An eco-sustainable green approach for the synthesis of 2,6-naphthyridines under microwave irradiation

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ABSTRACT

A microwave-promoted new easy, efficient, clean and environmentally benign method for the synthesis of 2,6-naphthyridine and its derivatives from 4-cyano-3-pyridylacetonitrile has been developed. The desired products were isolated in excellent yields and high purity under eco-friendly conditions. The synthesized compounds were characterized by the IR, UV-Visible and ¹H-NMR spectral analyses along with elemental analysis.

Keywords: Microwave, eco-friendly, pyridylacetonitrile, naphthyridines

INTRODUCTION

Among the nitrogen heterocycles, naphthyridines and their derivatives represent an important class of organic molecules that attract the interest of both synthetic and medicinal chemists. Naphthyridines have recently been used as pharmaceuticals, fungicides, bactericides, herbicides and insecticides as well as providing an important scaffold for the preparation of several important alkaloids.[1-3] Furthermore, literature shows naphthyridines as good DNA intercalators thereby showing potential against HIV/AIDS, malaria and tuberculosis [4]. Many syntheses of naphthyridines are known, but due to their importance, the development of new synthetic approaches remains an active research area. The biological and pharmacological importance of naphthyridines led to the present synthetic study of 2,6-naphthyridines from simple and readily available precursors using green chemistry methodologies.

Microwave dielectric heating uses the ability of some liquids and solids to transform electromagnetic energy into heat and thereby drive chemical reactions. This in situ mode of energy conversion has many attractions for chemists, [5-6] because its magnitude depends on the properties of the molecules. This allows some control of the material’s properties and may lead to reaction selectivity. There are a variety of methods for carrying out microwave assisted organic reactions using domestic or commercial ovens; this is basically known as microwave-induced organic reaction enhancement (MORE) chemistry [7].

Microwave irradiation is a clean, efficient, and economical technology; safety is largely increased, work up is considerably simplified, cost is reduced, increased amounts of reactants can be used in some equipment and the reactivities and sometimes selectivities are enhanced without dilution. Due to these advantages there is an increasing interest in the use of environmentally-benign reagents and procedures. The absence of solvents coupled with the high yields and short reaction times often associated with reactions of this type make these procedures very attractive for synthesis [8]. Thus, microwave assisted organic synthesis (MAOS) becomes a part of green chemistry. Now-a-days it is also termed as e-chemistry because it is easy, economic, effective and eco-friendly. The cyclization
of o-cyanobenzylcyanides to naphthyridines is well communicated [9]. However, no publications are available for the eco-friendly synthesis of 2,6-naphthyridines from cyclization of 4-cyano-3-pyridylacetonitriles. The present study reports a microwave assisted synthesis of 2,6-naphthyridines from easily available and cheap chemical namely ethyl-4-cyano-3-pyridylacetate.

MATERIALS AND METHODS

2.1: Instruments and Technique
All the chemicals were purchased from Merck. The microwave irradiations were performed using a commercial / kitchen microwave oven model BMO: 700T (BPL-make). The melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. The infrared spectra were recorded on a Perkin-Elmer 521 grating spectrophotometer. Solid compounds were sampled as KBr unless otherwise indicated, and liquid compounds as a film supported between sodium chloride plates. The ultraviolet spectra were obtained on a Perkin-Elmer Model 350 spectrophotometer using absolute methanol as solvent. Nuclear magnetic resonance spectra were determined on a Varian High Resolution Nuclear Magnetic Resonance Model A-60 spectrometer. Solvents used were deuteriochloroform (CDCl$_3$) and dimethyl-tetramethylsilane used as sulfoxide-d$_6$ (DMSO-d$_6$) an internal reference (TMS = 0 p.p.m.). The chemical shifts are expressed in δ-scale downfield from TMS and proton signals are indicated as $s$= singlet, $d$= doublet, $t$= triplet, $q$= quartet, $m$= multiplet. The TLC was run on silica gel plates using acetone-benzene (1:3) as the irrigant. All compounds were analysed satisfactorily for C, H and N using Carl-Ebra 1106 elemental analyser in micro analytical laboratory.

2.2: Experimental Methods

(a) Preparation of 3-Amino-1-bromo-2,6-naphthyridine (III)
4-Cyano-3-pyridylacetonitrile (II) (6.2 g; 0.043 moles) was suspended in 100 ml of dry ether and cooled to -50°C to 0°C in a dry ice-methanol bath. Anhydrous hydrogen bromide was bubbled through the mixture for two hours and the resulting mixture was poured slowly into a solution of excess sodium bicarbonate. The yellow precipitate was filtered and washed with several small portions of water yielding 7.8 g of 3-amino-1-bromo-2,6-naphthyridine (III) (80.3%). Recrystallization from methanol gave yellow needles, m.p. 199.5°C (with dec.).

Analytical Data:
Calculated for C$_8$H$_6$N$_3$Br: C, 42.88; H, 2.68; N, 18.76; Br, 35.6
Found: C, 42.82; H, 2.82; N, 18.66; Br, 35.59

(b) Preparation of 1,3-Dibromo-2,6-naphthyridine (IV)
3-Amino-1-bromo-2,6-naphthyridine (III) (1.42 g ; 6.4 mmoles) was suspended in 48% fuming hydrobromic acid (25 ml). Solid sodium nitrite (0.7 g; 0.010 moles) was added in small portions over a period of 30 min. with constant stirring: the temperature of the mixture was kept at -4 to -2°C. When the addition was completed, the mixture was stirred at 0°C for 30 min. and allowed to stand at room temperature overnight. It was poured slowly onto 200 g of crushed ice and made strongly alkaline with 20% sodium hydroxide. The solution was extracted three times with 150 ml portions of ether and the combined ethereal extract was evaporated to dryness leaving 1.08 g of yellow substance. Chromatography and recrystallization from hexane gave 0.4 g of 1,3-dibromo-2,6-naphthyridine (IV) (82.0% yield) as colorless needles, m.p.136-136.5°C.

Analytical Data:
Calculated for C$_8$H$_4$N$_2$Br$_2$: C, 33.36; H, 1.39; N, 9.73; Br, 55.56
Found: C, 33.50; H, 1.51; N, 9.66; Br, 55.41

(c) Preparation of 1,3-Dihydrazino-2,6-naphthyridine (V)
One gram of 3-amino-1-bromo-2,6-naphthyridine (III) (4.45 mmoles) was dissolved in 10 ml of dioxane and 5 ml of 85% hydrazine hydrate was added drop wise. The mixture was heated at 125°C for 6 minutes in the microwave oven and allowed to cool to room temperature. The yellow precipitate was filtered to give 0.74 g of 1,3-dihydrazino-2,6-naphthyridine (V) (86.0% yield) m.p. 214-216°C . A small sample was sent for elemental analysis without further purification.

Analytical Data:
Calculated for C$_8$H$_{10}$N$_6$: C, 50.51; H, 5.30; N, 44.19
One gram of 1,3-dihydrazino-2,6-naphthyridine (V) (5.30 mmoles) was dissolved in 15 ml of acetic acid and 30 ml of water. The mixture was poured slowly into 100 ml of 10% hot cupric sulfate solution. The resulting mixture was boiled for 15 min., made alkaline with 20% sodium hydroxide solution and extracted several times with ether (ca. 600 ml). The ethereal solution was dried over anhydrous sodium sulfate and the solvent was evaporated leaving 0.35 g of pale yellow solid (93.0% yield). Chromatography and recrystallization from hexane gave 2,6-naphthyridine (V) as white crystals, m.p. 118-119°C; lit. [10]; 114-115°C.

Analytical Data:
Calculated for C₈H₆N₂: C, 74.07; H, 4.81; N, 21.46
Found: C, 73.83; H, 4.65; N, 21.53

The i.r. spectrum (CS₂): 3055s, 3020m, 2980vw cm⁻¹; i.r. (KBr): 1665w, 1562s, 1481s, 1380s, 1298w, 1273s, 1247s, 1204m, 1128sh, 1115s, 1015s, 940s, 842vs, 804w, 800s, 660s + 650s (doublet), 447m cm⁻¹.

RESULTS AND DISCUSSION

The synthesis of 2,6-naphthyridine (I) from 4-cyano-3-pyridylacetonitrile (II) is outlined in scheme-1. 3-Amino-1-bromo-2,6-naphthyridine (III) was prepared in 80.3 per cent yield by the action of anhydrous hydrogen bromide on 4-cyano-3-pyridylacetonitrile under microwave irradiation for few minutes. Diazotization of compound (III) with sodium nitrite and hydrobromic acid gave 1,3-dibromo-2,6-naphthyridine (IV) in 72 percent yield. Treatment of compound (IV) with 85 per cent hydrazine hydrate gave a quantitative yield of 1,3-dihydrazino-2,6-naphthyridine (V). Reaction of (V) with 10 percent cupric sulfate solution in acetic acid under microwave irradiation for few minutes gave 2,6-naphthyridine (I) in 83 percent yield.

Scheme-1: Microwave assisted synthesis of 2,6-naphthyridines

The infrared spectrum of the product obtained no longer showed cyano-group absorptions but a primary amine group was shown by bands at 3310 and 3175 cm⁻¹ (NH₂asym. and sym. stretch respectively) and 1652 cm⁻¹ (NH₂ deformation). The cyclization of 4-cyano-3-pyridylacetonitrile (II) could yield two isomers, 3-amino-1-bromo-2,6-naphthyridine (III) or 1-amino-3-bromo-2,6-naphthyridine (IIIa). The NMR spectrum of the cyclization product and of its catalytic reduction product supported structure (III).
The NMR spectrum of the cyclization product showed two singlets at 8.89 and 6.65 p.p.m. for the two isolated protons, H₅ and H₆, respectively. The assignment of the lower field singlet to H₅ is analogous to the assignment made for H₅ of isoquinoline [11]. The two doublets at 8.09 and 7.41 ppm were assigned to H₇ and H₈, respectively (J₇,₈ = 6.0 cps). The H₇ doublet occurs at lower field because of its proximity to the ring nitrogen atom. The remaining broad band at 4.72 ppm is due to the primary amino group protons.

In this spectrum, both H₈ and H₄ are situated in positions meta to the ring nitrogen atom and the difference in their chemical shifts is 0.76 ppm. The up field displacement of the chemical shift of H₈ relative to that of H₈ shows that the amino group must be in the ortho position to H₄ [5-6] that the amino group must be in position 3. In compound IIIa, the difference in chemical shift of H₈ relative to that of H₈ should be approximately 0.4 ppm because the amino group would be para to H₈ [12-13] that the NMR evidence is not consistent with structure IIIa. This evidence shows that structure III is the correct one.

Another piece of evidence was showing that the bromine atom is in position 1 and the amino group in position 3 is the NMR spectrum of the catalytic reduction. This spectrum displays a broad band at 6.13 ppm for the primary amino group protons, two singlets at 6.63 and 8.88 ppm for H₄ and H₅, respectively, and two doublets at 8.03 and 7.47 ppm for H₇ and H₈ respectively (J₇,₈ = 5.5 cps).

Another singlet at 8.78 ppm, not present in the spectrum of III, is due to the proton that replaced the bromine atom. This band occurs very close to that of H₅, so that it must be produced by the proton in position 1 and not by the one in position 3. If the reduction product were 1-ami no-2,6-naphthyridine, its NMR spectrum would contain only one singlet for the isolated proton, H₅, and two sets of quartets for H₇ and H₈, and for H₇ and H₈ respectively. Since the NMR spectrum of the reduction product obtained cannot be interpreted this way, the NMR evidence is consistent with structure III but inconsistent with structure IIIa for the product of the cyclization of 4-cyano-3-pyridylacetonitrile (II).

Since only one of the two possible isomers was obtained in the reaction of the dinitrile II with anhydrous hydrogen bromide, it may be concluded that the mechanism of the cyclization is a nucleophilic attack of the cyano nitrogen in position 4 of the pyridine ring on the carbon atom of the cyano group in the side chain. It is probable that by resonance and inductive effects the electron-withdrawing ring nitrogen atom renders the cyano nitrogen at position 4 less susceptible to protonation than that on the side-chain, the latter being separated from the ring by the methylene group. After protonation, the lone pair electrons of the cyano nitrogen at position 4 are available for nucleophilic attack on the carbon atom of the protonated cyano group attached to the methylene group (Scheme-2).

In the NMR spectrum of IV(Fig. 9), the low field singlet at 9.21 ppm was assigned to the isolated proton (H₅) because of its proximity to the ring nitrogen atom, and the high field singlet at 8.05 ppm to the remaining isolated meta proton (F:14). This signal occurs at higher field because H₄ is not influenced by the resonance effect of the

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electron-withdrawing ring nitrogen atom. The two doublets at 8.86 and 8.01 ppm (J_{7,8} = 6.0 cps) were produced by H_{7} and H_{8}. The doublet at 8.01 ppm was assigned to the meta proton (H_{8}) on the basis of the fact that it was superimposed upon the singlet at 8.05 for the other meta proton (H_{4}). The remaining doublet at 8.86 ppm was then assigned to the remaining proton (H_{7}).

In the diazotization of 3-amino-1-bromo-2,6-naphthyridine (III) with sodium nitrite and hydrobromic acid, the major product was 1,3-dibromo-2,6-naphthyridine (IV). In addition, a minor product, which was identified by its NMR spectrum as 1,3,4-tribromo-2,6-naphthyridine(IVa), was obtained in 22 percent yield.

The NMR spectrum of IVa (Fig. 10) showed a low field singlet at 9.70 ppm which was assigned to H_{5} and two doublets at 8.99 and 8.04 ppm due to H_{7} and H_{8} respectively (J_{7,8} = 6.0 cps). The singlet at 8.05 ppm due to H_{4} in compound IV was absent in the spectrum of IVa, indicating that the proton in position 4 had been replaced by a bromine atom. The formation of the tribromo compound (IVa) in the diazotization of 3-amino-1-bromo-2,6-naphthyridine (IV) was unexpected. It was presumably formed by an electrophilic substitution at C-4 and it is believed that this reaction occurred before the diazotization of the amine group to give 1,3-dibromo-2,6-naphthyridine took place. In the diazotization of 3-amino-1-bromo-2,6-naphthyridine (III), though bromine was not used, the reaction of nitrous acid and hydrobromic acid could have liberated bromine to brominate III [14].

\[ 2\text{HNO}_2 + 2\text{HBr} \rightarrow \text{Br}_2 + 2\text{NO} + 2\text{H}_2\text{O} \]

It is known that nitrosation, which involves nucleophilic attack of amine nitrogen on the nitrous acidium ion (the addition product of nitrous acid and a proton), is the first step in diazotization [15], as is shown by the following scheme-3:

![Scheme-3: Mechanism of nucleophilic attack of amine nitrogen](image)

Therefore, a decrease in electron density on the amine nitrogen would hinder the reaction. It is probable that, in 3-amino-1-bromo-2,6-naphthyridine, the lone pair electrons on the amino nitrogen are involved in resonance interaction with the adjacent electron-attracting ring nitrogen atom and are thus not so readily available for the nucleophilic attack. This causes the diazotization to proceed very slowly and therefore the competing bromination reaction sometimes occurs first. In the case in which bromination occurred first, followed by diazotization, the tribromo derivative (IVa) was obtained, while in the case in which diazotization occurred first, the dibromo derivative (IV) was formed.

The next step in the synthesis of 2,6-naphthyridine was to replace both bromine atoms in IV by hydrogens. In the naphthyridine series, the catalytic reduction of halogenated naphthyridines is not a suitable method for dehalogenation because a partial reduction of the ring also occurs [16].

1,3-Dibromo-2,6-naphthyridine (IV) was treated with 85 percent hydrazine hydrate in dioxane solution at room temperature, and 1,3-dihydrazone-2,6-naphthyridine (V) was obtained in quantitative yield.

Compound V was also obtained, although in lower yield, by refluxing 3-amino-1-bromo-2,6-naphthyridine (III) and 85 per cent hydrazine hydrate in dioxane solution.
The replacement of the amine group in compound III by the hydrazino group could probably be due to the low electron density at C-3 caused by the inductive and resonance effects of the ring nitrogen atom. Thus C-3 was readily attacked by hydrazine as is shown in the following scheme-4:

Scheme-4: Mechanism of conversion of III into V

The dihydrazino derivative, V, was converted to the unsubstituted 2,6-naphthyridine by oxidation with cupric sulfate in acetic acid. The oxidation of compound V with cupric sulfate probably involves the formation of an intermediate diimide which immediately decomposes to give 2,6-naphthyridine and molecular nitrogen through a free radical mechanism [17].

Scheme-5: Free radical Mechanism

The results are compared to the conventional methods (Table-1).

<table>
<thead>
<tr>
<th>Compound</th>
<th>m.p.(in K)</th>
<th>% Yield</th>
<th>Conventional method</th>
<th>Green meth</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>391</td>
<td>28%</td>
<td>93%</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>472</td>
<td>36%</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>409</td>
<td>39%</td>
<td>82%</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>488</td>
<td>37%</td>
<td>86%</td>
<td></td>
</tr>
</tbody>
</table>
Table 2: NMR spectra of 2,6-naphthyridine and its derivatives

<table>
<thead>
<tr>
<th>Compound</th>
<th>R&lt;sub&gt;1&lt;/sub&gt;</th>
<th>R&lt;sub&gt;3&lt;/sub&gt;</th>
<th>R&lt;sub&gt;4&lt;/sub&gt;</th>
<th>H&lt;sub&gt;1&lt;/sub&gt;</th>
<th>H&lt;sub&gt;2&lt;/sub&gt;</th>
<th>H&lt;sub&gt;3&lt;/sub&gt;</th>
<th>H&lt;sub&gt;4&lt;/sub&gt;</th>
<th>H&lt;sub&gt;5&lt;/sub&gt;</th>
<th>H&lt;sub&gt;7&lt;/sub&gt;</th>
<th>H&lt;sub&gt;8&lt;/sub&gt;</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>I&lt;sub&gt;a&lt;/sub&gt;</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>9.39</td>
<td>8.77</td>
<td>7.80</td>
<td>9.39</td>
<td>8.77</td>
<td>7.80</td>
<td>7.41</td>
<td>4.72(NH&lt;sub&gt;2&lt;/sub&gt;)</td>
</tr>
<tr>
<td>III&lt;sub&gt;a&lt;/sub&gt;</td>
<td>Br</td>
<td>NH&lt;sub&gt;2&lt;/sub&gt;</td>
<td>H</td>
<td>6.65</td>
<td>8.89</td>
<td>8.09</td>
<td>7.41</td>
<td>4.72(NH&lt;sub&gt;2&lt;/sub&gt;)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV&lt;sub&gt;a&lt;/sub&gt;</td>
<td>Br</td>
<td>Br</td>
<td>H</td>
<td>8.05</td>
<td>9.21</td>
<td>8.86</td>
<td>8.01</td>
<td>7.41</td>
<td>4.72(NH&lt;sub&gt;2&lt;/sub&gt;)</td>
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<td></td>
</tr>
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</table>

(B) Spin-spin coupling constant J (in cps)

<table>
<thead>
<tr>
<th>Compound</th>
<th>R&lt;sub&gt;1&lt;/sub&gt;</th>
<th>R&lt;sub&gt;3&lt;/sub&gt;</th>
<th>R&lt;sub&gt;4&lt;/sub&gt;</th>
<th>J&lt;sub&gt;1,4&lt;/sub&gt;</th>
<th>J&lt;sub&gt;1,5&lt;/sub&gt;</th>
<th>J&lt;sub&gt;3,4&lt;/sub&gt;</th>
<th>J&lt;sub&gt;4,8&lt;/sub&gt;</th>
<th>J&lt;sub&gt;5,8&lt;/sub&gt;</th>
<th>J&lt;sub&gt;7,8&lt;/sub&gt;</th>
</tr>
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<tbody>
<tr>
<td>I&lt;sub&gt;a&lt;/sub&gt;</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>6.0</td>
<td>6.0</td>
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<td>6.0</td>
<td>6.0</td>
<td>6.0</td>
</tr>
<tr>
<td>III&lt;sub&gt;a&lt;/sub&gt;</td>
<td>Br</td>
<td>NH&lt;sub&gt;2&lt;/sub&gt;</td>
<td>H</td>
<td>6.0</td>
<td>6.0</td>
<td>6.0</td>
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<td>6.0</td>
<td>6.0</td>
<td>6.0</td>
<td>6.0</td>
<td>6.0</td>
</tr>
</tbody>
</table>

(a) In DMSO-d<sub>6</sub> solution (b) In CDCl<sub>3</sub> solution

Figure 1: NMR Spectrum of 2,6-Naphthyridine (I) in CDCl<sub>3</sub>

Figure 2: NMR Spectrum of 3-Amino-1-bromo-2,6-Naphthyridine (III) in DMSO-d<sub>6</sub>
Table 3: Infrared absorption bands of 2,6-naphthyridine and its derivatives in the 1600 - 1350 cm⁻¹ region

<table>
<thead>
<tr>
<th>Compound</th>
<th>Band-I</th>
<th>Band-II</th>
<th>Band-III</th>
<th>Band-IV</th>
<th>Band-V</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,6-Naphthyridine (I)</td>
<td>1564</td>
<td>1555</td>
<td>1492</td>
<td>1430</td>
<td>1375</td>
</tr>
<tr>
<td>3-Amino-1-bromo-2,6-Naphthyridine (III)</td>
<td>1610</td>
<td>1564</td>
<td>1481</td>
<td>1424</td>
<td>1355</td>
</tr>
<tr>
<td>1,3-Dibromo-2,6-Naphthyridine (IV)</td>
<td>1553</td>
<td>1536</td>
<td>1473</td>
<td>1431</td>
<td>1375</td>
</tr>
<tr>
<td>1,3,4-Tribromo-2,6-Naphthyridine (IVa)</td>
<td>1532</td>
<td>1525</td>
<td>1469</td>
<td>1435</td>
<td>1375</td>
</tr>
</tbody>
</table>

Figure 4: Infrared Spectrum of 2,6-Naphthyridine (I)

Table 4: Ultraviolet absorption maxima and their corresponding log ε values of 2, 6-naphthyridine and its derivatives in methanol

<table>
<thead>
<tr>
<th>Compound</th>
<th>α-band</th>
<th>ι-band</th>
<th>β-band</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,6-Naphthyridine (I)</td>
<td>331</td>
<td>3.61</td>
<td>263</td>
</tr>
<tr>
<td></td>
<td>326</td>
<td>3.57</td>
<td>254</td>
</tr>
<tr>
<td></td>
<td>317</td>
<td>3.61</td>
<td>246</td>
</tr>
<tr>
<td></td>
<td>305</td>
<td>3.42</td>
<td>238</td>
</tr>
<tr>
<td>3-Amino-1-bromo-2,6-Naphthyridine (III)</td>
<td>397</td>
<td>3.56</td>
<td>286</td>
</tr>
<tr>
<td></td>
<td>305</td>
<td>3.82</td>
<td>286</td>
</tr>
<tr>
<td></td>
<td>345</td>
<td>3.70</td>
<td>276</td>
</tr>
<tr>
<td></td>
<td>334</td>
<td>3.70</td>
<td>268</td>
</tr>
<tr>
<td>1,3-Dibromo-2,6-Naphthyridine (IV)</td>
<td>355</td>
<td>3.82</td>
<td>286</td>
</tr>
<tr>
<td></td>
<td>342</td>
<td>3.80</td>
<td>276</td>
</tr>
<tr>
<td>1,3,4-Tribromo-2,6-Naphthyridine (IVa)</td>
<td>355</td>
<td>3.82</td>
<td>286</td>
</tr>
<tr>
<td></td>
<td>342</td>
<td>3.80</td>
<td>276</td>
</tr>
<tr>
<td>1,3-Dihydrazino-2,6-Naphthyridine (V)</td>
<td>Above 400</td>
<td>312</td>
<td>3.94</td>
</tr>
</tbody>
</table>

* No α-band was found in the ultraviolet region. The intense yellow color of the compound indicated that the α-band had shifted to the visible region of the spectrum.

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The $\alpha$ - and $\rho$-bands of 2, 6-naphthyridine and its derivatives are assigned to the electronic transitions polarized parallel to the x- and y-axes, respectively, by analogy with the assignment of the bands of substituted naphthalenes [18] and isoquinolines [19]. These assignments are based on the effects shown by electron-donating substituents at C-3 and C-1 on the positions of the bands.

It is seen that compound with electron-donating groups at C-3, such as III have much greater bathochromic shifts of the $\alpha$-band than of the $\rho$-band. This indicates that the $\alpha$-band must be due to electronic transitions along the x-axis.

CONCLUSION

A new method for the synthesis of 2,6-naphthyridine from 4-cyano-3-pyridylacetonitrile was developed. It involved the cyclization of 4-cyano-3-pyridylacetonitrile to 3-amino-1-bromo-2,6-naphthyridine by the action of hydrogen bromide, diazotization of 3-amino-1-bromo-2,6-naphthyridine with sodium nitrite and hydrobromic acid to 1,3-dibromo-2,6-naphthyridine, conversion of the product to 1,3-dihydrazino-2,6-naphthyridine by reaction with hydrazine hydrate and oxidation of the latter compound with copper sulfate to unsubstituted 2,6-naphthryidine under microwave irradiation which is simple, mild, efficient and ecofriendly from green chemistry point of view. This simple method provides a convenient synthesis of 2,6-naphthyridine and its derivatives which otherwise would be difficult using conventional synthetic methodologies.

In conclusion, we observed better yields in a shorter period compared to the conventional methods in the present protocol. We describe here an efficient and environmentally benign synthesis of 2,6-naphthyridine and its derivatives.

REFERENCES


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