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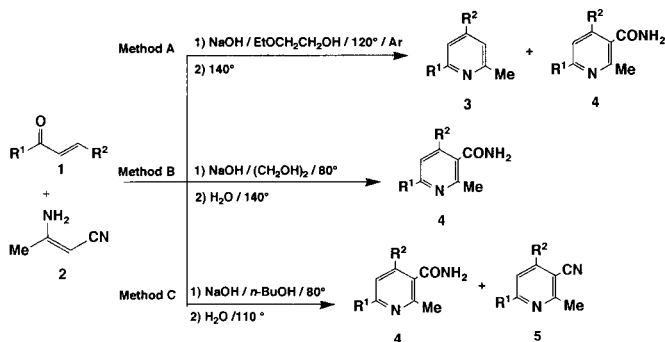
A new one-pot synthesis of title compounds by the reactions of α,β -unsaturated carbonyl compounds with β -aminocrotononitrile in the presence of sodium hydroxide is described.

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Although many methods have been reported for the synthesis of 4,6-disubstituted 2-methylpyridines **3** [1-6], all methods require drastic conditions or several steps. In our continuing study on the synthesis of pyridine derivatives [7a-d], this report describes a convenient synthesis of 4,6-disubstituted 2-methylpyridines **3** and their 3-carboxamides **4**.

The reactions of α,β -unsaturated carbonyl compound **1** with β -aminocrotononitrile (**2**) using following three methods (A, B, and C) were found to give different product distributions. The reaction processes and their results are shown in Scheme 1 and Table 1, respectively.

Scheme 1



Method A is suitable for the formation of **3**. Methods B and C are suitable for the formation of 2-methylpyridine-3-carboxamides **4** substituted with aryl groups and heteroatomics, respectively.

EXPERIMENTAL

Instruments.

Melting points were recorded with a Yanagimoto MP-S2 micro melting point apparatus and were uncorrected. The ¹H nmr spectra (270 MHz) were measured in deuteriochloroform with a JEOL 270-GX spectrometer. Tetramethylsilane (TMS) was used as an internal standard. Mass spectra (ionization potential: 70 eV) were measured with a Shimadzu QP-1000 mass spectrometer. The ir spectra were measured with a Perkin Elmer FT-IR 1640. Elemental analysis were recorded using a Yamato CHN recorder MT-3.

Synthesis of 4,6-Disubstituted 2-methylpyridines **3** and their 3-Carboxamides **4**.

Method A.

In a general procedure, to an ethylene glycol monoethyl ether solution (20 ml) of **2** (4 mmoles) and sodium hydroxide (50 mmoles) heated at 120° under argon atmosphere was added an ethylene glycol monoethyl ether solution (20 ml) of **1** (20 mmoles) dropwise for 15 minutes. The mixture was refluxed for 4 hours. After the reaction, the solution was poured into brine (50 ml) and extracted with dichloromethane. The extract was washed with 10% aqueous sodium hydrogen sulfate and brine, and dried over sodium sulfate. After evaporation of the solvent, the products were isolated by column chromatography on silica gel (dichloromethane) and recrystallized (**3**: ethyl alcohol-water (2:1 v/v), **4**: ethyl alcohol).

Method B.

In a general procedure, to an ethylene glycol solution (20 ml) of **1** (1 mmole), **2** (4 mmoles) and sodium hydroxide (25 mmoles) kept at 80° for 24 hours was added water (1 ml). The mixture was heated at 140° for 6 hours. After the reaction, the solution was poured into brine (50 ml) and extracted with dichloromethane. The extract was washed with 10% aqueous sodium hydrogen sulfate and brine, and dried over sodium sulfate. After evaporation of the solvent, the products were isolated by column chromatography on silica gel (dichloromethane) and recrystallized (ethyl alcohol).

Method C.

In a general procedure, to a *n*-butyl alcohol solution (20 ml) of **1** (1 mmole), **2** (4 mmoles), and sodium hydroxide (25 mmoles) kept at 80° for 24 hours was added water (1 ml). The mixture was heated at 110° for 4 hours. After the reaction, the solution was poured into brine (50 ml) and extracted with dichloromethane. The extract was washed with 10% aqueous sodium hydrogen sulfate and brine, and dried over sodium sulfate. After evaporation of the solvent, the products were isolated by column chromatography on silica gel (dichloromethane) and recrystallized (ethyl alcohol).

Physical and spectral data of the products are shown below.

2-Methyl-4,6-diphenylpyridine (**3a**).

This compound had mp 72-73° (lit [3] mp 73°).

6-(4-Methoxyphenyl)-2-methyl-4-phenylpyridine (**3b**).

This compound had mp 105-106°; ¹H nmr: δ 2.67 (s, 3H), 3.86

Table 1
Synthesis of 4,6-Disubstituted 2-Methylpyridines and their 3-Carboxamides

Compound	R ¹	Substituent	R ²	Yield (%)			
				Method A 3	Method B 4	Method C [a] 4	
a	phenyl		phenyl	63	18	56	—
b	4-methoxyphenyl		phenyl	61	20	65	—
c	4-methoxyphenyl		phenyl	64	25	61	—
d	4-chlorophenyl		phenyl	55	28	47	—
e	<i>t</i> -butyl		phenyl	49	16	37	—
f	phenyl		4-methoxyphenyl	53	23	43	—
g	phenyl		4-methoxyphenyl	61	28	39	—
h	phenyl		4-chlorophenyl	63	20	57	—
i	4-methoxyphenyl		4-methoxyphenyl	65	18	45	—
j	phenyl		2-furyl	41	20	trace	35
k	2-furyl		2-furyl	49	19	trace	29
l	phenyl		2-thienyl	51	35	trace	42
m	2-thienyl		2-thienyl	46	37	trace	47
n	2-pyridyl		phenyl	25	24	trace	35
o	2-pyridyl		4-methoxyphenyl	32	20	trace	33
p	2-pyridyl		4-chlorophenyl	23	18	trace	30
q	phenyl		2-pyridyl	63	trace	trace	trace
r	4-methoxyphenyl		2-pyridyl	55	trace	trace	trace
s	4-chlorophenyl		2-pyridyl	65	trace	trace	trace
t	ferrocenyl		phenyl	55	20	7	32
u	phenyl		ferrocenyl	50	trace	trace	trace
v	ferrocenyl		ferrocenyl	60	trace	trace	trace

[a] A small amount of **5** was obtained.

(s, 3H), 7.00 (d, *J* = 9.0 Hz, 2H), 7.26 (d, *J* = 1.5 Hz, 1H), 7.43-7.69 (m, 5H), 7.66 (d, *J* = 1.5 Hz, 1H), 8.00 (d, *J* = 9.0 Hz, 2H); ms: *m/z* (ion, relative intensity) 275 (M⁺, 100), 276 (26); ir (potassium bromide): 1605 cm⁻¹.

Anal. Calcd. for C₁₉H₁₇NO: C, 82.88; H, 6.22; N, 5.09. Found: C, 83.09; H, 6.27; N, 5.26.

2-Methyl-6-(4-methylphenyl)-4-phenylpyridine (**3c**).

This compound had mp 95-96°; ¹H nmr: δ 2.41 (s, 3H), 2.69 (s, 3H), 7.28 (d, *J* = 8.1 Hz, 2H), 7.29 (s, 1H), 7.45-7.69 (m, 5H), 7.69 (s, 1H), 7.94 (d, *J* = 8.1 Hz, 2H); ms: *m/z* (ion, relative intensity) 259 (M⁺, 100), 258 (33), 244 (53); ir (potassium bromide): 1600 cm⁻¹.

Anal. Calcd. for C₁₆H₁₇N: C, 87.99; H, 6.61; N, 5.40. Found: C, 88.15; H, 6.47; N, 5.18.

6-(4-Chlorophenyl)-2-methyl-4-phenylpyridine (**3d**).

This compound had mp 102-103°; ¹H nmr: δ 2.68 (s, 3H), 7.33 (d, *J* = 1.7 Hz, 1H), 7.45 (d, *J* = 8.5 Hz, 2H), 7.47-7.68 (m, 5H), 7.68 (d, *J* = 1.7 Hz, 1H), 7.99 (d, *J* = 8.5 Hz, 2H); ms: *m/z* (ion, relative intensity) 279 (M⁺, 34), 271 (20), 270 (100), 269 (77); ir (potassium bromide): 1600 cm⁻¹.

Anal. Calcd. for C₁₈H₁₄ClN: C, 77.28; H, 5.04; N, 5.01. Found: C, 77.49; H, 4.95; N, 5.21.

6-(*t*-Butyl)-2-methyl-4-phenylpyridine (**3e**).

This compound had mp 47.5-48°; ¹H nmr: δ 1.40 (s, 9H), 2.59 (s, 3H), 7.15 (d, *J* = 1.3 Hz, 1H), 7.32 (d, *J* = 1.3 Hz, 1H), 7.39-7.62 (m, 5H); ms: *m/z* (ion, relative intensity) 225 (M⁺, 34), 224 (45), 210 (100), 183 (48), 169 (22); ir (potassium bromide): 1610 cm⁻¹.

Anal. Calcd. for C₁₆H₁₉N: C, 85.29; H, 8.50; N, 6.22. Found: C, 85.08; H, 8.57; N, 6.31.

4-(4-Methoxyphenyl)-2-methyl-6-phenylpyridine (**3f**).

This compound had mp 87-89°; ¹H nmr: δ 2.64 (s, 3H), 3.79 (s, 3H), 7.00 (d, *J* = 8.5 Hz, 2H), 7.22 (d, *J* = 1.3 Hz, 1H), 7.37-7.48 (m, 3H), 7.57 (d, *J* = 8.5 Hz, 2H), 7.65 (d, *J* = 1.3 Hz, 1H), 8.01 (d, *J* = 8.5 Hz, 2H); ms: *m/z* (ion, relative intensity) 275 (M⁺, 100), 260 (40); ir (potassium bromide): 1610 cm⁻¹.

Anal. Calcd. for C₁₉H₁₇NO: C, 82.88; H, 6.22; N, 5.09. Found: C, 83.07; H, 6.26; N, 4.92.

2-Methyl-4-(4-methylphenyl)-6-phenylpyridine (**3g**).

This compound had mp 60-61°; ¹H nmr: δ 2.37 (s, 3H), 2.65 (s, 3H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.25 (d, *J* = 0.9 Hz, 1H), 7.34-7.48 (m, 3H), 7.53 (d, *J* = 8.1 Hz, 2H), 7.67 (d, *J* = 0.9 Hz, 1H), 8.02 (d, *J* = 8.1 Hz, 2H); ms: *m/z* (ion, relative intensity) 259 (M⁺, 100); ir (potassium bromide): 1600 cm⁻¹.

Anal. Calcd. for C₁₉H₁₇N: C, 87.99; H, 6.61; N, 5.40. Found: C, 87.77; H, 6.58; N, 5.49.

4-(4-Chlorophenyl)-2-methyl-6-phenylpyridine (**3h**).

This compound had mp 90-92°; ¹H nmr: δ 2.66 (s, 3H), 7.23 (s, 1H), 7.39-7.54 (m, 3H), 7.45 (d, *J* = 8.6 Hz, 2H), 7.56 (d, *J* = 8.6 Hz, 2H), 7.63 (s, 1H), 8.01 (d, *J* = 8.6 Hz, 2H); ms: *m/z* (ion relative intensity) 279 (M⁺, 100); ir (potassium bromide): 1605 cm⁻¹.

Anal. Calcd. for C₁₈H₁₄ClN: C, 77.28; H, 5.04; N, 5.01. Found: C, 77.42; H, 5.00; N, 5.01.

4,6-Di(4-methoxyphenyl)-2-methylpyridine (**3i**).

This compound had mp 115-116°; ¹H nmr: δ 2.66 (s, 3H), 3.87 (s, 6H), 7.00 (d, *J* = 9.0 Hz, 2H), 7.02 (d, *J* = 9.0 Hz, 2H), 7.23 (d,

J = 1.3 Hz, 1H), 7.63 (d, J = 1.3 Hz, 1H), 7.63 (d, J = 9.0 Hz, 2H), 7.98 (d, 9.0 Hz, 2H); ms m/z (ion, relative intensity) 305 (M⁺, 100), 290 (26); ir (potassium bromide): 1610 cm⁻¹.

Anal. Calcd. for C₂₀H₁₉NO₂: C, 78.66; H, 6.27; N, 4.59. Found: C, 78.85; H, 6.17; N, 4.79.

4-(2-Furyl)-2-methyl-6-phenylpyridine (3j).

This compound is an oil; ¹H nmr: δ 2.65 (s, 3H), 6.54 (dd, J = 3.4 and 1.7 Hz, 1H), 6.90 (d, J = 3.4 Hz, 1H), 7.35 (d, J = 1.3 Hz, 1H), 7.41-7.51 (m, 3H), 7.56 (d, J = 1.7 Hz, 1H), 7.77 (d, J = 1.3 Hz, 1H), 8.02 (d, J = 8.5 Hz, 2H); ms: m/z (ion, relative intensity) 235 (M⁺, 92), 234 (100); ir (neat): 1610 cm⁻¹.

Anal. Calcd. for C₁₆H₁₃NO: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.52; H, 5.71; N, 5.90.

4,6-Di(2-furyl)-2-methylpyridine (3k).

This compound had mp 98-99°; ¹H nmr: δ 2.59 (s, 3H), 6.48 (dd, J = 3.4 and 1.7 Hz, 1H), 6.51 (dd, J = 3.4 and 1.7 Hz, 1H), 6.85 (d, J = 3.4 Hz, 1H), 7.06 (d, J = 3.4 Hz, 1H), 7.23 (d, J = 1.3 Hz, 1H), 7.51 (d, J = 1.7 Hz, 1H), 7.53 (d, J = 1.7 Hz, 1H), 7.71 (d, J = 1.3 Hz, 1H); ms: m/z (ion, relative intensity) 225 (M⁺, 100); ir (potassium bromide): 1610 cm⁻¹.

Anal. Calcd. for C₁₄H₁₁NO₂: C, 74.65; H, 4.92; N, 6.22. Found: C, 74.89; H, 4.81; N, 6.42.

2-Methyl-6-phenyl-4-(2-thienyl)pyridine (3l).

This compound is an oil; ¹H nmr: δ 2.66 (s, 3H), 7.15 (dd, J = 5.2 and 3.7 Hz, 1H), 7.31 (d, J = 1.1 Hz, 1H), 7.41 (d, J = 5.2 Hz, 1H), 7.42-7.52 (m, 3H), 7.54 (d, J = 3.7 Hz, 1H), 7.70 (d, J = 1.1 Hz, 1H), 8.01 (d, J = 8.3 Hz, 2H); ms: m/z (ion, relative intensity) 251 (M⁺, 100); ir (neat): 1605 cm⁻¹.

Anal. Calcd. for C₁₆H₁₃NS: C, 76.46; H, 5.21; N, 5.57. Found: C, 76.34; H, 5.16; N, 5.73.

2-Methyl-4,6-di(2-thienyl)pyridine (3m).

This compound had mp 94.5-95.5°; ¹H nmr: δ 2.60 (s, 3H), 7.12 (dd, J = 5.1 and 3.4 Hz, 1H), 7.14 (dd, J = 5.1 and 3.4 Hz, 1H), 7.21 (d, J = 1.3 Hz, 1H), 7.38 (d, J = 5.1 Hz, 1H), 7.40 (d, J = 5.1 Hz, 1H), 7.52 (d, J = 3.4 Hz, 1H), 7.63 (d, J = 3.4 Hz, 1H), 7.63 (d, J = 1.3 Hz, 1H); ms: m/z (ion, relative intensity) 257 (M⁺, 100); ir (potassium bromide): 1600 cm⁻¹.

Anal. Calcd. for C₁₄H₁₁NS₂: C, 65.33; H, 4.31; N, 5.44. Found: C, 65.06; H, 4.24; N, 5.58.

2-Methyl-4-phenyl-6-(2-pyridyl)pyridine (3n).

This compound is an oil; ¹H nmr: δ 2.71 (s, 3H), 7.31-7.52 (m, 5H), 7.74-7.77 (m, 2H), 7.83 (t, J = 7.7 Hz, 1H), 8.44 (s, 1H), 8.46 (d, J = 7.7 Hz, 1H), 8.71 (d, J = 4.7 Hz, 1H); ms: m/z (ion, relative intensity) 246 (M⁺, 100), 245 (34), 231 (45); ir (neat): 1600 cm⁻¹.

Anal. Calcd. for C₁₇H₁₄N₂: C, 82.90; H, 5.73; N, 11.37. Found: C, 82.98; H, 5.81; N, 11.20.

4-(4-Methoxyphenyl)-2-methyl-6-(2-pyridyl)pyridine (3o).

This compound had mp 93.5-95°; ¹H nmr: δ 2.68 (s, 3H), 3.87 (s, 3H), 7.01 (d, J = 8.9 Hz, 2H), 7.31 (dd, J = 7.7 and 4.7 Hz, 1H), 7.38 (d, J = 1.5 Hz, 1H), 7.72 (d, J = 8.9 Hz, 2H), 7.82 (t, J = 7.7 Hz, 1H), 8.41 (d, J = 1.5 Hz, 1H), 8.45 (d, J = 7.7 Hz, 1H), 8.70 (d, J = 4.7 Hz, 1H); ms: m/z (ion, relative intensity) 276 (M⁺, 100), 261 (37); ir (potassium bromide): 1605 cm⁻¹.

Anal. Calcd. for C₁₈H₁₆N₂O: C, 78.24; H, 5.84; N, 10.14. Found: C, 78.51; H, 5.98; N, 10.01.

4-(4-chlorophenyl)-2-methyl-6-(2-pyridyl)pyridine (3p).

This compound had mp 91-93°; ¹H nmr: δ 2.70 (s, 3H), 7.32 (dd, J = 7.7 and 4.7 Hz, 1H), 7.37 (d, J = 1.5 Hz, 1H), 7.46 (d, J = 8.6 Hz, 2H), 7.69 (d, J = 8.6 Hz, 2H), 7.83 (t, J = 7.7 Hz, 1H), 8.42 (d, J = 1.5 Hz, 1H), 8.47 (d, J = 7.7 Hz, 1H), 8.70 (d, J = 4.7 Hz, 1H); ms: m/z (ion, relative intensity) 280 (M⁺, 100), 279 (77), 265 (62); ir (potassium bromide): 1595 cm⁻¹.

Anal. Calcd. for C₁₇H₁₃ClN₂: C, 72.73; H, 4.67; N, 9.98. Found: C, 72.61; H, 4.58; N, 9.79.

2-Methyl-6-phenyl-4-(2-pyridyl)pyridine (3q).

This compound is an oil; ¹H nmr: δ 2.72 (s, 3H), 7.33-7.52 (m, 4H), 7.71 (d, 1.3 Hz, 1H), 7.82-7.85 (m, 2H), 8.06-8.09 (m, 2H), 8.12 (d, J = 1.3 Hz, 1H), 8.76-8.78 (m, 1H); ms: m/z (ion relative intensity) 246 (M⁺, 100), 245 (32); ir (neat): 1600 cm⁻¹.

Anal. Calcd. for C₁₇H₁₄N₂: C, 82.90; H, 5.73; N, 11.37. Found: C, 83.17; H, 5.77; N, 11.28.

6-(4-Methoxyphenyl)-2-methyl-4-(2-pyridyl)pyridine (3r).

This compound is an oil; ¹H nmr: δ 2.70 (s, 3H), 3.87 (s, 3H), 7.01 (d, J = 8.5 Hz, 2H), 7.34-7.37 (m, 1H), 7.65 (s, 1H), 7.82-7.85 (m, 2H), 8.05 (d, J = 8.5 Hz, 2H), 8.06 (s, 1H), 8.76 (d, J = 4.7 Hz, 1H); ms: m/z (ion, relative intensity) 276 (M⁺, 100), 261 (35); ir (neat): 1605 cm⁻¹.

Anal. Calcd. for C₁₈H₁₆N₂O: C, 78.24; H, 5.84; N, 10.14. Found: C, 78.41; H, 5.90; N, 10.02.

6-(4-Chlorophenyl)-2-methyl-4-(2-pyridyl)pyridine (3s).

This compound had mp 97.5-98°; ¹H nmr: δ 2.71 (s, 3H), 7.37 (dd, J = 8.1 and 4.7 Hz, 1H), 7.45 (d, J = 8.5 Hz, 2H), 7.70 (d, J = 1.3 Hz, 1H), 7.82-7.85 (m, 2H), 8.04 (d, J = 8.5 Hz, 2H), 8.12 (d, J = 1.3 Hz, 1H), 8.77 (d, J = 4.7 Hz, 1H); ms: m/z (ion, relative intensity) 280 (M⁺, 100); ir (potassium bromide): 1600 cm⁻¹.

Anal. Calcd. for C₁₇H₁₃ClN₂: C, 72.73; H, 4.67; N, 9.98. Found: C, 72.68; H, 4.72; N, 10.09.

6-Ferrocenyl-2-methyl-4-phenylpyridine (3t).

This compound had mp 117-118°; ¹H nmr: δ 2.61 (s, 3H), 4.06 (s, 5H), 4.38 (s, 2H), 4.96 (s, 2H), 7.15 (s, 1H), 7.45-7.67 (m, 6H); ms: m/z (ion, relative intensity) 353 (M⁺, 100), 288 (46); ir (potassium bromide): 1595 cm⁻¹.

Anal. Calcd. for C₂₂H₁₉FeN: C, 74.80; H, 5.42; N, 3.97. Found: C, 74.88; H, 5.57; N, 3.82.

4-Ferrocenyl-2-methyl-6-phenylpyridine (3u).

This compound had mp 101-101.5°; ¹H nmr: δ 2.63 (s, 3H), 4.08 (s, 5H), 4.43 (t, J = 1.7 Hz, 2H), 4.77 (t, J = 1.7 Hz, 2H), 7.16 (d, J = 1.0 Hz, 1H), 7.41-7.52 (m, 3H), 7.56 (d, J = 1.0 Hz, 1H), 8.00 (d, J = 9.8 Hz, 2H); ms: m/z (ion, relative intensity) 353 (M⁺, 100), 352 (82); ir (potassium bromide): 1605 cm⁻¹.

Anal. Calcd. for C₂₂H₁₉FeN: C, 74.80; H, 5.42; N, 3.97. Found: C, 74.71; H, 5.34; N, 4.09.

4,6-Diferrocenyl-2-methylpyridine (3v).

This compound had mp 172-173°; ¹H nmr: δ 2.56 (s, 3H), 4.07 (s, 10H), 4.38 (t, J = 1.7 Hz, 2H), 4.42 (t, J = 1.7 Hz, 2H), 4.75 (t, J = 1.7 Hz, 2H), 4.95 (t, J = 1.7 Hz, 2H), 6.99 (s, 1H), 7.31 (s, 1H); ms: m/z (ion, relative intensity) 461 (M⁺, 100); ir (potassium bromide): 1600 cm⁻¹.

Anal. Calcd. for C₂₆H₂₃Fe₂N: C, 67.72; H, 5.03; N, 3.04. Found: C, 67.68; H, 5.09; N, 3.16.

2-Methyl-4,6-diphenylpyridine (**4a**).

This compound had mp 225-227° (lit [8] mp 216°).

6-(4-Methoxyphenyl)-2-methyl-4-phenylpyridine-3-carboxamide (**4b**).

This compound had mp 175-177°; ¹H nmr: δ 2.75 (s, 3H), 3.87 (s, 3H), 5.33 (br s, 1H), 5.53 (br s, 1H), 7.00 (d, J = 8.8 Hz, 2H), 4.5-7.56 (m, 6H), and 8.00 (d, J = 8.8 Hz, 2H); ms: m/z (ion, relative intensity) 318 (M⁺, 100); ir (potassium bromide): 3340, 3170 cm⁻¹.

Anal. Calcd. for C₂₀H₁₈N₂O₂: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.27; H, 5.85; N, 8.92.

2-Methyl-6-(4-methylphenyl)-4-phenylpyridine-3-carboxamide (**4c**).

This compound had mp 256-258°; ¹H nmr: δ 2.41 (s, 3H), 2.76 (s, 3H), 5.35 (br s, 1H), 5.56 (br s, 1H), 7.29 (d, J = 8.2 Hz, 2H), 7.45-7.57 (m, 6H), and 7.94 (d, J = 8.2 Hz, 2H); ms: m/z (ion, relative intensity) 302 (M⁺, 100); ir (potassium bromide): 3375, 3190 cm⁻¹.

Anal. Calcd. for C₂₀H₁₈N₂O: C, 79.44; H, 6.00; N, 9.26. Found: C, 79.18; H, 6.08; N, 9.12.

6-(4-Chlorophenyl)-2-methyl-4-phenylpyridine-3-carboxamide (**4d**).

This compound had mp 258-261°; ¹H nmr: δ 2.76 (s, 3H), 5.34 (br s, 1H), 5.57 (br s, 1H), 7.43-7.57 (m, 8H), and 7.99 (d, J = 8.8 Hz, 2H); ms: m/z (ion, relative intensity) 322 (M⁺, 100) and 321 (28); ir (potassium bromide): 3375, 3190, and 1690 cm⁻¹.

Anal. Calcd. for C₁₉H₁₅ClN₂O: C, 70.70; H, 4.68; N, 8.68. Found: C, 70.87; H, 4.81; N, 8.49.

6-(*t*-Butyl)-2-methyl-4-phenylpyridine-3-carboxamide (**4e**).

This compound had mp 196-198°; ¹H nmr: δ 1.37 (s, 9H), 2.66 (s, 3H), 5.31 (br s, 1H), 5.65 (br s, 1H), 7.14 (s, 1H), and 7.41-7.51 (m, 5H); ms: m/z (ion, relative intensity) 268 (M⁺, 41), 267 (44), 253 (100), and 226 (91); ir (potassium bromide): 3370, 3190, and 1650 cm⁻¹.

Anal. Calcd. for C₁₇H₂₀N₂O: C, 76.09; H, 7.51; N, 10.44. Found: C, 75.93; H, 7.59; N, 10.32.

4-(4-Methoxyphenyl)-2-methyl-6-phenylpyridine-3-carboxamide (**4f**).

This compound had mp 240-241°; ¹H nmr: δ 2.76 (s, 3H), 3.87 (s, 3H), 5.36 (br s, 1H), 7.00 (d, J = 8.4 Hz, 2H), 7.43-7.55 (m, 7H), and 8.02 (d, J = 8.4 Hz, 2H); ms: m/z (ion, relative intensity) 318 (M⁺, 100); ir (potassium bromide): 3370, 3190, and 1685 cm⁻¹.

Anal. Calcd. for C₂₀H₁₈N₂O₂: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.28; H, 5.79; N, 8.92.

2-Methyl-4-(4-methylphenyl)-6-phenylpyridine-3-carboxamide (**4g**).

This compound had mp 223-226°; ¹H nmr: δ 2.42 (s, 3H), 2.77 (s, 3H), 5.36 (br s, 1H), 5.55 (br s, 1H), 7.28 (d, J = 8.1 Hz, 2H), 7.43-7.51 (m, 5H), 7.56 (s, 1H), and 8.02 (d, J = 8.1 Hz, 2H); ms: m/z (ion, relative intensity) 302 (M⁺, 100); ir (potassium bromide): 3325, 3180, and 1655 cm⁻¹.

Anal. Calcd. for C₂₀H₁₈N₂O: C, 79.44; H, 6.00; N, 9.26. Found: C, 79.54; H, 5.82; N, 9.22.

4-(4-Chlorophenyl)-2-methyl-6-phenylpyridine-3-carboxamide (**4h**).

The compound had mp 258-161°; ¹H nmr (DMSO-d₆): δ 2.61 (s,

3H), 7.43-7.64 (m, 8H), 7.72 (s, 1H), 7.89 (br s, 1H), and 8.13 (br s, 2H); ms: m/z (ion, relative intensity) 322 (M⁺, 100); ir (potassium bromide): 3310, 3155, and 1670 cm⁻¹.

Anal. Calcd. for C₁₉H₁₅ClN₂O: C, 70.70; H, 4.68; N, 8.68. Found: C, 70.55; H, 4.52; N, 8.92.

4,6-Di(4-methoxyphenyl)-2-methylpyridine-3-carboxamide (**4i**).

This compound had mp 246-248°; ¹H nmr: δ 2.73 (s, 3H), 3.86 (s, 3H), 3.87 (s, 3H), 5.35 (br s, 1H), 5.56 (br s, 1H), 6.99-7.00 (m, 4H), 7.43 (s, 1H), 7.49-7.52 (m, 2H), and 7.98-8.00 (m, 2H); ms: m/z (ion, relative intensity) 348 (M⁺, 100), 332 (43), and 331 (27); ir (potassium bromide): 3360, 3190, and 1685 cm⁻¹.

Anal. Calcd. for C₂₁H₂₀N₂O₃: C, 72.40; H, 5.79; N, 8.04. Found: C, 72.46; H, 5.62; N, 8.25.

4-(2-Furyl)-2-methyl-6-phenylpyridine-3-carboxamide (**4j**).

This compound had mp 167-168°; ¹H nmr: δ 2.72 (s, 3H), 5.83 (br s, 1H), 5.92 (br s, 1H), 6.53 (dd, J = 3.4 and 1.7 Hz, 1H), 7.05 (d, J = 3.4 Hz, 1H), 7.43-7.52 (m, 3H), 7.58 (d, J = 1.7 Hz, 1H), 7.89 (s, 1H), and 8.02 (d, J = 8.1 Hz, 2H); ms: m/z (ion relative intensity) 278 (M⁺, 100), 250 (39), 249 (55), and 235 (55); ir (potassium bromide): 3325, 3180, and 1660 cm⁻¹.

Anal. Calcd. for C₁₇H₁₄N₂O₂: C, 73.37; H, 5.07; N, 10.08. Found: C, 73.46; H, 5.22; N, 9.89.

4,6-Di(2-furyl)-2-methylpyridine-3-carboxamide (**4k**).

This compound had mp 160-163°; ¹H nmr: δ 2.68 (s, 3H), 5.76 (br s, 1H), 5.85 (br s, 1H), 6.53 (dd, J = 3.4 and 1.7 Hz, 1H), 6.55 (dd, J = 3.4 and 1.7 Hz, 1H), 7.05 (d, J = 3.4 Hz, 1H), 7.12 (d, J = 3.4 Hz, 1H), 7.57 (d, J = 1.7 Hz, 1H), 7.59 (d, J = 1.7 Hz, 1H), and 7.85 (s, 1H); ms: m/z (ion, relative intensity) 268 (M⁺, 100); ir (potassium bromide): 3310, 3155, and 1665 cm⁻¹.

Anal. Calcd. for C₁₅H₁₂N₂O₃: C, 67.16; H, 4.51; N, 10.44. Found: C, 67.28; H, 4.35; N, 10.22.

2-Methyl-6-phenyl-4-(2-thienyl)pyridine-3-carboxamide (**4l**).

This compound had mp 201-201.5°; ¹H nmr: δ 2.73 (s, 3H), 5.68 (br s, 1H), 5.87 (br s, 1H), 7.12 (dd, J = 5.1 and 3.9 Hz, 1H), 7.45 (dd, J = 5.1 and 1.3 Hz, 1H), 7.49 (dd, J = 3.9 and 1.3 Hz, 1H), 7.43-7.52 (m, 3H), 7.64 (s, 1H), and 8.00 (d, J = 7.9 Hz, 2H); ms: m/z (ion, relative intensity) 294 (M⁺, 100); ir (potassium bromide): 3350, 3160, and 1660 cm⁻¹.

Anal. Calcd. for C₁₇H₁₄N₂OS: C, 69.36; H, 4.79; N, 9.52. Found: C, 69.17; H, 4.62; N, 9.48.

2-Methyl-4,6-di(2-thienyl)pyridine-3-carboxamide (**4m**).

This compound had mp 178-180°; ¹H nmr: δ 2.67 (s, 3H), 5.65 (br s, 1H), 5.85 (br s, 1H), 7.10-7.14 (m, 2H), 7.41-7.48 (m, 3H), 7.55 (s, 1H), and 7.63 (d, J = 3.9 Hz, 1H); ms: m/z (ion, relative intensity) 300 (M⁺, 100) and 284 (28); ir (potassium bromide): 3380, 3190, and 1690 cm⁻¹.

Anal. Calcd. for C₁₅H₁₂N₂O₂S: C, 59.98; H, 4.03; N, 9.33. Found: C, 59.78; H, 4.18; N, 9.17.

2-Methyl-4-phenyl-6-(2-pyridyl)pyridine-3-carboxamide (**4n**).

This compound had mp 199-200°; ¹H nmr: δ 2.63 (s, 3H), 7.45-7.61 (m, 7H), 7.92-8.00 (m, 2H), 8.18 (s, 1H), 8.43 (d, J = 8.1 Hz, 1H), and 8.68 (d, J = 4.7 Hz, 1H); ms: m/z (ion, relative intensity) 289 (M⁺, 100), 288 (32), and 273 (56); ir (potassium bromide): 3380, 3165, and 1655 cm⁻¹.

Anal. Calcd. for C₁₈H₁₅N₃O: C, 74.72; H, 5.23; N, 14.52. Found:

C, 74.52; H, 5.08; N, 14.68.

4-(4-Methoxyphenyl)-2-methyl-6-(2-pyridyl)pyridine-3-carboxamide (**4o**).

This compound had mp 229-230°; ¹H nmr: δ 2.61 (s, 3H), 3.81 (s, 3H), 7.05 (d, J = 8.6 Hz, 2H), 7.48 (dd, J = 7.7 and 4.7 Hz, 1H), 7.54-7.57 (m, 3H), 7.89 (br s, 1H), 7.97 (t, J = 7.7 Hz, 1H), 8.17 (s, 1H), 8.42 (d, J = 7.7 Hz, 1H), and 8.68 (d, J = 4.7 Hz, 1H); ms: m/z (ion, relative intensity) 319 (M⁺, 100) and 303 (12); ir (potassium bromide): 3325, 3155, and 1670 cm⁻¹.

Anal. Calcd. for C₁₉H₁₇N₃O₂: C, 71.46; H, 5.37; N, 13.16. Found: C, 71.31; H, 5.05; N, 13.32.

4-(4-Chlorophenyl)-2-methyl-6-(2-pyridyl)pyridine-3-carboxamide (**4p**).

This compound had mp 246-247°; ¹H nmr: δ 2.63 (s, 3H), 7.48 (dd, J = 7.9 and 4.9 Hz, 1H), 7.54-7.62 (m, 5H), 7.95-8.00 (m, 2H), 8.18 (s, 1H), 8.43 (d, J = 7.9 Hz, 1H), and 8.69 (d, J = 4.9 Hz, 1H); ms: m/z (ion, relative intensity) 323 (M⁺, 100), 322 (33), and 307 (17); ir (potassium bromide): 3335, 3190, and 1660 cm⁻¹.

Anal. Calcd. for C₁₈H₁₄ClN₃O: C, 66.78; H, 4.36; N, 12.98. Found: C, 66.59; H, 4.32; N, 13.07.

6-Ferrocenyl-2-methyl-4-phenylpyridine-3-carboxamide (**4t**).

This compound had mp > 300°; ¹H nmr: δ 2.69 (s, 3H), 4.06 (s,

5H), 4.42 (t, J = 1.7 Hz, 2H), 4.05 (t, J = 1.7 Hz, 2H), 5.30 (br s, 1H), 5.53 (br s, 1H), 7.24 (s, 1H), and 7.42-7.57 (m, 5H); ms: m/z (ion, relative intensity) 3.96 (M⁺, 100); ir (potassium bromide): 3345, 3190, and 1660 cm⁻¹.

Anal. Calcd. for C₂₃H₂₀FeN₂O: C, 69.71; H, 5.09; N, 7.07. Found: C, 69.57; H, 5.01; N, 13.23.

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