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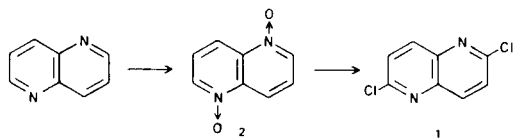
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The structure of 2,6-dichloro-1,5-naphthyridine (1) was established based on physical and spectral data; thus, correcting the numerous inaccurate literature reports.

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During our investigation of the construction of macrocycles possessing subheterocyclic rings (2), we found it necessary to prepare large quantities of 2,6-dichloro-1,5-naphthyridine (1). In 1954, Hart (3) prepared 1 as colorless plates (m.p. 236-238°) from 1,5-naphthyridine di-*N*-oxide (2) by treatment with phosphorus oxychloride at initially ice bath temperatures, followed by reflux for 20 minutes. Other workers have synthesized 1 by (A) treatment of 1,5-dimethyl-1,5-naphthyridine-2,6(1*H*,5*H*)-dione with a mixture of phosphorus pentachloride and phosphorus oxychloride at reflux for 9 hours (5), or (B) the reaction of 2-hydroxy-1,5-naphthyridine 5-oxide with phosphorus oxychloride (6) under conditions similar to Hart (3). Both groups (5,6) reported 1 to possess a melting point of 258-260° (yellow powder) (5) and comparable nmr spectral data. On the other hand in 1971, Rapoport, *et al.*, (4) purported the synthesis of 1 by reaction of 6-methoxy-1,5-naphthyridin-2(1*H*)-one with phosphorus oxychloride under reflux for 15 hours; however, they isolated a compound which melted at 190-194°, which could be converted into the known 2-chloro-1,5-naphthyridine.



Upon repetition of Hart's original conversion of 2 to 1 in separate reactions, we isolated a tan lower melting compound (m.p. 198-200°) and a yellow, higher melting component (m.p. 237-239°). The mixture melting point (m.p. < 200°) and solubility characteristics of our lower melting compound were evidence indicative of a mixture. After numerous repetitions of this reaction, we could only consistently reproduce the synthesis of the higher melting material, which after sublimation and recrystallization possessed an uncorrected average melting point of 253-254°, in agreement with others (5,6). The previously isolated (4) lower melting compound must have been either a mixture (see reference 5), a possible crystalline modification, or due to a typographical error. The nmr spectrum of 1 has been previously determined in DMSO (6), deuteriochloroform (5), and trifluoroacetic acid (4) (7).

EXPERIMENTAL

Preparation of 1,5-Naphthyridine di-*N*-Oxide (2).

1,5-Naphthyridine (m.p. 67-69°, 1.0 g., 0.007 mole) (8) in glacial acetic acid (25 ml.) and hydrogen peroxide (30%, 7 ml.) was heated at 60° for 2 hours. After cooling, the mixture was basified with potassium hydroxide, and extracted with chloroform. The extract was dried with anhydrous potassium carbonate and concentrated *in vacuo* affording a yellow solid, which was recrystallized from ethanol to give yellow crystals of 2, 1.2 g. (98%), m.p. 299-301° [lit (3) m.p. 299-301°]; nmr (deuterium oxide): δ 9.0 (d, 2,6-Naphth-H, J = 7 Hz, 2H), 8.8 (d, 4,8-Naphth-2H, J = 9 Hz, 2H), 8.0 (d, d, 3,7-Naphth-2H, J = 7.9 Hz, 2H).

Preparation of 2,6-Dichloro-1,5-naphthyridine (1).

Di-*N*-oxide 2 (1.0 g., 0.005 mole) was added to cold redistilled phosphorus oxychloride (35 ml.), then the mixture was refluxed for 20 minutes. After cooling, the solution was carefully poured onto ice, and neutralized with ammonium hydroxide. The resultant solid was filtered, dried *in vacuo*, and recrystallized from hexane to afford 1 (m.p. 240°). Sublimation (133 C/1 mm.) and recrystallization from cyclohexane gave analytically pure 1 as pale yellow crystals, 300 mg. (37%), m.p. 253-254°; ¹³C-nmr (chloroform-TMS): 126 ppm (C3), 138.5 (C4), 140 (C2), 150.5 (C5); ¹H-nmr (deuteriochloroform-1% TMS): δ 7.75 (d, 3,7-Naphth-H, J = 9 Hz, 2H), 8.35 (d, 4,8-Naphth-H, J = 9 Hz, 2H); ir (potassium bromide): 3500, 3100, 1599, 1425, 1350, 1285, 1225, 1140, 1100, 1000, 900, 840, 800 cm⁻¹; uv (ethanol) λ max (ϵ): 214 nm (240,000), 256 (4,300), 266 (3,400), 310 (5,800), 323 (5,800); ms m/e: 203 (P + 4, 11.3), 201 (P + 2, 63), 200 (P + 1, 9.8), 199 (C₈H₄Cl₂N₂, 97), 164 (C₈H₄ClN₂, 100), 166 (C₈H₄Cl, 35), 128 (C₈H₄N₂, 86), 102 (C₇H₄N, 39), 76 (C₅H₂N, 26).

Anal. Calcd. for C₈H₄Cl₂N₂: C, 48.27; H, 2.02; N, 14.07. Found: C, 47.91; H, 1.99; N, 14.23.

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