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NOVEL SYNTHESIS OF SOME NEW FLUOERESCENT 2-AMINO-3-CYANOPYRIDINES

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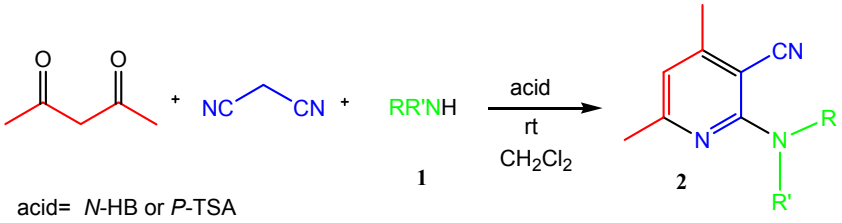
Abstract – Novel synthesis of some new fluorescent 2-amino-3-cyanopyridines **2a-m** in the presence of *N*-hydroxybenzamide or *p*-toluenesulfonic acid is described. Photophysical data including $\lambda_{Abs.}$ and $\lambda_{Flu.}$ of **2a-m** in CH_2Cl_2, MeCN and MeOH have been measured.

INTRODUCTION

Aminopyridine derivatives have attracted more attention due to their biological activities, such as cardioprotective,[1] antibacterial,[2] antioxidant,[3] anti-inflammatory[4] and anti-HIV-1.[5] For example sulfapyridine which contains 2-aminopyridine moiety is an old marked antibacterial drug. Synthesis of aminopyridine derivatives with cyano substitution is rather new. In 2005 Shi and coworkers have reported the synthesis of 2-amino-3-cyanopyridine derivatives using one-pot reaction of aromatic aldehydes, ketones and malononitrile in ammonium acetate under microwave irradiation.[6] In 2009 Sarda and coworkers have reported 2-amino-4,6-diphenylpyridine-3-carbonitrile through condensation of chalcones with malononitrile and ammonium acetate by ionic liquid ethylammonium nitrate as a catalyst.[7] In 2011, Tang and coworkers have used ytterbium perfluoroacetate as catalyst for the synthesis of similar 2-amino-4,6-diaryl-3-cyanopyridines in a similar manner.[8] Synthesis of heteroaromatic rings contain amino substitution is still desired[9] and in continuation of our quest for developing one-pot synthetic procedure for heterocyclic frameworks,[10-13] herein we wish to report the one-pot condensation of 2,4-pentanedione (acetylacetone), malononitrile and some different amines in acidic media at room temperature. In this procedure non hydrated *p*-toluenesulfonic acid (*P*-TSA) and *N*-hydroxybenzamide (*N*-HB) applied as catalysts and new compounds **2a-m** produced in fairly high yields (Scheme 1).



Scheme 1

RESULTS AND DISCUSSION

In this procedure primary and secondary amines, benzyl- and phenylethylamine, cyclic amines such as pyrrolidine, piperidine and morpholine also ethanolamine can be used. These amines could reacted a little different. In the similar condition, primary amines reacted faster (5-8 h), secondary amines reacted relatively slower (8-9 h) and cyclic amines reacted even slower (9-12 h). Ethanolamine reacted more slowly (15 h) probably as a result of hydroxyl group (Table 1). It has been already reported which *P*-TSA and *N*-HB can work as Brønsted acid.[14] Using *N*-hydroxybenzamide in CH_2Cl_2 catalyzed this reaction more efficient (shorter times and more yields). *P*-TSA in CH_2Cl_2 on the other hand was not as well as the other one. The results are compared in Table 1.

Table 1. Reaction times and yields of **2a-m** using *P*-TSA or *N*-HB as catalyst in CH_2Cl_2

Comp.**2**	R	R′	Time (h)		Yield *(%)		MP
			(*P*-TSA)	(*N*-HB)	(*P*-TSA)	(*N*-HB)	(˚C)
A	Me	H	12	7	55	90	126
B	Et	H	14	7	50	85	99
C	*n*-Pr	H	12	6	60	80	69
D	*i*-Pr	H	15	7	55	80	68
E	*n*-Bu	H	14	6	45	76	65
F	*i*-Bu	H	14	8	60	70	74
G	$(CH_2)_2OH$	H	28	15	40	54	75
H	$PhCH_2$	H	12	5	65	87	138
i	$Ph(CH_2)_2$	H	15	5	56	85	106
j	Me	Me	24	9	47	75	48
k	piperidino		24	8	50	70	46
l	pyrrolidino		28	12	42	60	-
m	morpholino		26	9	60	65	100

* The isolated yields

Structures **2a-m** were assigned on the basis of their elemental analysis, IR, ^1H, ^{13}C NMR, and mass spectral data. The mass spectra of these compounds displayed molecular ion peaks at the appropriate *m/z* values. IR spectra of compounds **2a-m** have shown a single sharp band at 2198-2215 cm^{-1} for C≡N group. The ^1H, ^{13}C NMR spectra of **2a-m** displayed resonances in agreement with their structure. In the ^1H NMR of compounds **2a-i** there are single N-H absorption at δ 5.03-5.58 ppm and for all of compounds there is a

distinguished single peak at δ 6.34-6.60 ppm for aromatic C-H protons (Experimental Section). Single crystals of **2h** were obtained from a mixture of EtOAc and *n*-hexane and its X-ray crystal structure was performed to confirm unambiguously the proposed structure.[15] X-Ray crystal analysis have shown a monoclinic crystal structure with space group= p 21/c, R=0.635, wR2=0.1760 and Z=4 for compound **2h**. Other crystallographic data can be obtained as supplementary publication No. CCDC 891215 (Figure 1).

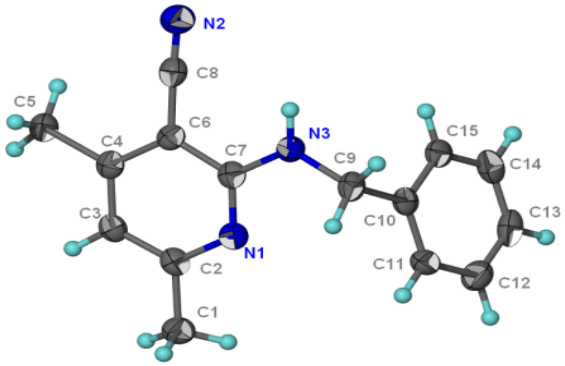
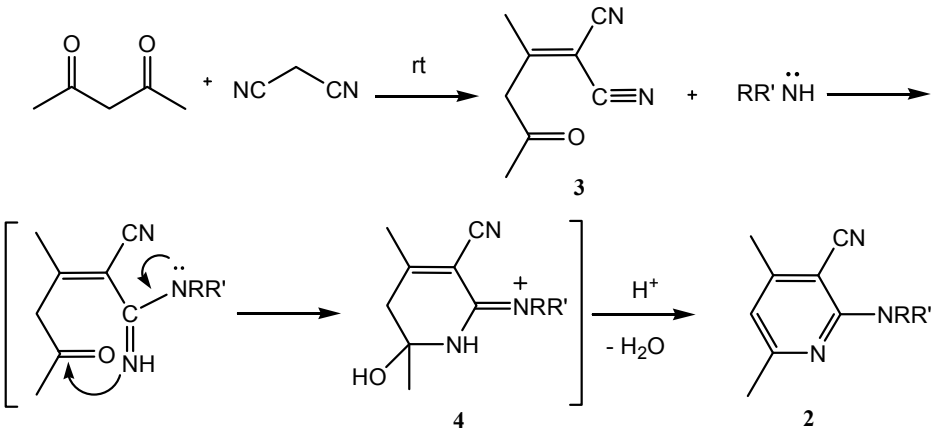


Figure 1. X-Ray crystal structure of **2h**

A possible mechanism for the formation of products **2** is shown in Scheme 2. Acetylacetone and malononitrile were initially condensed to produce adduct **3**. Nucleophilic addition of amine to one of the CN groups of **3,** cyclization followed by elimination of H_2O in acidic media converted intermediate **3** to the final product **2** through the cyclic structure **4.** Adduct **3** could be recognized as an intermediate in IR spectra of reaction mixture. Two sharp absorptions for CN groups (2054-2209 cm^{-1}) and a sharp absorption for carbonyl group (1738-1740 cm^{-1}) in the IR spectra of reaction mixture were evidences for **3** which were good for monitoring the progress of reactions. So, in the last stage of reactions the CO and one of the CN absorptions were highly decreased and in the IR spectra of final products only one of the CN absorptions (2198-2209 cm^{-1}) remained. Our attempt to isolate **3** was not successful. It seems that stability gained from aromatization led to rapid transformation of intermediate **3** to final product.



Scheme 2

Optoelectronic devices such as optical fiber switchers, tunable lasers and amplifiers, modulators with various applications need compounds emitting in blue spectral region,[16-18] there are some reports on using the fluorescent compounds in biochemical and medical research.[19] On the other hand 2-aminopyridine has already being used as one of the fluorescence quantum yield standards,[20] so developing a procedure for the synthesis of thermally stable, highly fluorescent materials emitting in blue spectral region can be urgently interesting for technology upgrading and biochemical researches. Figure 2 shows photograph of compound **2e** solutions to represent the fluorescence features of the synthesized compounds.

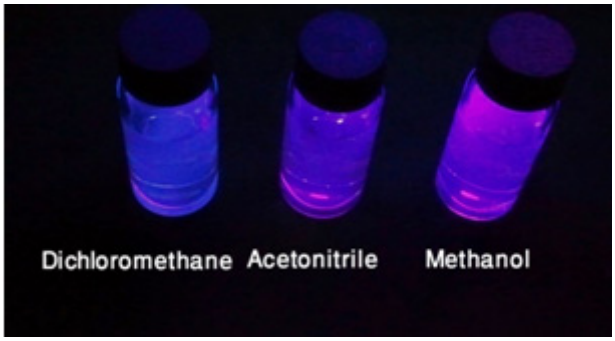


Figure 2. Photograph of **2e** solutions in dichloromethane, acetonitrile and methanol under lamp λ=366 nm

The photophysical data of compounds **2a-m** including $\lambda_{Abs.}$ (nm) and $\lambda_{Flu.}$ (nm) have been measured for 2×10^{-5} M solution in CH_2Cl_2, MeCN and MeOH. The maximum absorption and emission wavelengths of **2a-m** in different solvents have been in the range of 285-300 nm and 366-413 nm respectively. The results are shown in Table 2.

Table 2. The photophysical data: electronic absorption (*Abs.*) and fluorescence (*Flu.*) of **2a-m**

Comp.	$\lambda_{Abs.}$(nm) (CH_2Cl_2)	$\lambda_{Flu.}$(nm) (CH_2Cl_2)	$\lambda_{Abs.}$(nm) (CH_3CN)	$\lambda_{Flu.}$(nm) (CH_3CN)	$\lambda_{Abs.}$(nm) (CH_3OH)	$\lambda_{Flu.}$(nm) (CH_3OH)
2a	292	371	291	377	295	381
2b	295	393	295	400	292	380
2c	290	373	295	380	295	382
2d	295	373	290	373	295	378
2e	290	371	300	376	295	384
2f	285	370	295	375	295	380
2g	285	371	287	375	285	385
2h	290	366	290	374	293	380
2i	293	368	295	376	293	383
2j	294	389	295	396	294	402
2k	293	390	295	393	289	398
2l	285	413	285	402	285	398
2m	293	388	290	405	293	403

CONCLUSION

In summary, we have reported the novel acid catalyzed condensation of acetylacetone, malononitrile and different amines by a one-pot multi component reaction. Fluorescent 2-amino-3-cyanopyridine derivatives **2a-m** are synthesized in fairly high yields. High atom economy, easy procedure and high yields are the other advantages of this method. Photophysical data of compounds **2a-m** including $\lambda_{Abs.}$ and $\lambda_{Flu.}$ in CH_2Cl_2, MeCN and MeOH are measured. Further investigation of this method is currently in progress to establish its scope and utility.

EXPERIMENTAL

Chemicals and solvents were obtained from Merck (Germany) and Fluka (Switzerland). Melting points were measured on Barnstead Electrothermal melting point apparatus and are not corrected. Elemental analyses for C, H and N were performed using a Thermo Finnigan Flash EA1112 instrument. IR spectra were measured on a Bruker EQUINOX 55 spectrophotometer as ATR method. ^{1}H NMR and ^{13}C NMR spectra were determined on a Bruker at 500 MHz and 128 MHz. Mass spectra were recorded on a Finnigan-MAT 8430 spectrometer at an ionization potential of 70 ev. All fluorescence intensity measurements were made with a Carry Eclipse Fluorescence spectrophotometer. The photo is taken under lamp λ=366 nm TL8W/08F8T5/BLC Philips made in Holland.

General procedure for the synthesis of compounds 2

To a stirred mixture of acetylacetone (2 mmol, 0.2 mL), malononitrile (2 mmol, 0.132 g), amine **1** (2 mmol) in CH_2Cl_2 (5 mL) was added *N*-hydroxybenzamide (50 mol %, 0.137 g) or *p*-toluenesulfonic acid (50 mol%, 0.172 g). The solution was stirred at room temperature for 5-15 h for *N*-hydroxybenzamide or 12-28 h for *p*-toluenesulfonic acid. The reaction was monitored by IR. When one of the CN and the CO absorptions were disappeared the solvent was removed under reduced pressure and the product was purified using column chromatography (silica gel, EtOAc/*n*-hexane: 1/4). The colorless crystals of product (except **2i**) were obtained by recrystalization from EtOAc**.**

4,6-Dimethyl-2-(methylamino)pyridine-3-carbonitrile (2a):

Colorless crystals; mp 126 °C; ν_{max} (KBr) 3384 (N-H), 2204 (C≡N), 1570, 1517, 1467 (C-N) cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ_H 2.36, 2.40 (6H, 2s, $2CH_3$), 3.06 (3H, d, *J*=4.86 Hz, CH_3), 5.15 (1H, br s, NH), 6.35 (1H, s, C-H of pyridine) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ_H 20.57, 25.36 ($2CH_3$), 28.71 (CH_3-N), 89.38 (C≡N), 113.51 (C-H of pyridine), 117.37, 152.62, 159.73, 162.15 (pyridine carbons) ppm; MS: *m/z*: 161 (M^+), 131 (M^+- CH_3NH), 104 ($C_7H_7N^+$), 90 ($C_6H_4N^+$); Anal. Calcd for $C_9H_{11}N_3$: C, 67.06; H, 6.88; N, 26.07. Found: C, 67.12; H, 6.84; N, 26.12.

2-(Ethylamino)-4,6-dimethylpyridine-3-carbonitrile (2b):

Colorless crystals; mp 99 °C; ν_{max} (KBr) 3360 (N-H), 2207 (C≡N), 1571, 1528 (C-N) cm^{-1}; ^{1}H NMR

($CDCl_3$, 500 MHz): δ_H 1.26 (3H, t, *J*=7.2 Hz, CH_3), 2.35, 2.38 (6H, 2s, $2CH_3$), 3.51 (2H, q of d, *J*=14.18 Hz, 5.62 Hz, CH_2), 5.03 (1H, br s, NH), 6.34 (1H, s, C-H of pyridine) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ_C 15.34 (CH_3 of Et), 20.58, 25.37 ($2CH_3$), 36.64 (CH_2), 89.17 (C≡N), 113.46 (C-H of pyridine), 117.39, 152.60, 159.13, 162.15 (pyridine carbons) ppm; MS: *m/z*: 175 (M^+), 160 (M^+-CH_3), 146 (M^+-C_2H_5), 131 (M^+-C_2H_5N), 57 ($C_3H_7N^+$); Anal. Calcd for $C_{10}H_{13}N_3$: C, 68.54; H, 7.48; N, 23.98. Found: C, 68.50; H, 7.51; N, 23.99.

4,6-Dimethyl-2-(propylamino)pyridine-3-carbonitrile (2c):

Colorless crystals; mp 69 °C; ν_{max} (KBr) 3375 (N-H), 2209 (C≡N), 1568, 1524 (C-N), cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ_H 1.00 (3H, t, *J*=7.45 Hz, CH_3), 1.63-1.71 (2H, m, CH_2), 2.37, 2.40 (6H, 2s, $2CH_3$), 3.47-3.51 (2H, d of t, *J*=14.17 Hz, *J*=5.57 Hz, CH_2-N), 5.07 (1H, br s, NH), 6.35 (1H, s, C-H of pyridine) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ_C 11.84 (CH_3 of propyl.), 20.61, 25.40 ($2CH_3$ of pyridine), 23.27 (CH_2), 43.55 (CH_2-N), 89.15 (C≡N), 113.46 (C-H of pyridine), 117.44, 152.63, 159.28, 162.18 (pyridine carbons) ppm; MS: *m/z*: 189 (M^+), 174 (M^+-CH_3), 160 (M^+-C_2H_5), 132 (M^+-C_3H_7N), 106 (M^+-$C_4H_7N_2$), 91 ($C_6H_5N^+$), 57; Anal. Calcd for $C_{11}H_{15}N_3$: C, 69.81; H, 7.99; N, 22.20. Found: C, 69.78; H, 7.94; N, 22.25.

2-(Isopropylamino)-4,6-dimethylpyridine-3-carbonitrile (2d):

Colorless crystals; mp 68 °C, ν_{max} (KBr) 3356 (N-H), 2207 (C≡N), 1585, 1525 (C-N) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ_H 1.23-1.32 (6H, q of d, *J*=22.42 Hz, *J*=5.57 Hz, $2CH_3$ of *i*-propyl), 2.36, 2.40 (6H, 2s, $2CH_3$), 4.35-4.42 (1H, m, CH), 4.85 (1H, br s, NH), 6.34 (1H, s, C-H of pyridine) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ_C 20.63, 25.43 ($2CH_3$ of pyridine), 23.32 ($2CH_3$ of *i*-propyl), 43.14 (CH), 89.11 (C≡N), 113.30 (C-H of pyridine), 117.48, 152.63, 158.59, 162.20 (pyridine carbons) ppm; MS: *m/z*: 189 (M^+), 174 (M^+-CH_3), 132 (M^+-C_3H_7N), 91 ($C_6H_5N^+$), 57, 43; Anal. Calcd for $C_{11}H_{15}N_3$: C, 69.81; H, 7.99; N, 22.20. Found: C, 69.77; H, 7.97; N, 22.26.

2-(Butylamino)-4,6-dimethylpyridine-3-carbonitrile (2e):

Colorless crystals; mp 65 °C; ν_{max} (KBr) 3362 (N-H), 2208 (C≡N), 1570, 1525 (C-N), cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ_H 0.98 (3H, t, *J*=7.36 Hz, CH_3 of butyl), 1.40-1.48 (2H, m, CH_2 of butyl), 1.60-1.65 (2H, m, CH_2 of butyl), 2.36, 2.43 (6H, 2s, $2CH_3$), 3.50-3.54 (2H, d of t, *J*=14.10 Hz, *J*=5.59 Hz, CH_2-N), 5.04 (1H, br s, NH), 6.34 (1H, s, C-H of pyridine) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ_C 14.25 (CH_3), 20.49 (CH_2), 20.59, 25.39 ($2CH_3$ of pyridine), 32.17 (CH_2), 41.48 (CH_2-N), 89.12 (C≡N), 113.41 (C-H of pyridine), 117.42, 152.60, 159.27, 162.16 (pyridine carbons) ppm; MS: *m/z*: 203 (M^+), 188 (M^+-CH_3), 174 (M^+-C_2H_5), 131 (M^+-$C_4H_{10}N$), 91 ($C_6H_5N^+$), 57, 43; Anal. Calcd for $C_{12}H_{17}N_3$: C, 70.90; H, 8.43; N, 20.67. Found: C, 70.86; H, 8.42; N, 20.70.

2-(Isobutylamino)-4,6-dimethylpyridine-3-carbonitrile (2f):

Colorless crystals; mp 74 °C; ν_{max} (KBr) 3369 (N-H), 2208 (C≡N), 1574, 1535 (C-N), cm^{-1}; ^1H NMR

($CDCl_3$, 500 MHz): δ_H 1.00, 1.02 (6H, 2d, *J*=1.64 Hz, $2CH_3$), 1.90-1.95 (1H, m, CH), 2.36, 2.39 (6H, 2s, $2CH_3$), 3.34-3.37 (2H, m, CH_2), 5.12 (1H, br s, NH), 6.34 (1H, s, C-H of pyridine) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ_C 20.59, 25.39 ($2CH_3$ of pyridine), 20.62 ($2CH_3$ of *i*-butyl), 28.84 (CH_2), 49.15 (CH-N), 89.10 (C≡N), 113.43 (C-H of pyridine), 117.42, 152.60, 159.40, 162.13 (pyridine carbons) ppm; MS: *m/z*: 203 (M^+), 188 (M^+-CH_3), 160 (M^+-C_3H_7), 131 (M^+-$C_4H_{10}N$), 105 (M^+-$C_5H_{10}N_2$), 57, 43; Anal. Calcd for $C_{12}H_{17}N_3$: C, 70.90; H, 8.43; N, 20.67. Found: C, 70.93; H, 8.47; N, 20.71.

2-(2-Hydroxyethylamino)-4,6-dimethylpyridine-3-carbonitrile (2g):

Colorless crystals; mp 75 °C; ν_{max} (KBr) 3356 (N-H), 3465-3265 (O-H), 2209 (C≡N), 1568, 1536 (C-N), 1243 (C-O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ_H 2.41-2.45 (6H, 2s, $2CH_3$), 3.68-3.71 (2H, d of t, *J*=9.38 Hz, *J*=5.42 Hz, CH_2-NH), 3.84-3.86 (2H, t, *J*=4.69 Hz, CH_2-OH), 4.75 (1H, br s, OH), 5.58 (1H, br s, NH), 6.44 (1H, s, C-H of pyridine) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ_C 20.74, 24.92 ($2CH_3$), 45.84 (CH_2-NH), 64.62 (CH_2-OH), 90.18 (C≡N), 114.40 (C-H of pyridine), 116.82, 153.70, 159.58, 161.49 (pyridine carbons) ppm; MS: *m/z*: 190 (M^+-1), 173 (M^+-H_2O), 141 (M^+-H_2O, $C_2H_4N^+$), 131 (M^+-C_2H_6NO), 103 (M^+-$C_3H_6N_2O$), 91 ($C_6H_5N^+$); Anal. Calcd for $C_{10}H_{13}N_3O$: C, 62.81; H, 6.85; N, 21.97. Found: C, 62.84; H, 6.89; N, 22.04.

2-(Benzylamino)-4,6-dimethylpyridine-3-carbonitrile (2h):

Colorless crystals; mp 138 °C; ν_{max} (KBr) 3392 (N-H), 2198 (C≡N), 1574, 1522 (C-N) cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ_H 2.40, 2.43 (6H, 2s, $2CH_3$), 4.75 (2H, d, *J*=5.56 Hz, CH_2), 5.42 (1H, br s, NH), 6.42 (1H, s, C-H of pyridine), 7.29-7.33, 7.37-7.41 (5H, 2m, phenyl protons) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ_C 20.65, 25.39 ($2CH_3$), 45.71(CH_2), 89.48 (C≡N), 114.08 (C-H of pyridine), 127.82, 128.30, 129.05, 139.42 (phenyl carbons), 117.23, 152.84, 158.90, 162.22 (pyridine carbons) ppm; MS: *m/z*: 237 (M^+), 222 (M^+-CH_3), 146 (M^+-C_7H_7), 131 (M^+-$PhCH_2N$), 107 ($PhCH_2N^+$), 91, 77; Anal. Calcd for $C_{15}H_{15}N_3$: C, 75.92; H, 6.37; N, 17.71. Found: C, 75.90; H, 6.40; N, 17.74.

4,6-Dimethyl-2-(phenethylamino)pyridine-3-carbonitrile (2i):

Colorless crystals; mp 106 °C; ν_{max} (KBr) 3368 (N-H), 2208 (C≡N), 1566, 1518 (C-N) cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ_H 2.38, 2.42 (6H, 2s, $2CH_3$), 2.94-2.97 (2H, t, *J*=7.13 Hz, CH_2), 3.77-3.81 (2H, d of t, *J*=13.59 Hz, *J*=5.97 Hz, CH_2-N), 5.15 (1H, br s, NH), 6.38 (1H, s, C-H of pyridine), 7.26-7.30, 7.35-7.38 (5H, 2m, phenyl protons) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ_C 20.63, 25.42 ($2CH_3$ of pyridine), 36.28 (Ph-CH_2), 43.18 (CH_2-NH), 89.48 (C≡N), 113.74 (C-H of pyridine), 126.90, 129.05, 129.24, 139.58 (phenyl carbons), 117.18, 152.70, 159.02, 162.17 (pyridine carbons) ppm; MS: *m/z*: 251 (M^+), 160 (M^+-$PhCH_2$), 131 (M^+-$C_8H_{10}N$), 120 ($C_8H_{10}N^+$), 91 ($C_6H_5N^+$), 57, 43; Anal. Calcd for $C_{16}H_{17}N_3$: C, 76.46; H, 6.82; N, 16.72. Found: C, 76.49; H, 6.84; N, 16.77.

2-(Dimethylamino)-4,6-dimethylpyridine-3-carbonitrile (2j):

Colorless crystals; mp 48 °C; ν_{max} (KBr) 2198 (C≡N), 1581, 1557, 1513 (C-N) cm^{-1}; ^{1}H NMR ($CDCl_3$,

500 MHz): δ_H 2.40, 2.42 (6H, 2s, $2CH_3$), 3.27 (6H, s, $2CH_3$-N), 6.44 (1H, s, C-H of pyridine) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ_C 21.13, 25.20 ($2CH_3$ of pyridine), 40.97 ($2CH_3$-N), 89.75 (C≡N), 114.33 (C-H of pyridine), 118.82, 154.85, 160.92, 161.10 (pyridine carbons) ppm; MS: *m/z*: 175 (M^+), 160 (M^+-CH_3), 131 (M^+-C_2H_6N), 105 ($C_7H_7N^+$), 91 ($C_6H_5N^+$); Anal. Calcd for $C_{10}H_{13}N_3$: C, 68.54; H, 7.48; N, 23.98. Found: C, 68.56; H, 7.44; N, 24.03.

4,6-Dimethyl-2-(pyrrolidin-1-yl)pyridine-3-carbonitrile (2k):

Colorless crystals; mp 46 °C; ν_{max} (KBr) 2201 (C≡N), 1555, 1554 (C-N) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ_H 1.96-1.99 (4H, m, $2CH_2$ of pyrrolidine), 2.36, 2.39 (6H, 2s, $2CH_3$), 3.77-3.80 (4H, t, *J*=4.44 Hz, $2CH_2$-N of pyrrolidine), 6.35 (1H, s, C-H of pyridine) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ_C 21.15, 25.25 ($2CH_3$ of pyridine), 25.99 ($2CH_3$), 49.39 (CH_2 of pyrrolidine), 88.10 (C≡N), 113.29 (C-H of pyridine), 119.34, 154.40, 157.95, 161.46 (pyridine carbons) ppm; MS: *m/z*: 203 (M^+), 188 (M^+-CH_3), 131 (M^+-$C_4H_{10}N$), 116 (M^+-$C_4H_{10}N$, CH_3), 105 ($C_7H_7N^+$), 43; Anal. Calcd for $C_{12}H_{17}N_3$: C, 70.90; H, 8.43; N, 20.67. Found: C, 70.94; H, 8.46; N, 20.71.

4,6-Dimethyl-2-(piperidin-1-yl)pyridine-3-carbonitrile (2l):

Yellow liquid; IR (KBr) 2209 (C≡N), 1579, 1556 (C-N) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ_H 1.65-1.74 (6H, m, $3CH_2$), 2.39, 2.41 (6H, 2s, $2CH_3$), 3.61-3.63 (4H, t, *J*=5.59 Hz, $2CH_2$-N), 6.49 (1H, s, C-H of pyridine) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ_C 20.97, 25.05, 25.20, 26.38 ($2CH_3$, $2CH_2$ of piperidine, $2CH_2$-N of piperidine) 50.24 ($2CH_2$-N), 93.20 (C≡N), 115.49 (C-H of pyridine), 118.11, 152.30, 160.97, 162.54 (pyridine carbons) ppm; MS: *m/z*: 215 (M^+), 200 (M^+-CH_3), 131 (M^+-$C_5H_{10}N$), 105 ($C_7H_7N^+$), 84 ($C_5H_{10}N^+$), 91 ($C_6H_5N^+$); Anal. Calcd for $C_{13}H_{17}N_3$: C, 72.52; H, 7.96; N, 19.52. Found: C, 72.48; H, 7.91; N, 19.56.

4,6-Dimethyl-2-morpholinopyridine-3-carbonitrile (2m):

Colorless crystals; mp 100 °C; ν_{max} (KBr) 2209 (C≡N), 1557, 1580 (C-N), 1148, 1066 (C-O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ_H 2.44, 2.46 (6H, 2s, $2CH_3$), 3.67-3.69, (4H, 2t, *J*=4.59 Hz, CH_2 of morpholine), 3.86-3.88 (4H, 2t, *J*=4.89 Hz, CH_2 of morpholine), 6.60 (1H, s, C-H of pyridine) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ_C 20.94, 25.15 ($2CH_3$ of pyridine), 49.36, 67.26 (CH_2 of morpholine), 93.94 (C≡N), 116.62 (C-H of pyridine), 117.76, 154.52, 161.21, 162.10 (pyridine carbons) ppm; MS: *m/z*: 217 (M^+), 202 (M^+-CH_3), 131 (M^+-C_4H_8NO), 105 ($C_7H_7N^+$), 91 ($C_6H_5N^+$), 30; Anal. Calcd for $C_{12}H_{15}N_3O$: C, 66.34; H, 6.98; N, 19.34. Found: C, 66.39; H, 7.01; N, 19.39.

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