(1,2,5-TRIMETHYL-4-PIPERIDYLIDENE)-α-NAPHTHYLAMINES IN THE SYNTHESIS OF 9-METHYLNAPHTHO[1,2-b][1,6]NAPHTHYRIDINE AND 2,3-DIMETHYL-4-AZAPHENANTHRENE

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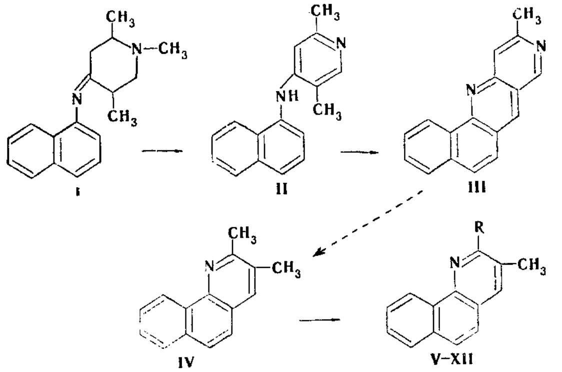
9-Methylnaphtho[1,2-b][1,6]naphthyridine and 2,3-dimethyl-4-azaphenanthrene were obtained by the catalytic dehydrocyclization of (1,2,5-trimethyl-4-piperidylidene)-α-naphthylamine.

Compounds of the naphthyridine series have received little chemical and pharmacological study. Of the six isomeric (with respect to the position of the nitrogen atoms) naphthyridines, the most accessible ones are 1,8- and 1,5-naphthyridines, the methods for the synthesis of which are based chiefly on the use of α- and β-aminopyridines [1, 2]. Data on methods for the preparation of the remaining four isomeric naphthyridines are extremely limited.

In our laboratory, we have established that (2,5-dimethyl-4-pyridyl)aniline and a very small amount of 8-methylbenzo[1,2-b][1,6]naphthyridine [3, 4] are formed during the catalytic transformations of (1,2,5-trimethyl-4-piperidylidene)aniline. This demonstrated that Schiff bases can be used for the synthesis of the as yet difficult-to-obtain naphthyridine systems. Considering this, we turned to a study of substances that are formed during the transformations of (1,2,5-trimethyl-4-piperidylidene)-α-naphthylamine (I) [5] on a K-16 dehydrogenating catalyst at 410-420°C.

N-(2,5-Dimethyl-4-pyridyl)-α-naphthylamine (II), 9-methylnaphtho[1,2-b][1,6]naphthyridine (III), and 2,3-dimethyl-4-azaphenanthrene (IV), which were characterized analytically and by means of their derivatives, several transformations, and spectroscopy, were isolated from the reaction products by means of column chromatography.



V $R=CH=CHC_6H_5$; VI $R=CHBrCHBrC_6H_5$; VII $R=C\equiv CC_6H_5$; VIII $R=COOH$; IX $R=COOC_2H_5$; X $R=CONHNH_2$; XI $R=CONHN=CHC_6H_5$; XII $R=H$

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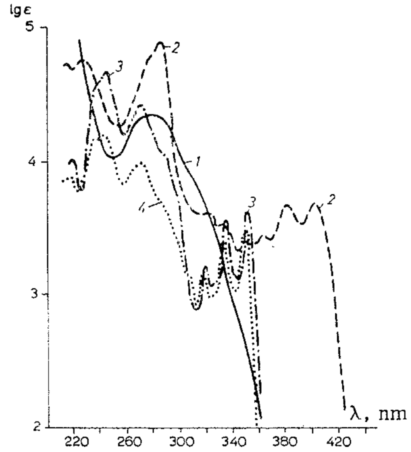

Fig. 1. UV spectrum (in ethanol): 1) N-(2,5-dimethyl-4-pyridyl)-α-naphthylamine (II); 2) 9-methylnaphtho[1,2-b][1,6]naphthyridine (III); 3) 2,3-dimethyl-4-azaphenanthrene (IV); 4) 2-methyl-4-azaphenanthrene (XII).

The IR spectrum of a CCl_4 solution of II contains a band of low intensity at 3400 cm^{-1}, which corresponds to an amino group of the ArNHAr type [3, 4, 6]; the IR spectrum of a KBr pellet contains bands at 3100-3250 cm^{-1}, which correspond to amino groups tied up in intermolecular hydrogen bonds. The UV spectrum of II [λ_{max} 280 nm (log ε 4.27)] attests to the absence of conjugation between the naphthalene and benzene rings (Fig. 1, curve 1).

The IR spectrum of III contains an intense band at 754 cm^{-1}, which corresponds to the out-of-plane deformation vibrations of four adjacent aromatic C–H bonds. The band of medium intensity at 836 cm^{-1} corresponds to solitary C–H bonds [7]. The intense band in the UV spectrum of III (Fig. 1, curve 2) at 225 nm (log ε 4.76) and 284 nm (log ε 4.92) as well as the group of bands centered at ~350 nm (log ε 3.4) are characteristic for a condensed aromatic system [4, 8, 9]. The singlet at 2.79 ppm in the PMR spectrum of III indicates the presence of one methyl group.

The IR spectra of IV and XII contain intense bands at 725-765 cm^{-1}, which are related to the out-of-plane deformation vibrations of four adjacent aromatic C–H bonds. The bands at 806-807 cm^{-1} attest to the presence of a tetrasubstituted ring, while the bands at 824-828 cm^{-1} correspond to isolated C–H bonds of the pyridine ring. The bands of medium intensity at 1450 cm^{-1} characterize the asymmetrical deformation vibrations of methyl groups. The signals at 2.60 and 2.27 ppm in the PMR spectrum of IV are affiliated with the methyl groups in the 3 and 2 positions, respectively.

From a comparison of the UV spectra of azaphenanthrene IV [λ_{max}, nm (log ε): 243 (4.66), 269 (4.44), 318 (3.21), 333 (3.52), and 349 (3.62)] and XII obtained from it [λ_{max}, nm (log ε): 236 (4.20), 242 (4.22), 269 (4.02), 318 (3.16), 333 (3.22), and 349 (3.52)] (Fig. 1, curves 3 and 4) with the absorption spectra of anthracene and phenanthrene [9], it follows that azaphenanthrenes IV and XII have angular condensed structures.

Azaphenanthrene IV is apparently formed from naphthyridine III. The methyl-substituted pyridine ring is hydrogenated initially, followed by thermal decomposition to give IV and ethylamine. Since N-dealkylation (for example, conversion of I to II) occurs readily on a K-16 catalyst, ammonia is formed from the latter, and its presence in the gaseous reaction products was established experimentally. Attention should be drawn to the fact that the yield of azaphenanthrene IV is considerably higher than the yield of amine II and naphthyridine III. In [10] it was demonstrated that when condensed hydrocarbons – phenanthrene, anthracene, chrysene, etc. – undergo destructive hydrogenation, they decompose in steps to form less condensed dialkyl-substituted hydrocarbons. The destructive transformation of acridine during its hydrogenation on a nickel catalyst to 2,3-dimethylquinoline has also been described [11].

Naphthyridine III was subjected to hydrogenation in the presence of rhenium heptasulfide. It was established (by chromatography) that azaphenanthrene IV is present in the reaction product.*

The syntheses that were accomplished on the basis of IV provide additional data regarding its structure. The condensation of IV with benzaldehyde gives 2-methyl-3-styryl-4-azaphenanthrene (V). The signal at 2.77 ppm in the PMR spectrum of V corresponds to a methyl group in the β position relative to the nitrogen atom. Conversion to 2-methyl-3-phenylethynyl-4-azaphenanthrene (VII) is accomplished from V through 2-methyl-3-(1,2-dibromo-2-phenylethyl)-4-azaphenanthrene (VI). The oxidation of V gave 2-methyl-4-azaphenanthrene-3-carboxylic acid (VIII), which was characterized by ethyl ester IX, hydrazide X, and benzylidenehydrazide XI.

2-Methyl-4-azaphenanthrene (XII) was isolated from the decarboxylation of acid VIII. The singlet at 2.44 ppm in the PMR spectrum of XII indicates the presence of only one methyl group.

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*This work was accomplished in collaboration with M. A. Ryashentseva; the results will be published in the future.

EXPERIMENTAL

The thin-layer chromatography in all of the experiments was carried out on activity II Al_2O_3. The gases were analyzed with a KhL-6 device. The IR spectra were recorded with a UR-20 spectrophotometer. The electronic spectra of alcohol solutions were measured with SF-4A and Hitachi spectrometers. The PMR spectra were measured with a Varian HA-100D spectrometer at 100 MHz. The positions of the signals in the PMR spectra for III, V, VI, VIII, and IX are indicated relative to tetramethylsilane, while those for IV are indicated relative to hexamethyldisiloxane. The solvent for samples of V was CCl_4-CF_3OOH, while the solvent for VIII was $CCl_4+CHCl_3+CF_3COOH$. The solvent for all of the remaining compounds was CCl_4. The molecular weights were measured with an MKh-1303 mass spectrometer.

(1,2,5-Trimethyl-4-piperidylidene)-α-naphthylamine (I). This compound was obtained in 92% yield by the method in [5] and had bp 177-179° (1 mm) and R_f 0.28 (benzene). IR spectrum, cm^{-1}: 2782 s ($N-CH_3$) and 1670 s (C=N). UV spectrum: λ_{max} 298 nm (log ε 3.94). Found: N 10.7%. $C_{18}H_{22}N_2$. Calculated: N 10.5%. The picrate had mp 154° (from alcohol). Found: N 14.2%. $C_{18}H_{22}N_2 \cdot C_6H_3N_3O_7$. Calculated: N 14.1%.

N-(2,5-Dimethyl-4-pyridyl)-α-naphthylamine (II), 9-Methylnaphtho[1,2-b][1,6]naphthyridine (III), and 2,3-Dimethyl-4-azapenanthrene (IV). A solution of 53.2 g (0.2 mole) of I in 170 ml of benzene was passed at a constant flow rate for 7 h through a contact tube (100 ml of K-16 catalyst) at 410-420°. A total of 12 liters of gas was collected (at 20° and 757 mm; 3.4% CH_4, 96.6% H_2). Removal of the benzene by distillation gave 40 g of catalyzate. A total of 79.5 g of catalyzate was collected from two similar experiments and distilled: the first fraction (1.43 g) had bp 53-120° (1 mm), the second fraction (7.3 g) had bp 120-135° (1 mm), the third fraction (60.4 g) had bp 135-181° (1 mm), and the fourth fraction (6.5 g) had bp 181-212° (1 mm). The first fraction [R_f 0.1 and 0.35 (benzene)] was primarily α-naphthylamine [R_f 0.34 (benzene)]. Chromatography of the third fraction [R_f 0.13 w and 0.82 s (benzene)] on a column (25-cm high with a diameter of 3.2 cm, 116 g of Al_2O_3), initially with benzene and then with ether, gave (from the ether eluate) 0.6 g of II with mp 156-156.5° (from benzene) and R_f 0.04 (benzene). Found: C 82.3; H 6.2; N 11.5%. $C_{17}H_{16}N_2$. Calculated: C 82.3; H 6.4; N 11.3%.

Repeated crystallization of the benzene eluate (57.8 g) gave 21.3 g of IV with mp 86-87° (from ether) and R_f 0.82 (benzene). Found: C 86.7; H 6.0; N 6.8%; M 207 (from the mass spectrum). $C_{15}H_{13}N$. Calculated: C 87.0; H 6.3; N 6.7%; M 207. The picrate had mp 223-224° (from alcohol). Found: N 12.9%. $C_{15}H_{13}N \cdot C_6H_3N_3O_7$. Calculated: N 12.8%. The perchlorate had mp 267-268° (from alcohol). Found: N 4.9%. $C_{15}H_{13}N \cdot HClO_4$. Calculated: N 4.6%. The hydrochloride had mp 240-241° (from acetone). Found: N 5.6%. $C_{15}H_{13}N \cdot HCl$. Calculated: N 5.7%. UV spectrum of the hydrochloride, λ_{max}, nm (log ε): 216 (3.86), 242 (4.66), 269 (4.44), 319 (3.21), 333 (3.50), 349 (3.58).

The fourth fraction partially crystallized in ether to give 3 g of III as yellow needles with mp 172-173.5° (from ether) and R_f 0.14 (benzene). Found: C 83.6; H 5.2; N 11.1%; M 244 (from the mass spectrum). $C_{17}H_{12}N$. Calculated: C 83.6; H 4.9; N 11.4%; M 244. The dipicrate had mp 272-273° (from alcohol). Found: N 15.6%. $C_{17}H_{12}N_2 \cdot 2C_6H_3N_3O_7$. Calculated: N 15.9%. The perchlorate had mp 230-232° (from alcohol). Found: N 8.0%. $C_{17}H_{12}N_2 \cdot HClO_4$. Calculated: N 8.1%. The ammonia contained in the reaction gases was isolated as ammonium chloride.

2-Methyl-3-styryl-4-azaphenanthrene (V). A mixture of 2.34 g (0.011 mole) of IV, 1.52 g (0.014 mole) of benzaldehyde, 0.78 g (0.013 mole) of glacial acetic acid, and 1.4 g (0.013 mole) of acetic anhydride was refluxed for 15 h. The acetic acid and anhydride were removed by vacuum distillation, and the residue was treated with 50 ml of hydrochloric acid (1 : 1). The neutral substances were extracted with two 100-ml portions of ether. The aqueous solution was treated with potassium hydroxide until it was alkaline. The organic bases were extracted with five 100-ml portions of ether, and the extracts were dried with sodium sulfate. Evaporation of the extract to a volume of 50 ml gave 1.86 g (56%) of yellow crystals of V with mp 150-151° and R_f 0.83 (benzene). IR spectrum, ν, cm^{-1}: 1638 w (C=C), 1600 m, 1500 m, 1455 m, 805 s, 767 vw, 694 s. UV spectrum, λ_{max}, nm (log ε): 243 (4.69), 264 (4.35) shoulder, 307 (4.39), 367 (4.28), 386 (4.27). Found: C 89.2; H 5.9; N 4.8%. $C_{22}H_{17}N$. Calculated: C 89.5; H 5.8; N 4.7%. The hydrochloride had mp 166-169° (from acetone). IR spectrum of the hydrochloride, ν, cm^{-1}: 1637 s (C=C), 1565 w, 1456 m, 767 s, 697 m. UV spectrum, λ_{max}, nm (log ε): 245 (4.97), 265 (4.63), 306 (4.62), 369 (4.52), 386 (4.51). Found: N 4.2%. $C_{22}H_{17}N \cdot HCl$. Calculated: N 4.2%. The picrate had mp 201-202° (from alcohol. Found: N 10.7%. $C_{22}H_{17}N \cdot C_6H_3N_3O_7$. Calculated N 10.7%.

2-Methyl-3-(1,2-dibromo-2-phenylethyl)-4-azaphenanthrene (VI). A solution of 0.8 ml of bromine in 30 ml of chloroform was added slowly to a solution of 1 g (3.4 mmole) of V in 40 ml of dry chloroform, and the mixture was heated at 100° for 1 h. The chloroform was removed by distillation to give 1.5 g (97%) of VI with mp 171-172° (from alcohol). IR spectrum, ν, cm^{-1}: 1604 w, 1500 w, 1461 m, 1448 m, 810 s, 765 s, 607 shoulder, 595 s. UV spectrum, λ_{max}, nm (log ε): 217 (4.47), 243 (4.72), 277 (4.35), 322 (3.66), 339 (3.74), and 356 (3.9). The PMR spectrum contains a signal of a methyl group at 2.68 ppm. Found: Br 35.2; N 3.0%. $C_{22}H_{17}Br_2N$. Calculated: Br 35.2; N 3.1%. The hydrochloride had mp 162-162.5° (from alcohol). Found: N 2.7%. $C_{22}H_{17}Br_2N \cdot HCl$. Calculated: N 2.8%.

2-Methyl-3-phenylethynyl-4-azaphenanthrene (VII). A solution of 2 g (0.035 mmole) of potassium hydroxide in 20 ml of alcohol was added to a solution of 1.5 g (3.3 mmole) of VI in 70 ml of anhydrous ethanol, and the mixture was refluxed for 2 h. The alcohol was removed by distillation, 50 ml of water was added to the residue, and the organic bases were extracted with ether to give 0.58 g (60%) of VII with mp 114-115.5° (from alcohol). IR spectrum, ν, cm^{-1}: 2211 w ($C \equiv C$), 1600 m, 1501 m, 1452, 805 m, 760 s, 694 m. UV spectrum, λ_{max}, nm (log ε): 244 (4.49), 302 (4.65), 351 (4.18), 368 (4.28), and388 (3.86) shoulder. Found: C 90.0; H 5.4; N 4.9%. $C_{22}H_{15}N$. Calculated: C 90.1; H 5.1; N 4.9%. The picrate had mp 191-192° (from alcohol). Found: N 10.8%. $C_{22}H_{15}N \cdot C_6H_3N_3O_7$. Calculated: N 10.8%.

2-Methyl-4-azaphenanthrene-3-carboxylic Acid (VIII). A total of 7.9 g (0.05 mole) of potassium permanganate was added in small portions with vigorous stirring in the course of 2 h at 0 to - 2° to a solution of 2.95 g (0.01 mole) of V in 200 ml of acetone. The mixture was stirred for 4 h at the same temperature. The manganese dioxide was removed by filtration and washed repeatedly with acetone and hot water (800 ml). The aqueous solution was evaporated to 100 ml and treated with 50% sulfuric acid until it was slightly acidic. The precipitate was removed by filtration and washed with 200 ml of warm water. The aqueous solution was evaporated to 50 ml to give 0.5 g of benzoic acid (mp 121°). The crystalline residue yielded 1.68 g (71%) of colorless crystals of VIII with mp 168-169° (from heptane). IR spectrum, ν, cm^{-1}: 1760 vs ($C=O$), 1600 vw, 1573 w, 1497 vw, 1446 s, 1390 s, 1364 vs, 828 m, 810 m, 764 w, 719 s, and 617 m. The band at 3200 cm^{-1} is due to an associated OH group. The PMR spectrum contained the signal of a CH_3 group at 2.92 ppm. UV spectrum, λ_{max}, nm (log ε): 243 (4.64), 271 (4.36), 319 (3.35), 335 (3.59), and 351 (3.66). Found: C 76.0; H 4.4; N 5.7%. $C_{15}H_{11}NO_2$. Calculated: C 76.0; H 4.6; N 5.9%.

The hydrochloride had mp 170.5-171° (from acetone). Found: Cl 13.0; N 5.0%. $C_{15}H_{11}NO_2 \cdot HCl$. Calculated: Cl 13.0; N 5.1%. IR spectrum, ν, cm^{-1}: 3200 w, 1760 s ($C=O$), 1705 m, 1448 s, 1230 s, 820, 761 s, 715 w, and 621 w.

Ethyl Ester IX. This compound was obtained in 76% yield from acid VIII as colorless needles with mp 108-109° (from heptane). IR spectrum, ν, cm^{-1}: 1725 vs ($C=O$), 1598 vw, 1508 w, 1398 m, 1307 vs, 1187 s, 807 m, and 762 s. UV spectrum, λ_{max}, nm (log ε): 237 (4.70), 266 (4.27) shoulder, 273 (4.31), 337 (3.54), 355 (3.49). Found: C 76.7; H 5.3; N 5.3%. $C_{17}H_{15}NO_2$. Calculated: C 77.0; H 5.5; N 5.3%.

Hydrazide X. This compound was obtained in 68% yield from ester IX as long, colorless needles with mp 187-189° (from alcohol). IR spectrum, ν, cm^{-1}: 3309 s, 1683 s ($C=O$), 1610 s, 1591 w, 1482 s, 1453 w, 950 s, 801 s, 750 s, and 696 s. Found: N 16.6%. $C_{15}H_{13}N_3O$. Calculated: 16.7%. The picrate had mp 201-202° (from alcohol). Found: N 17.4%. $C_{15}H_{13}N_3O \cdot C_6H_3N_3O_7$. Calculated: N 17.5%.

Benzylidenehydrazide XI. This compound was obtained in 74% yield from hydrazide X and had mp 219-220° (from alcohol). IR spectrum, ν, cm^{-1}: 3230 s (N−H), 1668 vs ($C=O$), 1607 w, 1542 s, 1491 s, 917 s, 757 s, and 698 s. Found: N 11.8%. $C_{22}H_{17}N_3O$. Calculated: N 12.4%.

2-Methyl-4-azaphenanthrene (XII). A mixture of 0.5 g (0.021 mole) of VIII and 30 ml of water was heated in an autoclave at 200° for 3 h. A total of 50 ml of 10% sodium carbonate solution was added, and the organic bases were extracted with ether to give 0.35 g (84%) of XII with mp 92-94° (from heptane). Found: C 87.1; H 5.6; N 7.3%. $C_{14}H_{11}N$. Calculated: C 87.1; H 5.7; N 7.3%. The picrate had mp 218-219° (from alcohol). Found: N 13.4%. $C_{14}H_{11}N \cdot C_6H_3N_3O_7$. Calculated: N 13.3%.

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