Fused s-Triazino Heterocycles. VI. 1,9,9b-Triazaphenalenes

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Derivatives of 1,9,9b-triazaphenalene have been prepared by reacting alkyl-*N*-cyanoimidates with 2,6-bis(cyanomethyl)pyridine.

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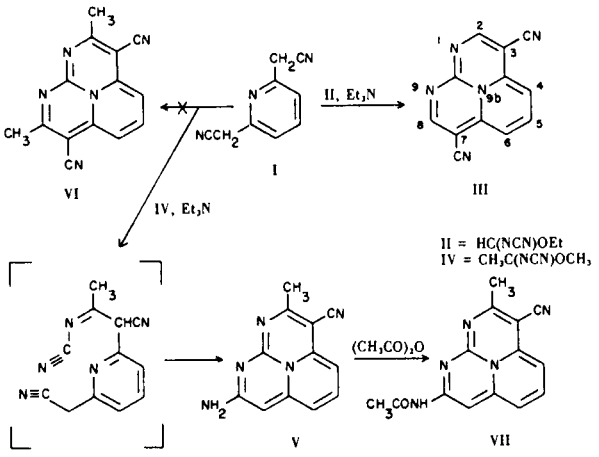
A previous paper (2) described a novel ring closure of 2,6-diaminopyridine to 1,3,4,6,9b-pentaazaphenalene derivatives using alkyl-*N*-cyanomidates as cyclizing agents. It was of interest to investigate whether an activated methyl group might serve as nucleophile in lieu of the amino group of 2,6-diaminopyridine in this reaction. We have found 2,6-bis(cyanomethyl)pyridine (I) to be a suitable substrate. A reported preparation of I (3) involved conversion of 2,6-bis(hydroxymethyl)pyridine with thionyl chloride to 2,6-bis(chloromethyl)pyridine hydrochloride and then displacing the halogen with potassium cyanide in aqueous methanol. The low yield obtained (10%) in the latter step prompted a search for an improved method for that step. It was found that use of the solvent pair 2-methoxyethanol/dimethyl sulfoxide and raising the reaction temperature from 70 to 90° increased the yield to 53%.

Base catalyzed(triethylamine or sodium methoxide) cyclization of I with ethyl *N*-cyanoformimidate (II) gave 3,7-dicyano-1,9,9b-triazaphenalene (III) in 8% yield (4). Interestingly, use of methyl *N*-cyanoacetimidate (IV) in place of II in the same reaction gave 8-amino-3-cyano-2-methyl-1,9,9b-triazaphenalene (V) (39% yield) rather than the expected 3,7-dicyano-2,8-dimethyl-1,9,9b-triazaphenalene (VI). Apparently only one of the cyanomethyl groups of I reacted with IV, while the second cyanomethyl group provided the moiety to complete the ring closure and the resulting amino group as shown in Scheme I. Acetylation of V with acetic anhydride gave 8-acetamido-3-cyano-2-methyl-1,9,9b-triazaphenalene (VII). Reactions of this interesting ring system are in progress and will be reported in a future paper.

Scheme I



EXPERIMENTAL

Melting points were determined in open capillaries on a Thomas-Hoover melting-point bath and are uncorrected. Infrared spectra were recorded using a Perkin-Elmer Infracord, Model 137. Pmr spectra were determined on a Varian EM-360 spectrometer using TMS as an internal reference. Analyses were performed by Micro-Analysis Inc., Marshallton, Delaware.

2,6-Bis(cyanomethyl)pyridine (I).

A mixture of 6.3 g. (0.03 mole) of 2,6-bis(chloromethyl)-pyridine hydrochloride (3), 6.5 g. (0.10 mole) of potassium cyanide and 70 ml. of 2-methoxyethanol was stirred at room temperature for 10 minutes and then 20 ml. of dimethyl sulfoxide was added; the stirring was continued for an additional 18 hours at room temperature followed by 5 hours at 90°. The reaction mixture was distilled (rotary evaporator/reduced pressure) to remove most of the 2-methoxyethanol. Dilution of the thick liquid remaining with 100 ml. of water was followed by extraction with six-100 ml. portions of ether. The combined ether extracts were dried (sodium sulfate), evaporated to dryness (rotary evaporator) and the residue was recrystallized from 95% ethanol to yield 2.5 g. (53%) yield of I, m.p. 94-95°, (Lit. (3) 97-98°).

3,7-Dicyano-1,9,9b-triazaphenalene (III).

A solution of 2.35 g. (0.015 mole) of I, 4.41 g. (0.045 mole) of II (5), 0.15 g. (0.0015 mole) of triethylamine, and 5 ml. of dry 1,2-dimethoxyethane (glyme) was stirred and refluxed for 18 hours and then filtered at room temperature. The filter cake was washed with glyme and then extracted with two-50 ml. portions of boiling chlorobenzene. The combined extracts on cooling deposited 0.26 g. (8%) of crude III, m.p. 343-345° dec. Recrystallization from 2-methoxyethanol gave beautiful green crystals, m.p. 347-349° dec.; ir λ (Nujol): 4.49 μm (CN); pmr (DMSO-d_6): δ 6.06 [d (J ~ 8 Hz), 2H, H_4 and H_6], δ 7.18 [t (J ~ 8 Hz) 1H, H_5], δ 7.36 (s, 2H, H_2 and H_8).

Anal. Calcd. for $C_{12}H_5N_5$: C, 65;75; H, 2.30; N, 31.95. Found: C, 65.93; H, 2.51; N, 31.68.

Use of an equivalent amount of sodium methoxide in the place of triethylamine in the above reaction gave essentially the same yield. Lowering the amount of II to 0.015 mole (all other reactants and conditions being the same) gave a 1% yield of III and no evidence of an amino derivative.

8-Amino-3-cyano-2-methyl-1,9,9b-triazaphenalene (V).

A solution of 2.82 g. (0.018 mole) of I, 1.57 g. (0.016 mole) of IV (5), 0.18 g. (0.0018 mole) of triethylamine and 6 ml. of dry glyme was stirred and refluxed for 18 hours and then filtered at room temperature. The filter cake after being washed successively with glyme and ether weighed 1.38 g. (39%), m.p. >360°. After several unsuccessful attempts at recrystallization, an analytical sample was obtained by boiling the crude material with 10 ml. of glyme for a few minutes, filtering hot and repeating the same operation on the filter cake, dark green solid, m.p. >360°; ir λ (Nujol): 2.93 and 3.15 μm (NH_2), 4.55 μm (CN); pmr

(DMSO-d_6): δ 1.85 (s, 3H, CH_3), δ 5.22 (s, 1H, H_7), δ 5.55 [d (J ~8 Hz), 1H, H_4 or H_6], δ 6.16 [d (J ~ 8 Hz) 1H, H_4 or H_6], δ 7.02 [t (J ~ 8 Hz) 1H, H_5], δ 7.35 [s, (broad) 2H, NH_2; treatment with D_2O removes this signal].

Increasing the amount of IV to 0.054 mole (other reagents the same molar amounts) did not alter the yield or nature of the product.

Anal. Calcd. for $C_{12}H_9N_5$: C, 64.56; H, 4.06; N, 31.38. Found: C, 64.73; H, 4.12; N, 31.20.

8-Acetamido-3-cyano-2-methyl-1,9,9b-triazaphenalene (VII).

A mixture of 0.5 g. (0.0022 mole) of V and 5 g. (0.049 mole) of acetic anhydride was stirred and refluxed for 3 hours. The solids were collected by filtration, washed with ether, and dried: 0.52 g. (87%), m.p. > 360°. Recrystallization from dimethylformamide gave dark, blue-green crystals, m.p. > 360°; ir λ (Nujol): 2.90 μm (NH), 4.55 μm (CN), 5.93 μm (CO); pmr (very low solubility precluded pmr analysis).

Anal. Calcd. for $C_{14}H_{11}N_5O$: C, 63.38; H, 4.17; N, 26.40. Found: C, 63.35; H, 3.75; N, 26.49.

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REFERENCES AND NOTES

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