PREPARATION AND PROPERTIES OF 14-CYANO-Δ^{10}-DODECAHYDROACRIDINE

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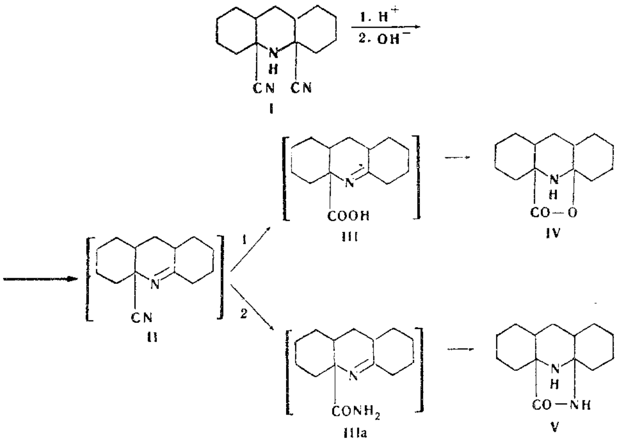
14-Cyano-Δ^{10}-dodecahydroacridine, the product of the partial dehydrocyanation of 11,14-dicyanoperhydroacridine, has been obtained. The behavior of this substance to acids and alkalies and also its hydrocyanation, autooxidation, disproportionation, and hydrogenation reactions have been studied. On the basis of IR spectral data, the hypothesis has been put forward that this substance exhibits imine-enamine tautomerism.

We have already reported that the hydrolysis of 11,14-dicyanoperhydroacridine (I) with strong solutions of acids at elevated temperatures gives the 5-oxazolidone derivative IV; hydrolysis of the dicyanide I with alcoholic alkali gives the 5-imidazolidone derivative V. In both cases, 14-cyano-Δ^{10}-dodecahydroacridine (II) was regarded as an intermediate [1].

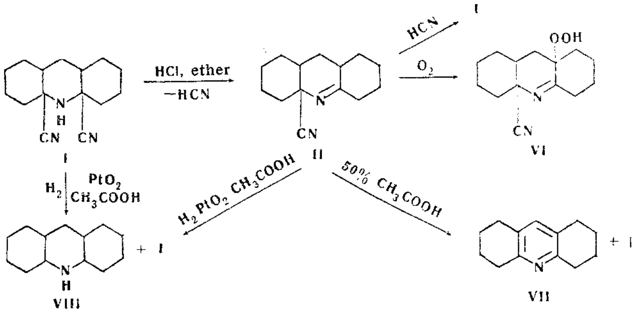


We have now found that if the dicyanide I is treated with a mixture of concentrated HCl and ether at 50–55° C, the process stops at the formation of the cyanomide II.

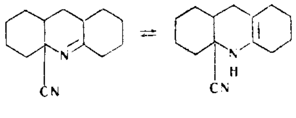
The structure of the compound obtained is confirmed by its reactions. Under the action of acetone cyanohydrin, it readily adds one molecule of hydrogen cyanide and is converted into the initial dicyanide I. On being boiled with 67% sulfuric acid, it is converted into the oxazolidone IV. Under the action of a 4% aqueous ethanolic solution of potassium hydroxide and, particularly, under the action of concentrated H_2SO_4, it gives the imidazolidone V. Even on standing in the air, solutions of compound II readily undergo autooxidation with the formation of 12-hydroperoxy-14-cyano-Δ^{10}-dodecahydroacridine (VI), behavior characteristic for a number of derivatives of Δ^1-tetrahydropyridine [2, 3].

When a solution of the cyanomide II in 50% acetic acid is allowed to stand, the dicyanide I gradually separates out. From the residue after the elimination of I we have isolated sym-octahydroacridine VII. This result can be explained only by the occurrence of a peculiar form of disproportionation, the intramolecular redistribution of hydrocyanic acid. The same transformation takes place when compound II is melted and when an attempt is made to recrystallize it from aqueous ethanol in an atmosphere of CO_2.

When substance II was hydrogenated over PtO_2 in ethanol or dioxane, hardly any hydrogen was absorbed. Hydrogenation took place in acetic acid, the hydrogenation product being the known β-perhydroacridine (VIII) [4]. In addition, the dicyanide I was isolated from the mixture after hydrogenation. It is obvious that this result is the consequence of the disproportionation of the cyanoimide II, which precedes hydrogenation. The dicyanide I itself slowly hydrogenates under the same conditions with the formation of the same compound VIII. Thus, the ratio of compounds VIII and I depends on the time of hydrogenation of the cyanoimide II.



The IR spectrum of compound II, taken in CCl_4, contains a medium-intensity band at 1650 cm^{-1}, a fairly weak band at 1690 cm^{-1}, and a very weak band at 3400 cm^{-1}. In the spectrum taken in KBr, the bands at 1690 and 3400 cm^{-1} appear far more clearly. The IR spectrum of the hydrochloride of II is the typical spectrum of an imine salt and contains a band at 1665 cm^{-1} ($C{=}\overset{+}{N}$). This permits the band at 1650 cm^{-1} in the spectrum of compound II itself to be assigned to the vibrations of the C=N bond, since it is known that on salt formation the vibrations of this bond are shifted to higher frequencies [5]. The appearance in the spectrum of compound II of bands at 1690 and 3400 cm^{-1} can be explained, in our opinion, by the existence of the tautomeric enamine form of the cyanoimide II; they correspond, respectively, to the absorption of C=C and N—H.



In favor of this hypothesis is, in particular, the fact that when a solution of the hydrochloride of compound II is made alkaline, a base is liberated whose IR spectrum is practically identical with that of the initial substance. Although the absorption of the C=C bond of the majority of enamines is found at about 1650 cm^{-1} [6], higher frequencies up to 1690 cm^{-1} [7] have been observed for some simple enamines. Furthermore, for the tautomeric enamine form of the cyclohexylimine derivative of acetophenone, a band at 1693 cm^{-1} is assigned to the vibrations of the C=C bond [8]. In the 1,4-dihydropyridine recently synthesized, a band is found at 1680 cm^{-1} [9].

EXPERIMENTAL

14-Cyano-Δ^{10}-dodecahydroacridine (II). A mixture of 20 g of I, 200 ml of ether, and 400 ml of concentrated HCl was heated in the water bath at 50–55° C for 10 hr. Then 300 ml of water was added and the mixture was neutralized with solid $(NH_4)_2CO_3$ to pH 5–6. The solution was filtered and a saturated solution of $(NH_4)_2CO_3$ was added to the clear filtrate until the reaction was alkaline. After several hours, a crystalline precipitate formed. Yield 13 g (73%). Mp 84–89° C. For purification from contamination with the initial dicyanide I, the product was treated with 10% H_2SO_4 solution, the insoluble I was filtered off, and the filtrate was neutralized with $(NH_4)_2CO_3$. (The presence or absence of contamination with the dicyanide I was checked by chromatography on a thin layer of Al_2O_3). Further purification was carried out by freezing a saturated solution of the substance in acetone with dry ice. In this way it was possible to exclude both the oxidation and the disproportionation of the product. After two such recrystallizations, we obtained a sample with mp 95–100° C. Melting was accompanied by a change in the substance: a chromatogram of the melt in a thin layer of Al_2O_3 showed spots corresponding to the dicyanide I and to octahydroacridine (VII). The chromatogram of a sample before melting did not show these spots. The substance was soluble in benzene, carbon tetrachloride, chloroform, acetone, acetic acid, and dioxane, less readily in ethanol and ether, sparingly in heptane, and insoluble in water. Found, %: C 77.57, 77.87; H 9.45, 9.45; N 13.27, 13.17%; Mol. Wt. 226–235 (in benzene). Calculated for $C_{14}H_{20}N_2$, %: C 77.78; H 9.26; N 12.96; Mol. Wt. 216. IR spectrum (in CCl_4), cm^{-1}: 1650 (C=N), 1690 (C=C), 2250 (C≡N), 3400 (N–H).

Hydrochloride. The base II was dissolved in benzene saturated with gaseous hydrochloric acid; when the solution was diluted with heptane the hydrochloride precipitated. Mp 150–152° C. Found, %: Cl 14.4. Calculated for $C_{14}H_{20}N_2 \cdot HCl$, %: Cl 14.1. IR spectrum (in KBr), cm^{-1}: 2700–2300, 1900–2000, 1665 ($C{=}\overset{+}{N}$).

Hydrogenation of the cyanoimide II. A mixture of 0.49 g of II, 1 g of acetone cyanohydrin, and 3 ml of a saturated solution of K_2CO_3 in methanol was kept at room temperature for 48 hr. Then it was diluted with water and the precipitate that deposited was separated off. Yield 0.47 g (86%). Mp 168–170° C (from ethanol). The product was shown to be identical with the dicyanide I by a mixed melting point with a reference sample.

Action of 67% sulfuric acid on the cyanoimide (II). 0.5 g of II was boiled for 20 min with a mixture of 2.5 ml of concentrated H_2SO_4 and 2.5 ml of water. The cooled mixture was carefully neutralized with concentrated NH_3 to pH 9 and the reaction product that had separated was extracted with chloroform; after the elimination of the solvent from the extract, 0.4 g (74%) of reaction product was obtained. Mp 127–128° C (from heptane). The product was shown to be identical with the oxazolidone IV by a mixed melting point with a reference sample.

Action of aqueous alcoholic alkali on the cyanoimide II. 0.5 g of II was boiled with a mixture of 7 ml of ethanol, 0.8 ml of water, and 0.25 g of KOH for 6 hr. Then the mixture was diluted with 5 volumes of water and extracted with chloroform, the extract was evaporated, and the residue treated with heptane. The part insoluble in heptane, 0.21 g (39%), formed a substance with mp 208–209° C [from chloroform-heptane (1:2)]. A mixture with a reference sample of the imidazolidone V gave no depression of the melting point.

Action of concentrated sulfuric acid on the cyanoimide II. 0.5 g of II was dissolved in 4 ml of concentrated H_2SO_4 at 0° C. After 18 hours' standing at room temperature, the mixture was heated at 50–60° C for 1 hr. The cooled mixture was poured onto ice and neutralized with sodium carbonate to give 0.43 g (83%) of substance V (identification as described above).

Disproportionation of the cyanoimide II. 1.06 g of II was dissolved in 4 ml of glacial acetic acid, 4 ml of water was added, and the mixture was left at room temperature for four days. After this time, the crystals that had deposited were separated off. Yield 0.55 g (92%). The product was shown to be identical with the dicyanide I by a mixed melting point with a reference sample. The filtrate after the removal of the I was acidified with NaOH and extracted with heptane; after evaporation of the extract, 0.33 g (70.6%) of an incompletely crystallizing mass was obtained. This gave a picrate with mp 199–200° C. A mixture with the picrate of sym-octahydroacridine gave no depression of the melting point. By treatment with NaOH solution, the picrate yielded the base, mp 69° C, shown to be identical with sym-octahydroacridine by a mixed melting point with a reference sample.

Hydrogenation of the cyanoimide II. 0.8 g of II was hydrogenated over 0.065 g of PtO_2 in 12 ml of dioxane. 8 ml of hydrogen was absorbed, after which its absorption ceased. After the addition of 12 ml of acetic acid, the absorption of hydrogen began again at the rate of 4–5 ml/min and then more slowly, about 0.5 ml/min. After 3 hr, 125 ml of hydrogen had been absorbed. The catalyst was filtered off, the solution was neutralized with sodium carbonate, and the precipitate formed was separated off. Yield 0.34 g. The product was shown to be identical with the dicyanide I by a mixed melting point. The filtrate after the separation of the I was made strongly alkaline with KOH solution and the crystals that deposited were separated off; in this way 0.35 g of a product with mp 46–48° C was obtained. For purification, the substance was converted into the hydrochloride and the latter was recrystallized from dioxane–ethanol (3:1) and the base was freed. After purification, mp 50–51° C. A mixture with a reference sample of β-perhydroacridine gave no depression of the melting point. The picrate of the hydrogenation product had mp 149–151° C and was identical with the picrate of β-perhydroacridine according to a mixed melting point test with a reference sample.

Hydrogenation of the dicyanide I. 0.95 g of I was hydrogenated over 0.1 g of PtO_2 in a mixture of 15 ml of acetic acid and 15 ml of dioxane. At room temperature, hydrogen was absorbed at the rate of 0.3 ml/min. At 45° C, the rate of absorption was 1–1.2 ml/min. After 8 hr, 300 ml of hydrogen had been absorbed. In the same way as described above, 0.55 g of the initial dicyanide I and 0.32 g of VIII were isolated.

12-Hydroperoxy-14-cyano-Δ^{10}-dodecahydroacridine (VI). a) A solution of 0.49 g of the cyanoimide II in 4.5 ml of benzene was treated with 4.5 ml of heptane. After standing at room temperature 48 hours, 0.43 g (76%) of the hydroperoxide VI separated.

b) A solution of 1.66 g of the cyanoimide II in 20 ml of CCl_4 was stirred at 46° C in a flask connected with a burette filled with oxygen. In the first 3 min, 90 ml of O_2 was absorbed, and then the rate gradually fell and the oxidation was complete in 20 min. The amount of oxidation was complete in 20 min. The amount of oxygen absorbed was 140 ml (81.5%). This gave 1.46 g (77%) of the hydroperoxide VI, which crystallized in the form of white rods; soluble in ethanol, chloroform, and acetone, less readily in dioxane, sparingly in benzene, very sparingly in heptane and carbon tetrachloride, insoluble in water. Mp 119° C (decomp, from benzene). Found, %: C 68.05, 67.81; H 8.29, 8.08; N 11.31, 11.29; O_{act} 6.11. Calculated for $C_{14}H_{20}N_2O_2$, %: C 67.75; H 8.06; N 11.29; O_{act} 6.45. IR spectrum (in KBr), cm^{-1}: 1670 (C=N), 2240 (C≡N), 3180 (OH, hydrogen bond).

REFERENCES

1. E. A. Kaminskii and M. N. Tilichenko, KhGS [Chemistry of Heterocyclic Compounds], 712, 1967.
2. L. Cohen and B. Witkop, J. Am. Chem. Soc., 77, 6595, 1955.
3. R. F. Parcell and F. R. Hauck, J. Am. Chem. Soc., 85, 346, 1963.

4. T. Masamune and S. Wakamatsu, C. A., 11850d, 1958.

5. K. Nakanishi, Absorption Spectroscopy. Practical [Russian translation], Mir, Moscow, p. 47, 1965.

6. J. A. West, J. Chem. Educ., 40, 194, 1963.

7. R. Dulou, E. Elkik, and A. Neillard, Bull. Soc. Chim., 967, 1960.

8. E. D. Bergmann, E. Zimkin, and S. Pinchas, Rec. trav. Chim., 71, 186, 1952.

9. N. C. Cook and J. E. Lyons, J. Am. Chem. Soc., 87, 3283, 1965.

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