Synthesis of 3-Cyano-2-methylpyridines Substituted with Heteroaromatics

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A series of title compounds were easily prepared by the sonication of α,β-unsaturated carbonyl compound in acetonitrile in the presence of potassium *t*-butoxide.

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Introduction.

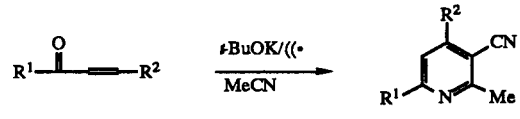
Many synthetic methods have been reported for substituted pyridines [1]. However, there are a few reports on the preparation of pyridines substituted with heteroaromatics [2]. Ultrasound has proved to be a convenient and effective method to accelerate slow reactions. Recently, we have reported syntheses of pyridines under ultrasound irradiation [3]. Since 3-cyanopyridines can be easily converted into the corresponding nicotinic acids, synthesis of heteroaromatic 3-cyanopyridines is of interest from a medicinal viewpoint. In this report, a convenient synthesis of the title compounds has been explored.

Results and Discussion.

In a typical procedure, an acetonitrile suspension (20 ml) containing potassium *t*-butoxide (110 mg) was sonicated for 15 minutes at 35°. 1,3-Di-(2-furyl)propen-1-one (**1n**, 10 mmoles) was added to the suspension, followed by sonication for another 2 hours. After the reaction, the suspension was poured into brine (50 ml) and extracted with ether (30 ml x 2). The extract was dried over sodium sulfate. The solvent was removed and the residue was recrystallized from ethanol. 3-Cyano-4,6-di-(2-furyl)-2-methylpyridine (**2n**) was obtained in 93% yield and identified on the basis of the following spectral data. The ^{1}H nmr spectrum showed δ at 2.79 (s, 3H, Me), 6.57 (dd, J = 3.6 and 1.8 Hz, 1H, H^f), 6.61 (dd, J = 3.6 and 1.8 Hz, 1H, H^b), 7.20 (d, J = 3.6 Hz, 1H, H^e), 7.57 (d, J = 3.6 Hz, 1H, H^a), 7.59 (d, J = 1.8 Hz, 1H, H^g), 7.62 (d, J = 1.8 Hz, 1H, H^c), and 7.91 (s, 1H, H^d) ppm as shown in Figure 1. The ^{13}C nmr spectrum showed δ at 24.3 (q), 99.5 (s), 110.6 (d), 111.9 (d), 112.6 (d), 112.8 (d), 113.9 (d), 117.7 (s), 140.3 (s), 144.8 (2 peaks, d and d), 148.2 (s), 150.7 (s), 152.6 (s), and 163.2 (s) ppm. The ir spectrum showed characteristic absorption at 2250 cm^{-1}, suggesting a cyano group in the molecule. Surprisingly the EI mass spectrum revealed M^+ ion peak at m/z 250 with few fragmentation. The elemental analysis gave satisfactory data consistent with the structure.

A wide variety of 3-cyano-2-methylpyridines **2** substituted with heteroaromatics at 4 and 6 positions were obtained in satisfactory yields as shown in Table 1. When the R^1 was 2-pyrrolyl group or R^1 and R^2 were heteroaromatics and 2-pyridyl groups respectively in the α,β-unsaturated carbonyl compound **1**, no corresponding 3-cyano-2-methylpyridines were obtained.

Table 1
Synthesis of 3-Cyano-2-methylpyridines
Substituted with Heteroaromatics



1 **2**

Run	Compound	R^1	R^2	Isolated yield of **2**, %
1	**a**	phenyl	2-furyl	87
2	**b**	phenyl	2-thienyl	80
3	**c**	phenyl	2-pyrrolyl	62
4	**d**	phenyl	2-pyridyl	54
5	**e**	4-chlorophenyl	2-furyl	85
6	**f**	4-chlorophenyl	2-thienyl	71
7	**g**	4-chlorophenyl	2-pyrroyl	86
8	**h**	4-chlorophenyl	2-pyridyl	72
9	**i**	4-methoxyphenyl	2-furyl	36
10	**j**	4-methoxyphenyl	2-thienyl	69
11	**k**	4-methoxyphenyl	2-pyrrolyl	62
12	**l**	4-methoxyphenyl	2-pyridyl	70
13	**m**	2-furyl	phenyl	77
14	**n**	2-furyl	2-furyl	93
15	**o**	2-furyl	2-thienyl	66
16	**p**	2-furyl	2-pyrrolyl	63
17	**q**	2-thienyl	phenyl	59
18	**r**	2-thienyl	2-furyl	71
19	**s**	2-thienyl	2-thienyl	86
20	**t**	2-thienyl	2-pyrrolyl	74
21	**u**	2-pyridyl	phenyl	63
22	**v**	2-pyridyl	2-furyl	63
23	**w**	2-pyridyl	2-thienyl	67
24	**x**	2-pyridyl	2-pyrrolyl	75

EXPERIMENTAL

Instruments.

Sonication was carried out using a Branson ultra sonic cleaner (150 W, 47 KHz). Melting points were measured with a Yanagimoto micro melting point apparatus and uncorrected.

Nmr spectra were recorded with a JEOL GX-270 spectrometer. The sample was dissolved in deuteriochloroform and referred to internal TMS. Mass spectra were obtained on a Shimadzu QP-1000 spectrometer (EI, 70 eV, direct insertion). Elemental analyses were recorded using a Yamato CHN recorder MT-3.

Syntheses of α,β-Unsaturated Carbonyl Compounds.

In a general procedure, to an ethanol solution (15 ml) containing the acetyl compound (0.02 mole) and 10% aqueous potassium hydroxide (15 ml) was added the aldehyde (0.02 mole) and stirred for 2 hours at room temperature. After the reaction, the precipitate was filtered and recrystallized from methanol. Their physical data are shown below:

3-(2-Furyl)-1-phenylpropen-1-one (**1a**).

This compound had mp 44-45° [lit [4] mp 46°].

1-Phenyl-3-(2-thienyl)propen-1-one (**1b**).

This compound had mp 57-58° [lit [5] mp 58.4-59.2°].

1-Phenyl-3-(2-pyrrolyl)propen-1-one (**1c**).

This compound had mp 128-129° [lit [6] mp 133-134°].

1-Phenyl-3-(2-pyridyl)propen-1-one (**1d**).

This compound had mp 121-122° [lit [7] mp 119-121°].

1-(4-Chlorophenyl)-3-(2-furyl)propen-1-one (**1e**).

This compound had mp 72-73° [lit [8] mp 101°]; ^{1}H nmr: δ 6.51 (dd, J = 3.3 and 1.5 Hz, 1H), 6.72 (d, J = 3.3 Hz, 1H), 7.39 (d, J = 15.4 Hz, 1H), 7.46 (d, J = 8.4 Hz, 1H), 7.52 (d, J = 1.5 Hz, 1H), 7.59 (d, J = 15.4 Hz, 1H), 7.96 (d, J = 8.4 Hz, 1H); ms: m/z (ion, relative intensity) 232 (M^+, 61), 141 (48), 139 (100), 65 (47).

1-(4-Chlorophenyl)-3-(2-thienyl)propen-1-one (**1f**).

This compound had mp 116-118°; ^{1}H nmr: δ 7.10 (dd, J = 5.1 and 3.8 Hz, 1H), 7.27 (d, J = 15.4 Hz, 1H), 7.37 (d, J = 3.8 Hz, 1H), 7.43 (d, J = 5.1 Hz, 1H), 7.47 (d, J = 8.9 Hz, 2H), 7.95 (d, J = 8.9 Hz, 2H), 7.95 (d, J = 15.4 Hz, 1H); ms: (ion, relative intensity) m/z 248 (M^+, 45), 213 (100), 139 (35), 137 (59), 111 (41), 109 (48), 65 (31).

Anal. Calcd. for $C_{13}H_9OSCl$: C, 62.78; H, 3.65. Found: C, 62.86; H, 3.43.

1-(4-Chlorophenyl)-3-(2-pyrrolyl)propen-1-one (**1g**).

This compound had mp 191-193°; ^{1}H nmr: δ 6.37 (dd, J = 3.8 and 2.6 Hz, 1H), 6.71 (d, J = 2.6 Hz, 1H), 7.00 (d, J = 3.8 Hz, 1H), 7.06 (d, J = 15.6 Hz, 1H), 7.44 (d, J = 8.5 Hz, 2H), 7.72 (d, J = 15.6 Hz, 1H), 7.92 (d, J = 8.5 Hz, 2H), 8.71 (br s, 1H); ms: m/z (ion, relative intensity) 231 (M^+, 100), 202 (21), 196 (38), 167 (28), 120 (54), 92 (46), 67 (47), 65 (25).

Anal. Calcd. for $C_{13}H_{10}NOCl$: C, 67.40; H, 4.35; H, 6.05. Found: C, 67.58; H, 4.28; N, 6.19.

1-(4-Chlorophenyl)-3-(2-pyridyl)propen-1-one (**1h**).

This compound had mp 96-97° [lit [7] mp 85-86°]; ^{1}H-nmr: δ 7.06 (dd, J = 7.7 and 3.8 Hz, 1H), 7.37 (d, J = 4.7 Hz, 2H), 7.38 (d, J = 11.3 Hz, 1H), 7.56 (dd, 7.7 and 7.7 Hz, 1H), 7.85 (d, J = 7.7 Hz, 1H), 7.86 (d, J = 11.3 Hz, 1H), 7.87 (d, J = 4.7 Hz, 2H), 8.45 (d, J = 3.8 Hz, 1H); ms: m/z (ion, relative intensity) 243 (M^+, 32), 214 (100), 132 (41), 104 (40).

3-(2-Furyl)-1-(4-methoxyphenyl)propen-1-one (**1i**).

This compound had mp 79-80°; ^{1}H nmr: δ 3.87 (s, 3H), 6.50 (dd, J = 2.9 and 1.5 Hz, 1H), 6.69 (d, J = 2.9 Hz, 1H), 6.97 (d, J = 8.8 Hz, 2H), 7.45 (d, J = 15.4 Hz, 1H), 7.51 (d, J = 1.5 Hz, 1H), 7.58 (d, J = 15.4 Hz, 1H), 8.04 (d, J = 8.8 Hz, 2H); ms: m/z (ion, relative intensity) 228 (M^+, 100), 174 (37), 135 (90).

Anal. Calcd. for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30. Found: C, 73.58; H, 5.12.

1-(4-Methoxyphenyl)-3-(2-thienyl)propen-1-one (**1j**).

This compound had mp 100-102° [lit [9] mp 106-107°].

1-(4-Methoxyphenyl)-3-(2-pyrrolyl)propen-1-one (**1k**).

This compound had mp 113-115°; ^{1}H nmr: δ 3.87 (s, 3H), 6.32 (dd, J = 2.6 and 2.6 Hz, 1H), 6.69 (d, J = 2.6 Hz, 1H), 6.92 (d, J = 2.6 Hz, 1H), 6.94-6.98 (m, 2H), 7.18 (d, J = 15.4 Hz, 1H), 7.74 (d, J = 15.4 Hz, 1H), 7.95 (m, 2H), 9.11 (br s, 1H); ms: m/z (ion, relative intensity) 227 (M^+, 100), 198 (27), 150 (27), 130 (38), 92 (32).

Anal. Calcd. for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 74.12; H, 5.58; N, 6.24.

1-(4-Methoxyphenyl)-3-(2-pyridyl)propen-1-one (**1l**).

This compound had 59-61°; ^{1}H nmr: δ 3.88 (s, 3H), 6.98 (dd, J = 9.2 and 4.4 Hz, 1H), 7.28 (s, 4H), 7.47 (d, J = 7.7 Hz, 1H), 7.76 (d, J = 16.0 Hz, 1H), 8.11 (dd, J = 9.2 and 7.7 Hz, 1H), 8.14 (d, J = 16.0 Hz, 1H), 8.68 (d, J = 4.4 Hz, 1H); ms: m/z (ion, relative intensity) 239 (M^+, 44), 210 (100), 135 (40), 104 (22).

Anal Calcd. for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.42; H, 5.31; N, 5.98.

1-(2-Furyl)-3-phenylpropen-1-one (**1m**).

This compound had mp 89-90° [lit [10] mp 89-89.5°].

1,3-Di-(2-furyl)propen-1-one (**1n**).

This compound had mp 88-89° [lit [4] mp 88-89°].

1-(2-Furyl)-3-(2-thienyl)propen-1-one (**1o**).

This compound had mp 74-75° [lit [4] mp 82°].

1-(2-Furyl)-3-(2-pyrrolyl)propen-1-one (**1p**).

This compound had mp 182-183°; ^{1}H nmr: δ 6.33 (dd, J = 2.5 and 2.1 Hz, 1H), 6.57 (dd, J = 1.7 and 1.7 Hz, 1H), 6.72 (d, J = 2.5 Hz, 1H), 7.00 (d, J = 2.1 Hz, 1H), 7.06 (d, J = 15.7 Hz, 1H), 7.27 (d, J = 1.7 Hz, 1H), 7.61 (d, J = 1.7 Hz, 1H), 7.80 (d, J = 15.7 Hz, 1H), 9.00 (br s, 1H); ms: m/z (ion, relative intensity) 187 (M^+, 100), 158 (43), 130 (53), 92 (23).

Anal. Calcd. for $C_{11}H_9NO_2$: C, 70.58; H, 4.85; N, 7.48. Found: C, 70.68; H, 4.68; N, 7.61.

3-Phenyl-1-(2-thienyl)propen-1-one (**1q**).

This compound mp had 73-74° [lit [5] mp 83.6-84.0°].

3-(2-Furyl)-1-(2-thienyl)propen-1-one (**1r**).

This compound had mp 71-72° [lit [5] mp 70.8-71.6°].

1,3-Di-(2-thienyl)propen-1-one (**1s**).

This compound had mp 99-100° [lit [5] mp 99-100°].

3-(2-Pyrrolyl)-1-(2-thienyl)propen-1-one (**1t**).

This compound had mp 159-160° [lit [11] mp 158-160°].

3-Phenyl-1-(2-pyridyl)propen-1-one (**1u**).

This compound had mp 64-65° [lit [7] mp 75°].

3-(2-Furyl)-1-(2-pyridyl)propen-1-one (**1v**).

This compound had mp 51-53° [lit [12] mp 53-54°].

1-(2-Pyridyl)-3-(2-thienyl)propen-1-one (**1w**).

This compound had mp 155-156°; ^{1}H nmr δ 7.07 (dd, J = 4.9 and 3.4 Hz, 1H), 7.39-7.49 (m, 3H), 7.84 (td, J = 7.2 and 1.5 Hz, 1H), 8.06 (s, 2H), 8.16 (d, J = 7.2 Hz, 1H), 8.72 (dd, J = 4.3 and 1.5 Hz, 1H); ms: m/z (ion, relative intensity) 215 (M^+, 100), 186 (90), 137 (50), 109 (45).

Anal. Calcd. for $C_{12}H_9NOS$: C, 66.95; H, 4.21; N, 6.51. Found: C, 66.88; H, 4.08; N, 6.58.

1-(2-Pyridyl)-3-(2-pyrrolyl)propen-1-one (**1x**).

This compound had mp 122-123°; ^{1}H nmr: δ 6.32 (s, 1H), 6.73 (s, 1H), 6.98 (s, 1H), 7.44 (dd, J = 7.7 and 4.8 Hz, 1H), 7.82 (dd, J = 7.7 and 7.7 Hz, 1H), 7.83 (d, J = 15.4 Hz, 1H), 7.85 (d, J = 15.4 Hz, 1H), 8.18 (d, J = 7.7 Hz, 1H), 8.67 (d, J = 4.8 Hz, 1H), 9.17 (br s, 1H); ms: m/z (ion, relative intensity) 198 (M^+, 93), 169 (100), 104 (60).

Anal. Calcd. for $C_{12}H_{10}N_2O$: C, 72.71; H, 5.09; N, 14.13. Found: C, 72.67; H, 4.92; N, 14.01.

Synthesis of 3-Cyano-2-methylpyridines.

In a general procedure, an acetonitrile suspension (20 ml) containing potassium *t*-butoxide (110 mg) was sonicated using a Branson ultrasonic cleaner (150 W, 47 KHz) for 15 minutes 35°. α,β-Unsaturated carbonyl compound (**1**, 10 mmoles) was added to the suspension and sonicated for another 2 hours. After the reaction, the suspension was poured into brine (50 ml) and extracted with ether (30 ml x 2). The extract was dried with sodium sulfate. The solvent was removed and the residue was recrystallized from ethanol. Their physical and spectral data are shown below:

3-Cyano-4-furyl-2-methyl-6-phenylpyridine (**2a**).

This compound had mp 120.0-120.5°; ^{1}H nmr: δ 2.85 (s, 3H), 6.62 (dd, J = 3.7 and 1.8 Hz, 1H), 7.47-7.50 (m, 3H), 7.61 (d, J = 3.7 Hz, 1H), 7.62 (d, J = 1.8 Hz, 1H), 8.01 (s, 1H), 8.06-8.09 (m, 2H); ms: m/z (ion, relative intensity) 260 (M^+, 100); ir (potassium bromide): ν 2220 cm^{-1}.

Anal. Calcd. for $C_{17}H_{12}N_2O$: C, 78.44; H, 4.65; N, 10.76. Found: C, 78.20; H, 4.32; N, 10.73.

3-Cyano-2-methyl-6-phenyl-4-(2-thienyl)pyridine (**2b**).

This compound had mp 134.5-135.0°; ^{1}H nmr: δ 2.87 (s, 3H), 7.20 (dd, J = 5.1 and 3.7 Hz, 1H), 7.49-7.51 (m, 3H), 7.53 (d, J = 5.1 Hz, 1H), 7.71 (s, 1H), 7.89 (d, J = 3.7 Hz, 1H), 8.03-8.07 (m, 2H); ms: m/z (ion, relative intensity) 276 (M^+, 100); ir (potassium bromide): ν 2240 cm^{-1}.

Anal. Calcd. for $C_{17}H_{12}N_2S$: C, 73.88; H, 4.38; N, 10.14. Found: C, 73.96; H, 4.17; N, 10.21.

3-Cyano-2-methyl-6-phenyl-4-(2-pyrrolyl)pyridine (**2c**).

This compound had mp 178-180°; ^{1}H nmr: δ 2.83 (s, 3H), 6.41 (dd, J = 3.7 and 1.5 Hz, 1H), 7.06 (dd, J = 3.7 and 1.4 Hz, 1H), 7.10 (dd, J = 1.5 and 1.4 Hz, 1H), 7.48 (m, 3H), 7.73 (s, 1H), 8.63 (m, 2H), 9.60 (br s, 1H); ms: m/z (ion, relative intensity) 259 (M^+, 100); ir (potassium bromide): ν 2205 cm^{-1}.

Anal. Calcd. for $C_{17}H_{13}N_3$: C, 78.74; H, 5.05; N, 16.20. Found: C, 78.52; H, 4.83; N, 16.34.

3-Cyano-2-methyl-6-phenyl-4-(2-pyridyl)pyridine (**2d**).

This compound had mp 155-157°; ^{1}H nmr: δ 2.95 (s, 3H), 7.44 (dd, J = 8.8 and 4.8 Hz, 1H), 7.48-7.53 (m, 3H), 7.89 (dd, J = 8.8 and 6.3 Hz, 1H), 7.91 (d, J = 6.3 Hz, 1H), 8.03 (s, 1H), 8.12 (m, 2H), 8.83 (d, J = 4.8 Hz, 1H); ms: m/z (ion, relative intensity) 271 (M^+, 100); ir (potassium bromide): ν 2220 cm^{-1}.

Anal. Calcd. for $C_{18}H_{13}N_3$: C, 79.68; H, 4.83; N, 15.49. Found: C, 79.58; H, 4.54; N, 15.62.

6-(4-Chlorophenyl)-3-cyano-4-(2-furyl)-2-methylpyridine (**2e**).

This compound had mp 169.5-170.0°; ^{1}H nmr: δ 2.87 (s, 3H), 6.65 (dd, J = 3.9 and 1.8 Hz, 1H), 7.48 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 3.9 Hz, 1H), 7.65 (d, J = 1.8 Hz, 1H), 8.03 (s, 1H), 8.06 (d, J = 8.4 Hz, 2H); ms: m/z (ion, relative intensity) 294 (M^+, 100); ir (potassium bromide): δ 2230 cm^{-1}.

Anal. Calcd. for $C_{17}H_{11}N_2OCl$: C, 69.28; H, 3.76; N, 9.51. Found: C, 69.22; H, 3.56; N, 9.47.

6-(4-Chlorophenyl)-3-cyano-2-methyl-4-(2-thienyl)pyridine (**2f**).

This compound had mp 182.0-183.0°; ^{1}H nmr: δ 2.90 (s, 3H), 7.23 (dd, J = 5.1 and 3.8 Hz, 1H), 7.48 (d, J = 8.5 Hz, 2H), 7.57 (dd, J = 5.1 and 0.9 Hz, 1H), 7.73 (s, 1H), 7.91 (dd, J = 3.8 and 0.9 Hz, 1H), 8.02 (d, J = 8.5 Hz, 1H); ms: m/z (ion, relative intensity) 310 (M^+, 100); ir (potassium bromide): δ 2210 cm^{-1}.

Anal. Calcd. for $C_{17}H_{11}N_2SCl$: C, 65.70; H, 3.57; N, 9.01. Found: C, 65.80; H, 3.28; N, 9.15.

6-(4-Chlorophenyl)-3-cyano-2-methyl-4-(2-pyrrolyl)pyridine (**2g**).

This compound had mp 188-190.5°; ^{1}H nmr: δ 2.74 (s, 3H), 6.36 (s, 1H), 7.25 (s, 1H), 7.19 (s, 1H), 7.63 (d, J = 8.4 Hz, 2H), 8.17 (s, 1H), 8.23 (d, J = 8.4 Hz, 2H), 9.45 (br s, 1H); ms: m/z (ion, relative intensity) 293 (M^+, 100); ir (potassium bromide): ν 2215 cm^{-1}.

Anal. Calcd. for $C_{17}H_{12}N_3Cl$: C, 69.51; H, 4.12; N, 14.30. Found: C, 69.42; H, 3.88; N, 14.38.

6-(Chlorophenyl)-3-cyano-2-methyl-4-(2-pyridyl)pyridine (**2h**).

This compound had mp 171-173°; ^{1}H nmr: δ 2.94 (s, 3H), 7.43-7.48 (m, 1H), 7.48 (d, J = 8.4 Hz, 2H), 7.90-7.92 (m, 2H), 8.02 (s, 1H), 8.08 (d, J = 8.4 Hz, 2H), 8.83 (d, J = 4.8 Hz, 1H); ms: m/z (ion, relative intensity) 305 (M^+, 100); ir (potassium bromide): ν 2220 cm^{-1}.

Anal. Calcd. for $C_{18}H_{12}N_3Cl$: C, 70.71; H, 3.96; N, 13.74. Found: C, 70.49; H, 3.78; N, 13.83.

3-Cyano-4-(2-furyl)-6-(4-methoxyphenyl)-2-methylpyridine (**2i**).

This compound had mp 120-121°; ^{1}H nmr: δ 2.85 (s, 3H), 3.88 (s, 3H), 6.63 (dd, J = 3.5 and 1.5 Hz, 1H), 7.02 (d, J = 8.8 Hz, 2H), 7.60 (d, J = 3.5 Hz, 1H), 7.64 (d, J = 1.5 Hz, 1H), 7.98 (s, 1H), 8.07 (d, J = 8.8 Hz, 2H); ms: m/z (ion, relative intensity) 290 (M^+, 100); ir (potassium bromide): ν 2230 cm^{-1}.

Anal. Calcd. for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.22; H, 4.59; N, 9.73.

3-Cyano-6-(4-methoxyphenyl)-2-methyl-4-(2-thienyl)pyridine (**2j**).

This compound had mp 139-141°; ^{1}H nmr: δ 2.88 (s, 3H), 3.88 (s, 3H), 7.02 (d, J = 6.8 Hz, 2H), 7.22 (dd, J = 5.1 and 3.9 Hz, 1H), 7.54 (dd, J = 5.1 and 1.3 Hz, 1H), 7.69 (s, 1H), 7.89 (dd, J = 3.9 and 1.3 Hz, 1H), 8.05 (d, J = 6.8 Hz, 2H); ms: m/z (ion, relative intensity) 306 (M^+, 100); ir (potassium bromide): ν 2220 cm^{-1}.

Anal. Calcd. for $C_{18}H_{14}N_2OS$: C, 70.56; H, 4.61; N, 9.14. Found: C, 70.49; H, 4.36; N, 9.24.

3-Cyano-6-(4-methoxyphenyl)-2-methyl-4-(2-pyrrolyl)pyridine (**2k**).

This compound had mp 179-181°; ^{1}H nmr: δ 2.82 (s, 3H), 3.87

(s, 3H), 6.40 (dd, J = 2.5 and 2.5 Hz, 1H), 7.00 (d, J = 8.5 Hz, 2H), 7.07 (d, J = 2.5 Hz, 1H), 7.08 (d, J = 2.5 Hz, 1H), 7.67 (s, 1H), 7.99 (d, J = 8.5 Hz, 2H), 9.59 (br s, 1H); ms: m/z (ion, relative intensity) 289 (M^+, 100); ir (potassium bromide): ν 2210 cm^{-1}.

Anal. Calcd. for $C_{18}H_{15}N_3O$: C, 74.72; H, 5.23; N, 14.52. Found: C, 74.53; H, 5.02; N, 14.68.

3-Cyano-6-(4-methoxyphenyl)-2-methyl-4-(2-pyridyl)pyridine (**2l**).

This compound had mp 168-170°; ^1H nmr: δ 2.92 (s, 3H), 3.88 (s, 3H), 7.01 (d, J = 8.8 Hz, 2H), 7.44 (dd, J = 5.2 and 4.8 Hz, 1H), 7.88 (d, J = 1.5 Hz, 1H), 7.90 (dd, J = 5.2 and 1.5 Hz, 1H), 7.96 (s, 1H), 8.10 (d, J = 8.8 Hz, 2H), 8.82 (d, J = 4.8 Hz, 1H); ms: m/z (ion, relative intensity) 301 (M^+, 100); ir (potassium bromide): ν 2220 cm^{-1}.

Anal. Calcd. for $C_{19}H_{15}N_3O$: C, 75.73; H, 5.02; N, 13.94. Found: C, 75.87; H, 4.77; N, 14.01.

3-Cyano-6-(2-furyl)-2-methyl-4-phenylpyridine (**2m**).

This compound had mp 139-130°; ^1H nmr: δ 2.85 (s, 3H), 6.57 (dd, J = 2.9 and 1.5 Hz, 1H), 7.24 (d, J = 2.9 Hz, 1H), 7.52 (m, 3H), 7.58 (d, J = 1.5 Hz, 1H), 7.60 (m, 2H), 7.61 (s, 1H); ms: m/z (ion, relative intensity) 260 (M^+, 100); ir (potassium bromide): 2220 cm^{-1}.

Anal. Calcd. for $C_{17}H_{12}N_2O$: C, 78.44; H, 4.65; N, 10.76. Found: C, 78.19; H, 4.41; N, 10.60.

3-Cyano-4,6-di(2-furyl)-2-methylpyridine (**2n**).

This compound had mp 145-146°; ^1H nmr: δ 2.79 (s, 3H), 6.57 (dd, J = 3.6 and 1.8 Hz, 1H), 6.61 (dd, J = 3.6 and 1.8 Hz, 1H), 7.20 (d, J = 3.6 Hz, 1H), 7.57 (d, J = 3.6 Hz, 1H), 7.59 (d, J = 1.8 Hz, 1H), 7.62 (d, J = 1.8 Hz, 1H), 7.91 (s, 1H); ms: m/z (ion, relative intensity) 250 (M^+, 100); ir (potassium bromide): ν 2250 cm^{-1}.

Anal. Calcd. for $C_{15}H_{10}N_2O_2$: C, 71.99; H, 4.03; N, 11.19. Found: C, 72.26; H, 4.11; N, 11.16.

3-Cyano-6-(2-furyl)-2-methyl-4-(2-thienyl)pyridine (**2o**).

This compound had mp 146-147°; ^1H nmr: δ 2.85 (s, 3H), 6.59 (dd, J = 3.5 and 1.5 Hz, 1H), 7.22 (dd, J = 5.1 and 3.9 Hz, 1H), 7.24 (d, J = 3.5 Hz, 1H), 7.58 (dd, J = 5.1 and 1.3 Hz, 1H), 7.61 (d, J = 1.5 Hz, 1H), 7.72 (s, 1H), 7.91 (dd, J = 3.9 and 1.3 Hz, 1H); ms: m/z (ion, relative intensity) 266 (M^+, 100); ir (potassium bromide): ν 2230 cm^{-1}.

Anal. Calcd. for $C_{15}H_{10}N_2OS$: C, 67.65; H, 3.78; N, 10.52. Found: C, 67.52; H, 3.52; N, 10.58.

3-Cyano-6-(2-furyl)-2-methyl-4-(2-pyrrolyl)pyridine (**2p**).

This compound had mp 207-208°; ^1H nmr: δ 2.78 (s, 3H), 6.40 (dd, J = 2.5 and 2.5 Hz, 1H), 6.57 (dd, J = 1.7 and 1.7 Hz, 1H), 7.07 (d, J = 2.5 Hz, 1H), 7.13 (d, J = 2.5 Hz, 1H), 7.21 (d, J = 1.7 Hz, 1H), 7.58 (d, J = 1.7 Hz, 1H), 7.70 (s, 1H), 9.56 (br s, 1H); ms: m/z (ion, relative intensity) 249 (M^+, 100); ir (potassium bromide): ν 2235 cm^{-1}.

Anal. Calcd. for $C_{15}H_{11}N_3O$: C, 72.28; H, 4.45; N, 16.86. Found: C, 71.98; H, 4.21; N, 16.73.

3-Cyano-2-methyl-4-phenyl-6-(2-thienyl)pyridine (**2q**).

This compound had mp 137-138°; ^1H nmr: δ 2.86 (s, 3H), 7.15 (dd, J = 5.1 and 3.9 Hz, 1H), 7.51 (d, J = 5.1 and 0.9 Hz, 1H), 7.52-7.55 (m, 3H), 7.56 (s, 1H), 7.60-7.64 (m, 2H), 7.71 (dd, J = 3.9 and 0.9 Hz, 1H); ms: m/z (ion, relative intensity) 276 (M^+, 100); ir (potassium bromide): ν 2220 cm^{-1}.

Anal. Calcd. for $C_{17}H_{12}N_2S$: C, 73.88; H, 4.38; N, 10.14. Found: C, 73.55; H, 4.19; N, 10.01.

3-Cyano-4-(2-furyl)-2-methyl-6-(2-thienyl)pyridine (**2r**).

This compound had mp 136-138°; ^1H nmr: δ 2.78 (s, 3H), 6.61 (dd, J = 3.7 and 1.8 Hz, 1H), 7.13 (dd, J = 5.1 and 3.8 Hz, 1H), 7.49 (d, J = 5.1 Hz, 1H), 7.58 (d, J = 3.7 Hz, 1H), 7.62 (d, J = 1.8 Hz, 1H), 7.72 (d, J = 3.8 Hz, 1H), 7.87 (s, 1H); ms: m/z (ion, relative intensity) 266 (M^+, 100); ir (potassium bromide): ν 2260 cm^{-1}.

Anal. Calcd. for $C_{15}H_{10}N_2OS$: C, 67.65; H, 3.78; N, 10.52. Found: C, 67.71; H, 3.54; N, 10.76.

3-Cyano-4,6-di(2-thienyl)-2-methylpyridine (**2s**).

This compound had mp 158-159°; ^1H nmr: δ 2.82 (s, 3H), 7.13 (dd, J = 4.5 and 3.7 Hz, 1H), 7.19 (dd, J = 4.5 and 3.7 Hz, 1H), 7.49 (d, J = 4.5 Hz, 1H), 7.53 (d, J = 4.5 Hz, 1H), 7.60 (s, 1H), 7.69 (d, J = 3.7 Hz, 1H), 7.86 (d, J = 3.7 Hz, 1H); ms: m/z (ion, relative intensity) 282 (M^+, 100); ir (potassium bromide): ν 2250 cm^{-1}.

Anal. Calcd. for $C_{15}H_{10}N_2S_2$: C, 63.80; H, 3.56; N, 9.92. Found: C, 63.52; H, 3.46; N, 9.81.

3-Cyano-2-methyl-4-(2-pyrrolyl)-6-(2-thienyl)pyridine (**2t**).

This compound had mp 212-214°; ^1H nmr: δ 2.78 (s, 3H), 6.40 (dd, J = 3.0 and 2.5 Hz, 1H), 7.07 (d, J = 3.0 Hz, 1H), 7.14 (d, J = 2.5 Hz, 1H), 7.15 (dd, J = 3.8 and 3.4 Hz, 1H), 7.50 (d, J = 3.8 Hz, 1H), 7.63 (s, 1H), 7.71 (d, J = 3.4 Hz, 1H), 9.56 (br s, 1H); ms: m/z (ion, relative intensity) 265 (M^+, 100); ir (potassium bromide): ν 2210 cm^{-1}.

Anal. Calcd. for $C_{15}H_{11}N_3S$: C, 67.90; H, 4.18; N, 15.84. Found: C, 67.94; H, 3.98; N, 15.95.

3-Cyano-2-methyl-4-phenyl-6-(2-pyridyl)pyridine (**2u**).

This compound had mp 173-175°; ^1H nmr: δ 2.93 (s, 3H), 7.37 (dd, J = 7.7 and 4.8 Hz, 1H), 7.51-7.70 (m, 5H), 7.87 (ddd, J = 7.7, 7.7 and 1.5 Hz, 1H), 8.43 (s, 1H), 8.52 (d, J = 7.7 Hz, 1H), 8.70 (dd, J = 4.8 and 1.5 Hz, 1H); ms: m/z (ion, relative intensity) 271 (M^+, 100); ir (potassium bromide): ν 2240 cm^{-1}.

Anal. Calcd. for $C_{18}H_{13}N_3$: C, 79.68; H, 4.83; N, 15.49. Found: C, 79.82; H, 4.59; N, 15.63.

3-Cyano-4-(2-furyl)-2-methyl-6-(2-pyridyl)pyridine (**2v**).

This compound had mp 177-178°; ^1H nmr: δ 2.85 (s, 3H), 6.61 (dd, J = 3.0 and 1.7 Hz, 1H), 7.35 (dd, J = 7.7 and 4.5 Hz, 1H), 7.58 (d, J = 3.0 Hz, 1H), 7.64 (d, J = 1.7 Hz, 1H), 7.83 (dd, J = 7.8 and 7.7 Hz, 1H), 8.46 (d, J = 7.8 Hz, 1H), 8.70 (s, 1H), 8.72 (d, J = 4.5 Hz, 1H); ms: m/z (ion, relative intensity) 261 (M^+, 100); ir (potassium bromide): ν 2220 cm^{-1}.

Anal. Calcd. for $C_{16}H_{11}N_3O$: C, 73.55; H, 4.24; N, 16.08. Found: C, 73.56; H, 3.91; N, 16.04.

3-Cyano-2-methyl-4-(2-thienyl)-6-(2-pyridyl)pyridine (**2w**).

This compound had mp 186-188°; ^1H nmr: δ 2.90 (s, 3H), 7.21 (dd, J = 5.1 and 3.7 Hz, 1H), 7.36 (dd, J = 7.6 and 4.7 Hz, 1H), 7.56 (d, J = 5.1 Hz, 1H), 7.84 (dd, J = 8.0 and 7.6 Hz, 1H), 7.94 (d, J = 3.7 Hz, 1H), 8.48 (d, J = 8.0 Hz, 1H), 8.53 (s, 1H), 8.71 (d, J = 4.7 Hz, 1H); ms: m/z (ion, relative intensity) 277 (M^+, 100); ir (potassium bromide): ν 2215 cm^{-1}.

Anal. Calcd. for $C_{16}H_{11}N_3S$: C, 69.29; H, 4.00; N, 15.15. Found: C, 69.52; H, 3.73; N, 15.33.

3-Cyano-2-methyl-6-(2-pyridyl)-4-(2-pyrrolyl)pyridine (**2x**).

This compound had mp 194-196°; ^{1}H nmr: δ 2.84 (s, 3H), 6.41 (dd, J = 5.2 and 3.7 Hz, 1H), 7.06 (d, J = 3.7 Hz, 1H), 7.28 (d, J = 5.2 Hz, 1H), 7.36 (dd, J = 7.4 and 4.8 Hz, 1H), 7.85 (dd, J = 7.4 and 7.4 Hz, 1H), 8.47 (s, 1H), 8.49 (d, J = 7.4 Hz, 1H), 8.68 (d, J = 4.8 Hz, 1H), 9.64 (br s, 1H); ms: m/z (ion, relative intensity) 260 (M^+, 100); ir (potassium bromide): ν 2220 cm^{-1}.

Anal. Calcd. for $C_{16}H_{12}N_4$: C, 73.83; H, 4.65; N, 21.52. Found: C, 74.01; H, 4.39; N, 21.49.

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