HYDROACRIDINES AND RELATED COMPOUNDS

XII.* SYNTHESIS OF HYDROGENATED DERIVATIVES OF ACRINDOLINE AND DIBENZO[b,j][1,10]PHENANTHROLINE FROM 4-HYDROACRIDINONES

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5,6,8,9,10,11-Hexahydroacrindoline and 6,7-dihydro- and 1,2,3,4,6,7-hexahydrodibenzo-[b,j][1,10]phenanthroline-8-carboxylic acids were synthesized. Decarboxylation of the acids gives the corresponding bases.

Dibenzo[b,j][1,10]phenanthroline derivatives are good complexing agents and can be used for the detection and quantitative determination of some metal cations [1, 2]. Compounds of this type are obtained by condensation of 1,2-cycloalkanols with o-aminoacetophenone [3].

It has been found that partially hydrogenated dibenzophenanthroline-8-carboxylic acids (III and IV), which are difficult-to-dissolve high-melting substances, are formed in good yield on refluxing equimolecular amounts of sym-octahydro-4-acridinone (I), 1,2,3,4-tetrahydro-4-acridinone (II), and isatin in aqueous alcoholic alkali. When III and IV are subjected to prolonged heating at their melting points, they readily undergo decarboxylation to give the corresponding five-ring bases (V and VI). Compounds V and VI form intensely colored alcohol-soluble complexes with beryllium, iron, and copper cations (yellow, brown, and crimson, respectively). The color does not vanish when the solutions are refluxed or when concentrated alkali is added.

Ketone II was obtained by oxidation of 1,2,3,4-tetrahydro-4-acridinol with active manganese dioxide. The IR spectrum of the synthesized ketone contains an absorption band at 1700 cm^{-1}, which is due to the stretching vibrations of the conjugated carbonyl group. It should be noted that the chief process in the direct oxidation of the active methylene group in 1,2,3,4-tetrahydroacridine to a carbonyl group by means of selenium dioxide is dehydrogenation to give acridine [4].

In order to obtain the little-studied acrindoline system, we carried out the Fischer reaction with the phenylhydrazone of ketone I. We used various reagents – formic acid, a mixture of concentrated acetic and sulfuric acids, and hydrogen chloride – for the cyclization. The optimum variant is refluxing of an alcohol solution of the phenylhydrazone saturated with dry hydrogen chloride. The reaction gives hexahydroacrindoline VII, the skeleton of which is isosteric with alkaloids of the yohimbane series. A similar compound was previously synthesized from 1,2,3,4-tetrahydro-4-acridinone phenylhydrazone [5].

The IR spectrum of synthesized VII contains an absorption band at 3200 cm^{-1}, which is characteristic for the imino group. An intense green fluorescence, which vanishes on alkalization, is characteristic for this base in acid media.

EXPERIMENTAL

The IR spectra of KBr pellets and of a mineral oil suspension (II) were recorded with a UR-20 spectrophotometer. Activity-II aluminum oxide was used for the chromatography.

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*See [8] for communication XI.

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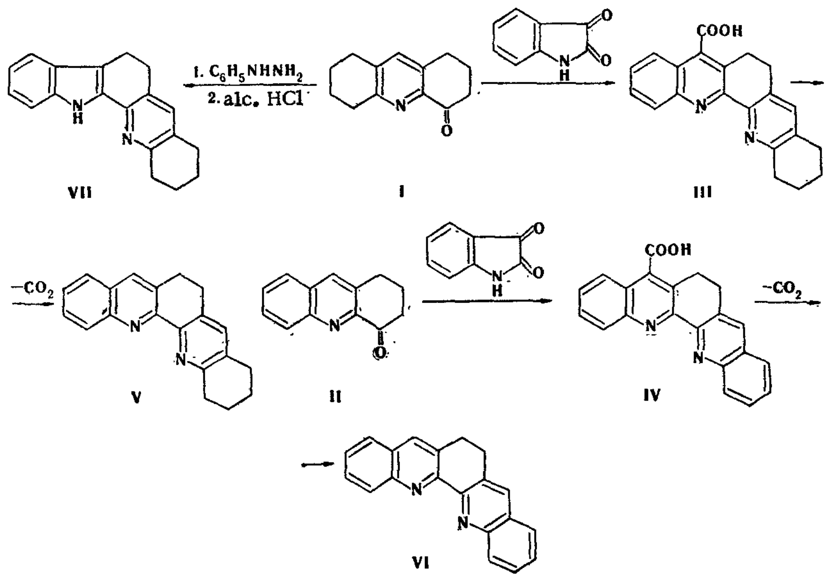

Phenylhydrazone of Ketone I. This compound was obtained by mixing alcohol solutions of I and phenylhydrazine to give pale-yellow rods with mp 175-176° [from chloroform–alcohol (1 : 3)] and R_f 0.59 (in chloroform). Found: C 78.3; H 7.2%. $C_{19}H_{21}N_3$. Calculated: C 78.3; H 7.3%.

1,2,3,4-Tetrahydro-4-acridinone (II). A mixture of 5.5 g (0.026 mole) of 1,2,3,4-tetrahydro-4-acridinol [7], 10 g (0.115 mole) of active manganese dioxide [6], and 280 ml of a mixture of petroleum ether with chloroform (6 : 1) was stirred at room temperature for 6 h and refluxed for 1 h, after which the solid was removed by filtration and washed with 90 ml of hot chloroform. The solvent was removed by distillation, and the residue was treated with 20 ml of petroleum ether to give 2.9 g (52%) of crystalline ketone II as long colorless needles with mp 140-142° (from petroleum ether) and R_f 0.12 [ethyl acetate–petroleum ether (2 : 3)]. Found: C 79.1; H 5.8%. $C_{13}H_{11}NO$. Calculated· C 79.2; H 5.7%. The phenylhydrazone was obtained as yellow prisms with mp 109.5° (from alcohol) (mp 110° [5]).

1,2,3,4,6,7-Hexahydrodibenzo[b,j][1,10]phenanthroline-8-carboxylic Acid (III). A mixture of 2.4 g (0.01 mole) of ketone I, 1.5 g (0.01 mole) of isatin, 7 ml of 30% potassium hydroxide solution, and 20 ml of alcohol was refluxed for 8 h, after which the alcohol was removed by distillation, and the residue was diluted with 20 ml of water and filtered. The filtrate was acidified to pH 5 with 10 ml of 50% acetic acid, and the precipitate was removed by filtration to give 2.7 g (78%) of the monohydrate of acid III as yellowish needles with mp 218-220° (dec., from n-propanol); the product was only slightly soluble in the usual organic solvents. Found: C 72.5; H 6.1; N 8.1%. $C_{21}H_{18}N_2O_2 \cdot H_2O$. Calculated: C 72.4; H 5.8; N 8.0%. A weighed sample (0.3783 g) of the acid lost 0.0227 g of water (calculated: 0.0205 g of H_2O) on heating in vacuo. The anhydrous acid had mp 225-226° (dec.). Equivalent wt. $_{\text{found}}$ 334. $C_{21}H_{18}N_2O$. Equiv. wt. $_{\text{calc}}$ 330.

6,7-Dihydrodibenzo[b,j][1,10]phenanthroline-8-carboxylic Acid (IV). This compound was similarly obtained from ketone II in 78% yield as yellowish needles with mp 289-289.5° (dec., from 50% acetic acid); the product was only slightly soluble in the usual organic solvents. Found: C 77.0; H 5.5%; Equiv. wt. 323. $C_{21}H_{14}N_2$. Calculated: C 77.3; H 5.3%; Equiv. wt. 326.

1,2,3,4,6,7-Hexahydrodibenzo[b,j][1,10]phenanthroline (V). A 1.2-g (3.45 mmole) sample of acid III was heated to the melting point and held at this temperature for 15 min. The solid was dissolved in chloroform and passed through a column filled with aluminum oxide. Base V was eluted with ether to give a quantitative yield of yellowish needles with mp 185-185.5° (from nonane). Found: C 84.0; H 6.6%. $C_{20}H_{18}N_2$. Calculated: C 83.9; H 6.4%. The picrate was obtained as dark-yellow needles with mp 220-221° [from alcohol–chloroform (1 : 2), dec.]. Found: N 13.8%. $C_{20}H_{18}N_2 \cdot C_6H_3N_3O_7$. Calculated N 13.6%.

6,7-Dihydrodibenzo[b,j][1,10]phenanthroline (VI). This compound was similarly obtained from acid IV in 95% yield as colorless rods with mp 181-181.5° (from heptane). Found: C 84.9; H 5.2%. $C_{10}H_{14}N_2$. Calculated: C 85.1; H 5.0%. IR spectrum: 2930 and 2840 cm^{-1} (methylene groups). The picrate was obtained as yellow rods with mp 277-280° [dec., from alcohol–chloroform (10 : 1)]. Found: N 14.1%. $C_{20}H_{24}N_2 \cdot C_6H_3N_3O_7$. Calculated: N 13.7%.

5,6,8,9,10,11-Hexahydroacrindoline (VII). Dry hydrogen chloride was passed through a refluxing alcohol solution of 0.293 g (1 mmole) of the phenylhydrazone of ketone I for 4 h, after which the mixture was refluxed for another 7 h and allowed to stand overnight. The precipitated hydrochloride of base VII was removed by filtration, washed with alcohol, and dried to give 0.2 g (63%) of yellow needles that were almost insoluble in water and had mp 289-290° (from methanol). Found: Cl 11.3%. $C_{19}H_{18}N_2 \cdot HCl$. Calculated: Cl 11.4%. Free base VII was isolated by shaking a chloroform solution of the salt with aqueous alkali until the intense green fluorescence vanished. Evaporation of the solvent gave base VII as acicular mustard-colored plates with mp 184.5-185° [from chloroform–methanol (1 : 3)] and R_f 0.64 (in chloroform). Found: C 83.5; H 7.0%. $C_{19}H_{18}N_2$. Calculated: C 83.2; H 6.6%.

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