H. O. Jones, J. Am. Chem. Soc., 101, 1376, 1912.

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