SYNTHESIS OF METHYL-SUBSTITUTED BENZOFURO-, BENZOTHIENO-, AND BENZOSELENOPHENO]2,3-b]PYRIDINES

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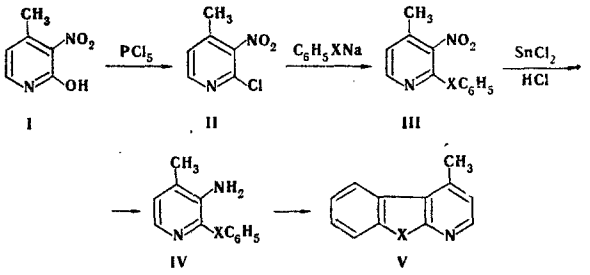
Three-ring benzo[b]furan, benzo[b]selenophene, and benzo[b]thiophene systems condensed with a pyridine ring and having a methyl group in the γ position of the pyridine ring were synthesized.

In the present communication we describe the synthesis of trinuclear heterocycles containing a pyridine ring starting from 2-hydroxy-3-nitro-4-methylpyridine (I) via the scheme:



III-V a X=O; b X=Se; c X=S

Bases Va-c form quaternary salts when they are heated with alkylating reagents. The IR spectra of V contain characteristic frequencies of the stretching vibrations of the pyridine ring, respectively, at 3000-3100 and 1555-1580 cm^{-1}.

EXPERIMENTAL

The UV spectra of 0.0001 M alcohol solutions were recorded with an SF-4 spectrophotometer. The IR spectra of mineral oil suspensions were obtained with a UR-10 spectrometer (NaCl prism).

2-Hydroxy-3-nitro-4-methylpyridine (I). A 2.6-g (0.017 mole) sample of 2-amino-3-nitro-4-methylpyridine [1] was dissolved in a mixture of 36 ml of water and 2.5 ml of concentrated sulfuric acid, after which 10 g of ice and a solution of 1.38 g (0.02 mole) of sodium nitrite in 4.72 ml of water were added while the mixture was cooled with ice. The mixture was stirred for 20 min, after which it was refluxed for 10 min and cooled. The resulting precipitate was removed by filtration and recrystallized from water to give 2.0 g (77%) of light-brown needles with mp 223-224°. UV spectrum: λ_{max} 308 nm, log ε 4.20. Found: N 18.0%. $C_6H_6N_2O_3$. Calculated: N 18.2%.

2-Chloro-3-nitro-4-methylpyridine (II). In analogy with [2], a mixture of 2.7 g (17.5 mmole) of I, 0.98 g (4.7 mmole) of phosphorus pentachloride, and 0.49 g (3.2 mmole) of phosphorus oxychloride was heated at 110-120° for 4 h, after which 0.46 g (2.2 mmole) of phosphorus pentachloride was added, and the mixture was heated for 2 h. The mixture was then cooled and washed with water, and the resinous product was steam distilled. The solid material was removed by filtration, washed with water, and dried to give 2.3 g (76.6%) of colorless needles (from petroleum ether) with mp 47.5-48°. Found: Cl 20.5%. $C_6H_5ClN_2O_2$. Calculated: Cl 20.6%.

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2-Phenoxy-3-nitro-4-methylpyridine (IIIa). A 2.3-g (0.1 g-atom) sample of sodium was dissolved in 40 ml of anhydrous ethanol, and 9.4 g (0.1 mole) of phenol and 17.2 g (0.1 mole) of II (in portions) were added successively with stirring under nitrogen. The mixture was refluxed for 10-12 h, after which it was evaporated in vacuo, and the residue was treated with water. The mixture was made alkaline with 5% sodium hydroxide solution and extracted with ether. The extract was washed successively with 5% sodium hydroxide solution and water and dried with magnesium sulfate. The ether was removed by distillation, and the residue was vacuum distilled to give 13.4 g (58%) of a fraction with bp 173-177° (7 mm). The colorless prism (from petroleum ether) had mp 56-57°. UV spectrum: λ_{max} 269 nm, log ε 4.15. Found: N 12.0%. $C_{12}H_{10}N_2O_3$. Calculated: N 12.1%.

2-Phenylseleno-3-nitro-4-methylpyridine (IIIb) [in 38% yield as a light-yellow oil, with mp 170-175° (5 mm), that began to crystallize on standing. Found: N 9.4%. $C_{12}H_{10}N_2O_2Se$. Calculated: N 9.6%] and 2-phenylthio-3-nitro-4-methylpyridine (IIIc) [in 46% yield as a light-yellow oil, with bp 178-181° (7 mm), that began to crystallize on standing. Found: N 11.1%. $C_{12}H_{10}N_2O_2S$. Calculated: N 11.3%] were similarly obtained.

2-Phenoxy-3-amino-4-methylpyridine (IVa). A 60-g sample of stannous chloride was added with vigorous stirring at 45-47° to a solution of 11.5 g (0.05 mole) of IIIa in 180 ml of concentrated hydrochloric acid, after which the mixture was stirred at 45-47° for 3 h. It was then cooled, made alkaline with sodium hydroxide solution while cooling with ice water, and extracted with chloroform. The extract was washed with 5% sodium hydroxide solution and water and dried with potassium carbonate. The chloroform was removed by distillation to give 9 g (90%) of colorless prisms (from petroleum ether) with mp 64-65°. UV spectrum: λ_{max} 244, 292 nm, log ε 4.27, 4.22. Found: C 71.8; H 5.9; N 13.8%. $C_{12}H_{12}N_2O$. Calculated: C 72.0; H 6.0; N 14.0%.

A similar procedure was used to obtain 2-phenylseleno-3-amino-4-methylpyridine (IVb) [in 86% yield as light-yellow needles with mp 47-48°. Found: C 54.7; H 4.4; N 10.5%. $C_{12}H_{12}N_2Se$. Calculated: C 54.9; H 4.6; N 10.7%] and 2-phenylthio-3-amino-4-methylpyridine (IVc) [in 88% yield as light-rose-colored needles with mp 61-62°. Found: C 66.4; H 4.3; N 12.7%. $C_{12}H_{12}N_2S$. Calculated: C 66.6; H 4.4; N 12.9%].

4-Methylbenzofuro[2,3-b]pyridine (Va). A solution of 4.6 g (0.066 mole) of sodium nitrite in 20 ml of water was added with stirring in the course of 10 min at 0-5° to a solution of 6.0 g (0.03 mole) of IVa in 120 ml of 25% sulfuric acid. The mixture was held at 0-5° for 1 h, after which it was filtered, and urea and 6 g of copper powder were added to the filtrate with stirring under nitrogen in the course of 3-5 min. The mixture was stirred at room temperature for 4 h, heated to the boiling point, cooled, and made slightly alkaline with dilute sodium hydroxide solution while cooling with ice water. The reaction product was extracted with ether, and the extract was washed with 5% sodium hydroxide solution and water. It was then dried with potassium carbonate, and the ether was removed by distillation. The residue was vacuum distilled to give 2.2 g (40%) of a product with bp 155-157° (12 mm). The colorless prisms (from petroleum ether) had mp 82-83°. UV spectrum: λ_{max} 281 nm, log ε 4.20. Found: C 78.5; H 4.8; N 7.4%. $C_{12}H_9NO$. Calculated: C 78.7; H 4.9; N 7.6%. The ethiodide was obtained as light-brown prisms (from anhydrous ethanol) with mp 208-209°. Found: I 37.3%. $C_{14}H_{14}INO$. Calculated: I 37.5%.

A similar procedure was used to obtain 4-methylbenzoselenopheno[2,3-b]pyridine (Vb) [in 22% yield as a light-yellow oil with bp 158-162° (4-5 mm). Found: C 58.3; H 3.5; N 5.5%. $C_{12}H_9NSe$. Calculated: C 58.5; H 3.6; N 5.7%] and 4-methylbenzothieno[2,3-b]pyridine (Vc) [in 31% yield as colorless plates with mp 101-102°. UV spectrum: λ_{max} 231, 294 nm, log ε 4.71, 4.47. Found: N 6.9%. $C_{12}H_9NS$. Calculated: N 7.0%]. The ethiodide was obtained as grayish prisms with mp 216-217° (from anhydrous ethanol, mp 216-217° [3]).

LITERATURE CITED

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