

## NOTE

## Synthesis and Spectral Characteristics of 5-Amino-4-Cyanoimidazoles from Amidines

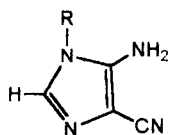
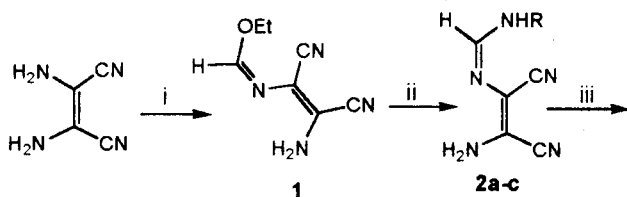
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Imidazole derivatives have been synthesized in high yields by reaction between amidine and strong base depending on reaction conditions and mainly on the nature of the base used to induce cyclization.

**Key words:** Synthesis, Spectral, 5-Amino-4-cyanoimidazoles, Amidines.

5-Amino-4-cyanoimidazoles have long been recognized as useful synthetic precursors for compounds such as a series of biologically active purines and their derivatives<sup>1–4</sup>, but there is no simple, general synthesis available for 1-aryl derivatives of these compounds. Sen and Ray<sup>5</sup> reported the synthesis of 5-amino-4-cyano-1-(3-diethylaminopropyl)imidazole and 5-amino-4-cyano-1-benzylimidazole *via* a multistep synthesis.

The compounds **3** can be synthesized directly from the corresponding amidines **2** under similar strongly basic conditions<sup>6–10</sup>. We thus attempted to cyclize the amidines **2a–c** to obtain compounds of type **3a–c**, which would be important intermediates for the synthesis of a range of 9-aryl-purines and 9-aryl-1,2-dihydropurines<sup>11–13</sup>.



**3a-c**

<b>2, 3</b>		yield (%) of <b>3</b>
<b>a</b>	R=2-ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> -	80
<b>b</b>	R=4-HOC <sub>6</sub> H <sub>4</sub> -	61
<b>c</b>	R=NH <sub>2</sub>	87

**Scheme-1:** Reagents and conditions; (i) HC(OEt)<sub>3</sub>, dioxane, heat; (ii) RNH<sub>2</sub>, PhNH<sub>3</sub><sup>+</sup>Cl<sup>-</sup>, room temp., 3–4 h; (iii) 1 mol dm<sup>-3</sup> KOH, aq., room temp.

The preparation of 5-amino-1-aryl-4-cyanoimidazoles **3a-c** were attempted from the corresponding amidines **2a-c** in the presence of an aqueous potassium hydroxide solution (1 M) at room temperature. Imidate **1** was prepared in high yield from diaminomaleonitrile and triethyl orthoformate, according to areported procedure<sup>7-9</sup>. After the preparation of imidate **1** in good yield (94%) it was treated with aryl or benzylamine in a 1 : 1 molar ratio in ethanol in the presence of a catalytic amount of anilinium hydrochloride<sup>8,9</sup>. The cyanoimidazoles **3a-c** were isolated in good yields.

Compounds **3a-c** were recrystallized from a mixture of ethanol/methanol (1 : 1) and gave pale yellow to off-white crystals respectively. These were fully characterized by TLC, IR and <sup>1</sup>H NMR spectroscopy. The infrared spectrum confirmed the presence of the NH and C=N stretching vibrations within the region of 3400–3100 and 1660–1650 cm<sup>-1</sup> respectively. The infrared spectrum also showed a sharp absorption band within the range of 2220–2200 cm<sup>-1</sup> for the C=N stretching vibration. In the <sup>1</sup>H NMR spectra of the isolated 5-amino-1-aryl-4-cyanoimidazoles, the primary amine protons were observed in the region of 5.60–6.60 ppm and in several cases the assignments were confirmed by D<sub>2</sub>O exchange. The proton of the imidazole ring appeared as a sharp singlet in the range of 7.14–7.42 ppm.

The <sup>1</sup>H NMR spectra were recorded on Hitachi-Perkin-Elmer R24B (60 MHz) or Bruker XL 500 (500 MHz) instruments, and IR spectra on a Shimadzu IR-470 spectrophotometer. The melting points were measured on an electrothermal digital melting point apparatus and are uncorrected.

**General procedure for the preparation of the 5-amino-4-cyanoimidazoles 3a-c:** A suspension of the corresponding aryl-(Z)-N-[2-amino-1,2-dicyanovinyl] formamidine or (amidrazone) **2a-c**<sup>6-8</sup> (1.00 g) in potassium hydroxide solution (1 M, 10 mL) was stirred at room temperature until TLC showed complete consumption of the starting material. The precipitated product was filtered off, washed with water (8–10 mL), followed by a mixture of dry diethyl ether/ethanol (10 : 1) and air-dried in the absence of light to give the desired products **3a-c**.

**5-Amino-1-(2-chlorobenzyl)-4-cyanoimidazole 3a:** Recrystallization of the product from dry diethyl ether/ethanol (1 : 1) and air-dried in the absence of light to give white crystals of **3a** (0.71 g, 3.08 mmol, 80%). mp. 112–114°C (decomp.); δ<sub>11</sub> (500 MHz, d<sub>6</sub>-DMSO) 5.40 (s, 2H, CH<sub>2</sub>), 6.60 (s, 2H, NH<sub>2</sub>), 7.01 (dd, 1H, ArH), 7.42 (s, 1H, H-imidazole), 7.63–7.68 (m, 2H, Ar—H), 7.85 (dd, 1H, Ar—H) ppm; ν<sub>max</sub> (Nujol mull) 3400 m, 3370 s, 3310 s, 3210 s, ν(N—H), 2220 s ν(CN), 1650 s ν(C=N), 1570 s ν(N—H), 1520 s, 1475 s, 1430 s, 1365 s, 1280 s, 1200 s, 1060 s, 1065 s, 980 s, 860 m, 820 m, 780 s, 730 m, 700 m cm<sup>-1</sup>.

**5-Amino-1-(4-hydroxyphenyl)-4-cyanoimidazole 3b:** Recrystallization of the product from ethanol/methanol (1 : 1) give pale yellow crystals of **3b** (0.54 g, 2.7 mmol, 61%). m.p. 171–172.5°C (decomp.); (500 MHz, d<sub>6</sub>-DMSO) 5.71 (s, 2H, NH<sub>2</sub>), 6.32 (dd, 2H, Ar—H), 6.80 (dd, 2H, Ar—H), 7.14 (s, 1H, H-imidazole) ppm; ν<sub>max</sub> (Nujol mull) 3390 s, 3210 s, 3160 s, 3100 w ν(N—H), 2220 s, 2210 s ν(CN), 1650 s ν(C=N), 1610 s ν(N—H), 1570 s, 1520 s, 1260 s, 1160 s, 1145 s, 1020 s, 865 s, 815 m, 770 s, 735 m cm<sup>-1</sup>.

**1,5-Diamino-4-cyanoimidazole 3c:** Recrystallization of the product from ethanol/methanol (1 : 1) gave pale yellow crystals of **3c** (0.72 g, 5.85 mmol, 87%). m.p. 214–215°C (decomp.);  $\delta_{\text{H}}$  (500 MHz,  $d_6$ -DMSO) 5.60 (s, 2H, NH<sub>2</sub>), 6.04 (s, 2H, NH<sub>2</sub>) and 7.20 (s, 1H, H-imidazole) ;  $\nu_{\text{max}}$  (Nujol mull) 3385 s, 3350 s, 3280 s, 3100 s  $\nu$ (N—H), 2220 s, 2200 s  $\nu$ (CN), 1660 s  $\nu$ (C=N), 1610 s  $\nu$ (N—H) and 1515 w, 1255 s, 1170 s, 1155 s, 1010 s, 860 s, 810 m, 760 s  $\text{cm}^{-1}$ .

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