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Highly Efficient and Direct Heterocyclization of Dipyridyl Ketone to *N,N*-Bidentate Ligands

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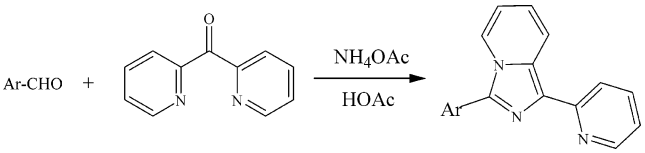
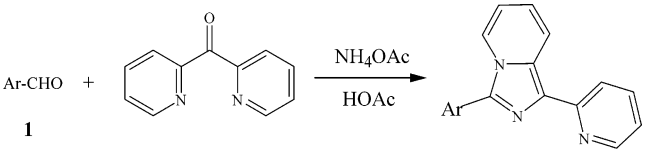


Reaction of various aromatic aldehydes with 2,2′-dipyridyl ketone and ammonium acetate in hot acetic acid provides ready access to a series of substituted 1-pyridylimidazo[1,5-*a*]pyridines, a class of ligands possessing an *N,N*-bidentate feature, in good yields.

N,N-Bidentate ligands such as 2,2′-bipyridine and 1,10-phenanthroline play a pivotal role in key areas such as photovoltaics,[1] OLEDs,[2] molecular sensors,[3] DNA intercalation,[4] molecular wires,[5] and supramolecular structures (network, helical, box, etc.).[6] The diverse applications stem from the facts that the ligands are capable of chelating various metal ions and the resultant complexes possess a wide range of magnetic, photophysical, and electrochemical properties. Thus, the development of synthetic methodologies for *N,N*-bidentate ligands is of paramount importance in chemistry.

N,N-Bidentate ligands with mixed five- and six-membered heterocycles are a desirable class of compounds in the pursuit of structural diversity for property performance. In particular, 1-pyridylimidazo[1,5-*a*]pyridines possess a bidentate structural feature with a pyridyl unit directly next to a fused imidazole and have emerged as a new class of ligands.[7,8] In contrast, there is a lack of an efficient synthetic method for their preparation. The only two methods for such ligands reported so far involve the use of amines to react with dipyridyl ketone in the presence of a sensitive Lewis acid, BF_3,[9] or the oxidization of Schiff bases in the presence of molecular sieves[9] or metal ions requiring two to three steps from dipyridyl ketone.[10] These approaches are encountered with overall yields usually below 30%. Recently, we have disclosed a direct method for the heterocyclization of 2,2′-pyridyl to form imidazo[1,5-*a*]pyridines.[11,12] Here we report a direct cyclization of 2,2′-dipyridyl ketone with aldehydes in the presence of ammonium acetate for the synthesis of desirable *N,N*-bidentate ligands. The significance of this approach is that the reaction is straightforward with only one step without the use of any metal catalysts or highly sensitive Lewis acids. Another advantage is that the reaction scope is significantly wide because the reaction is tolerant with various aldehyde substrates.

SCHEME 1



1 **2**

The first reaction that was examined involved the use of benzaldehyde whose reaction with 2,2′-dipyridyl ketone and ammonium acetate was carried out in acetic acid. The desired product **2a** was obtained in 69% yield (Scheme 1, entry 1 in Table 1), demonstrating that such a direct approach was indeed working and the yield was good as well. A series of benzaldehyde derivatives with different substituents was then examined to study the reaction scope. The results (entries 2−10, Table 1) clearly demonstrated that all the reactions led to the target products without exception. In addition to the wide scope of the application, the yields are moderate to excellent. For example, **2d** and **2g** are obtained in 95% and 64% yield, respectively, while **2h** and **2j** are obtained in 81% and 87% yield, respectively.

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TABLE 1. Yields from 1:1.5:4 Ketone/Aldehyde/NH_4OAc[a]

entry	**1**: Ar in **1**	**2**: yield (%)
1	**1a**: Ph	**2a**: 69
2	**1b**: 2-MeC_6H_4	**2b**: 78
3	**1c**: 3-MeC_6H_4	**2c**: 87
4	**1d**: 4-i-PrC_6H_4	**2d**: 95
5	**1e**: 3-$OMeC_6H_4$	**2e**: 68
6	**1f**: 4-$OEtC_6H_4$	**2f**: 90
7	**1g**: 4-$NMe_2C_6H_4$	**2g**: 64
8	**1h**: 2-FC_6H_4	**2h**: 81
9	**1i**: 3-ClC_6H_4	**2i**: 88
10	**1j**: 3-$NO_2C_6H_4$	**2j**: 87

[a] Molar ratio.

TABLE 2. Yields of 2a Obtained under Various Ratios

run	molar ratio[a]	yield of **2a** (%)
1	1:1.5:4	69
2	1:2:4	75
3	1:3:4	66
4	1:2:3	66
5	1:2:5	81
6	1:2:6	57
7	1:2:7	55

[a] Ketone/benzaldehyde/ammonium acetate.

TABLE 3. Yields Using Optimal Conditions[a]

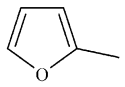
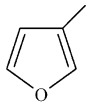
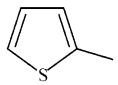
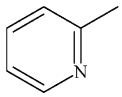
entry	product	yield (%)
1	**2a**	81
2	**2b**	79
3	**2e**	75
4	**2g**	70
5	**2h**	88
6	**2j**	90

[a] Ketone/aldehyde/NH_4OAc 1:2:5 (molar ratio).

Other reaction conditions have been also investigated using benzaldehyde as a model substrate (Table 2). The optimal conditions are established to have a 1:2:5 molar ratio of ketone/aldehyde/NH_4OAc. Several aldehydes were then examined under these optimal conditions (Table 3), and yields are generally improved compared to those from the 1:1.5:4 ratio conditions. Other aldehydes which have already given high yields in the 1:1.5:4 conditions have not been examined further. For example, **2d** was already obtained in 95% yield while **2f** was obtained in 90% yield.

This strategy was further applied for the preparation of potential multi-dentate ligands using aromatic heterocyclic aldehydes. Results from a series of aldehydes containing thiophene, furan, and pyridine showed that all the reactions led to the desired products with no exception (Table 4). These reactions only need a short period of reaction time (1.5 h) and a moderately elevated temperature (80 °C). The extended reaction time and reflux temperature are not only unnecessary but should be also avoided since the yields of the formed products will decrease. For example, the reaction using 2-carboxaldehyde furan (**1k**) afforded **2k** only in 5% yield at 110 °C for 5 h but in 52% yield at 80 °C for 1.5 h. Compounds **2k** and **2m** are potential tridentate ligands because the heteroatom (O or S) from the heterocyclic ring is in close proximity with the *N*,*N*-bidentate unit. For the same reason, compound **2n** is another potential tridentate

TABLE 4. Yields Using Heterocyclic Aldehydes[a]

1:	Ar in **1**	**2:** Yield (%)
1k		**2k:** 52
1l		**2l:** 55
1m		**2m:** 53
1n		**2n:** 12

[a] Ketone/aldehyde/NH_4OAc 1:2:5 (molar ratio).

ligand with intrinsic terpyridine[13] character. Most importantly, a significantly wide application scope was further demonstrated with the use of these heterocyclic aldehydes.

Triphenylamine is known to be a charge-transporting species and a thermally stable electron-donating group,[14] used in nonlinear optical,[15] two-photon absorption,[16] and OLED materials.[17] The treatment of aldehyde **1o**[18] with dipyridyl ketone and ammonium acetate gave **2o** in 84% yield (Scheme 2).

The plausible reaction mechanism involves the initial addition of ammonia to aldehyde to form an imine, followed by the nucleophilic attack of the in situ generated imine to carbonyl of the ketone (Scheme 3). These two steps bring the three individual components together. The subsequent intramolecular interaction leads to the cyclization and eventually to the formation of the desirable imidazopyridine.

In conclusion, a new method for the development of bidentate and multiple dentate ligands has been established to be both straightforward and highly efficient. The strategy involves the use of three easily accessible substrate−aldehydes, dipyridyl ketone, and ammonium acetate without the use of any highly sensitive Lewis acids or metal-based catalysts. This approach is tolerant with various aromatic aldehydes with different types of substituted groups. The wide scope of this application also includes heterocyclic aromatic aldehydes. Since the new ligands also possess an inherent imidazopyridine, a class of compounds of medicinal importance,[19,20] this approach will offer a new and direct route not only for

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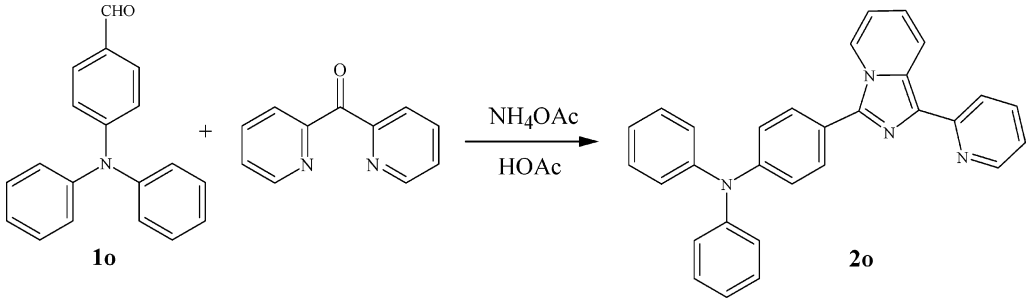
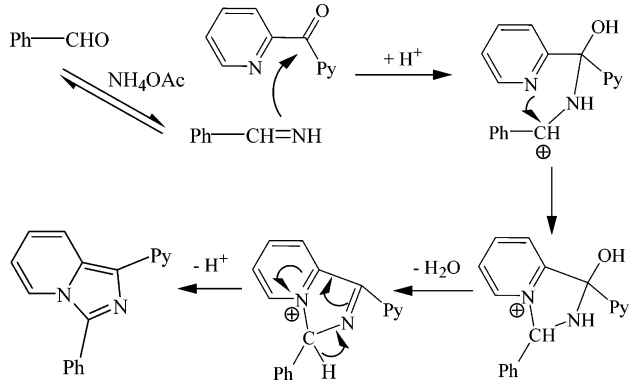
SCHEME 2



SCHEME 3



the ligand synthesis but also for the potential pharmaceutical synthesis.

Experimental Section

General Methods. All the reactions were manipulated in nitrogen atmosphere. All the chemicals were used as received. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded with TMS as an internal standard for reference. The C, H, and N contents were obtained through combustion analysis. Melting points are uncorrected.

Method A: General Procedure for the Preparation of Compound 2a−j. A mixture consisting of either 2,2′-dipyridyl ketone (0.92 g, 5.0 mmol), substituted benzaldehyde (10.0 mmol), NH_4OAc (1.93 g, 25.0 mmol), or 2,2′-dipyridyl ketone (0.92 g, 5.0 mmol), substituted benzaldehyde (7.5 mmol), and NH_4OAc (1.54 g, 20.0 mmol) in 50 mL of glacial acetic acid was stirred at 110 °C under N_2. After 5 h, the reaction mixture was cooled to room temperature and poured into 250 mL of ice water. The formed solid was then filtered, dried, and recrystallized with appropriate mixed solvent. If there no solid formed, the mixture was extracted with CH_2Cl_2 and washed with brine and then water. The organic layer was separated and dried over Na_2SO_4. Upon the removal of solvent, the residue was recrystallized to afford analytically pure compound.

Method B: General Procedure for the Preparation of Compounds 2k−o. To a 100 mL three-necked round-bottom flask was added 30 mL of glacial acetic acid and 2,2′-dipyridyl ketone (0.92 g, 5.0 mmol). The mixture was allowed to stir at room temperature under nitrogen until all the solid was dissolved. Aldehyde (10.0 mmol) was then added, followed by the addition of ammonium acetate (25.0 mmol). The reaction was monitored by the TLC. The reaction mixture was stirred at 80 °C for 1.5 h and then cooled to room temperature. The mixture was added to 200 mL of ice−water and then extracted with methylene chloride. The organic phase was washed with water (100 mL and then 2 × 75 mL) and then dried over sodium sulfate. Upon the removal of solvent under reduced pressure, the residue was purified by chromatography on a silica column, followed by further recrystallization from solvents.

1-(2-Pyridyl)-3-phenylimidazo[1,5-*a*]pyridine (2a): 81% (method A, ketone/aldehyde/NH_4OAc = 1:2:5, molar ratio); yellow solid; mp 92−93 °C (EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 8.66 (1H, d, J = 9.0 Hz), 8.58 (1H, d, J = 4.5 Hz), 8.21 (2H, d, J = 7.5 Hz), 7.80 (2H, d, J = 7.5 Hz), 7.67 (1H, t, J = 7.5 Hz), 7.50 (2H, t, J = 7.5 Hz), 7.42 (1H, t, J = 7.5 Hz), 7.05 (1H, t, J = 6.5 Hz), 6.88 (1H, dd, J = 9.0 Hz), 6.60 (1H, t, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 155.2, 149.2, 138.3, 136.5, 130.8, 130.5, 130.4, 129.3, 129.2, 128.6, 122.1, 121.8, 121.3, 120.7, 120.2, 114.1; GC−MS *m/z* 271 (M^+). Anal. Calcd for $C_{18}H_{13}N_3$: C, 79.68; H, 4.83; N, 15.49. Found: C, 79.55; H, 4.82; N, 15.41.

1-(2-Pyridyl)-3-(2-methylphenyl)imidazo[1,5-*a*]pyridine (2b): 79% (method A, ketone/aldehyde/NH_4OAc = 1:2:5, molar ratio); yellow solid; mp 112−113 °C (EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 8.66 (1H, d, J = 9.0 Hz), 8.58 (1H, d, J = 4.5 Hz), 8.19 (1H, d, J = 8.0 Hz), 7.65 (1H, t, J = 8.0 Hz), 7.57 (1H, d, J = 7.5 Hz), 7.45 (1H, d, J = 7.5 Hz), 7.38−7.21 (3H, m), 7.03 (1H, t, J = 6.5 Hz), 6.86 (1H, dd, J = 9.0 Hz), 6.54 (1H, t, J = 6.5 Hz), 2.21 (3H, s); ^{13}C NMR ($CDCl_3$) δ 155.2, 149.0, 139.14, 138.6, 137.8, 136.3, 130.9, 130.6, 129.9, 129.7, 129.3, 126.2, 121.7, 121.6, 121.0, 120.4, 119.9, 113.6, 19.8; GC−MS *m/z* 285 (M^+). Anal. Calcd for $C_{19}H_{15}N_3$: C, 79.98; H, 5.30; N, 14.73. Found: C, 80.04; H, 5.29; N, 14.75.

1-(2-Pyridyl)-3-(3-methylphenyl)imidazo[1,5-*a*]pyridine (2c): 87.0% (method A, ketone/aldehyde/NH_4OAc = 1:1.5:4, molar ratio); yellow solid; mp 105−107 °C (EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 8.65 (1H, d, J = 9.0 Hz), 8.58 (1H, d, J = 4.5 Hz), 8.20 (2H, t, J = 8.0 Hz), 7.68−7.63 (2H, m), 7.57 (1H, d, J = 8.0 Hz), 7.38 (1H, t, J = 8.0 Hz), 7.22 (1H, d, J = 8.0 Hz), 7.04 (1H, t, J = 7.0 Hz), 6.85 (1H, dd, J = 9.0 Hz), 6.57 (1H, d, J = 7.0 Hz), 2.57 (3H, s); ^{13}C NMR ($CDCl_3$) δ 155.1, 149.0, 139.0, 138.2, 136.2, 130.5, 130.1, 130.0, 129.7, 129.3, 128.9, 125.2, 121.8, 121.7, 121.0, 120.4, 120.0, 113.8, 21.6; GC−MS *m/z* 285 (M^+). Anal. Calcd for $C_{19}H_{15}N_3$: C, 79.98; H, 5.30; N, 14.73. Found: C, 80.01; H, 5.29; N, 14.79.

1-(2-Pyridyl)-3-(4-isopropylphenyl)imidazo[1,5-*a*]pyridine (2d): 95% (method A, ketone/aldehyde/NH_4OAc = 1:1.5:4, molar ratio); yellow solid; mp 100−101°C (hexanes); ^{1}H NMR ($CDCl_3$) δ 8.65 (1H, d, J = 9.0 Hz), 8.58 (1H, d, J = 4.5 Hz), 8.20 (1H, d, J = 8.0 Hz), 7.71 (2H, d, J = 8.0 Hz), 7.66 (1H, t, J = 8.0 Hz), 7.35 (2H, d, J = 8.0 Hz), 7.03 (1H, t, J = 6.5 Hz), 6.85 (1H, dd, J = 9.0 Hz), 6.56 (1H, t, J = 6.5 Hz), 2.95 (1H, hept, J = 7.0 Hz), 1.26 (6H, d, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 155.4, 145.1, 148.9, 138.5, 136.2, 130.6, 130.3, 128.4, 127.6, 127.1, 121.8, 121.7, 120.9, 120.4, 119.9, 113.7, 34.1, 23.9; GC−MS *m/z* 313 (M^+). Anal. Calcd for $C_{21}H_{19}N_3$: C, 80.48; H, 6.11; N, 13.41. Found: C, 80.47; H, 6.13; N, 13.39.

1-(2-Pyridyl)-3-(3-methoxyphenyl)imidazo[1,5-*a*]pyridine (2e): 75% (method A, ketone/aldehyde/NH_4OAc = 1:2:5, molar ratio); yellow solid; mp 96−98 °C (EtOAc/hexanes); IR/cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.66 (1H, d, J = 9.0 Hz), 8.57 (1H, d, J = 4.5 Hz), 8.21 (2H, d, J = 8.0 Hz), 7.66 (1H, t, J = 8.0 Hz), 7.41−7.34 (3H, m), 7.04 (1H, t, J = 6.5 Hz), 6.95 (1H, d, J = 8.0

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Hz), 6.86 (1H, dd, J = 9.0 Hz), 6.58 (1H, t, J = 6.5 Hz), 3.84 (3H, s); ^{13}C NMR ($CDCl_3$) δ 160.2, 155.1, 149.0, 137.9, 136.3, 131.4, 130.5, 130.3, 130.1, 121.9, 121.7, 121.1, 120.5, 120.0, 115.0, 113.9, 113.8, 55.3; GC−MS m/z 301 (M^+). Anal. Calcd for $C_{19}H_{15}N_3O$: C, 75.73; H, 5.02; N, 13.94. Found: C, 75.72; H, 4.99; N, 13.94.

1-(2-Pyridyl)-3-(4-ethoxyphenyl)imidazo[1,5-*a*]pyridine (2f): 90% (method A, ketone/aldehyde/NH_4OAc = 1:1.5:4, molar ratio); yellow solid; mp 130−131 °C (EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 8.63 (1H, d, J = 9.0 Hz), 8.57 (1H, d, J = 4.5 Hz), 8.19 (1H, d, J = 8.0 Hz), 8.12 (1H, d, J = 7.0 Hz), 7.70−7.63 (3H, m), 7.04−6.99 (3H, m), 6.83 (1H, dd, J = 9.0 Hz), 6.56 (1H, t, J = 7.0 Hz), 4.06 (2H, tetra, J = 7.0 Hz), 1.41 (4H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 159.5, 155.1, 149.0, 136.2, 130.2, 129.8, 123.0, 121.8, 121.6, 120.8, 120.3, 119.9, 115.0, 113.7, 63.6, 14.8; GC−MS m/z 315 (M^+). Anal. Calcd for $C_{20}H_{17}N_3O$: C, 76.17; H, 5.43; N, 13.32. Found: C, 76.06; H, 5.40; N, 13.29.

1-(2-Pyridyl)-3-(4-dimethylaminophenyl)imidazo[1,5-*a*]pyridine (2g): 70% (method A, ketone/aldehyde/NH_4OAc = 1:2:5, molar ratio); yellow solid; mp 180−182 °C (EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 8.61 (1H, d, J = 9.0 Hz), 8.57 (1H, d, J = 4.5 Hz), 8.21 (1H, t, J = 6.5 Hz), 8.14 (1H, d, J = 7.0 Hz), 7.67−7.63 (3H, m), 7.01 (1H, t, J = 6.0 Hz), 6.82−6.78 (3H, m), 6.52 (1H, t, J = 7.0 Hz), 2.97 (6H, s); ^{13}C NMR ($CDCl_3$) δ 155.3, 150.7, 148.9, 139.0, 130.2, 129.9, 129.8, 129.4, 121.9, 121.7, 120.6, 120.2, 119.9, 117.6, 113.3, 112.3, 40.4; GC−MS m/z 314 (M^+). Anal. Calcd for $C_{20}H_{18}N_4$: C, 76.41; H, 5.77; N, 17.82. Found: C, 76.22; H, 5.71; N, 17.70.

1-(2-Pyridyl)-3-(2-fluorophenyl)imidazo[1,5-*a*]pyridine (2h): 88% (method A, ketone/aldehyde/NH_4OAc = 1:2:5, molar ratio); yellow solid; mp 127−128 °C (EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 8.68 (1H, d, J = 9.0 Hz), 8.58 (1H, d, J = 4.5 Hz), 8.18 (1H, d, J = 8.0 Hz), 7.75 (2H, t, J = 6.0 Hz), 7.67 (1H, t, J = 8.0 Hz), 7.47−7.42 (1H, m), 7.30 (1H, t, J = 8.0 Hz), 7.21 (1H, t, J = 9.0 Hz), 7.05 (1H, t, J = 7.0 Hz), 6.92 (1H, dd, J = 9.0 Hz), 6.64 (1H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 161.2, 159.6, 155.2, 149.2, 136.5, 133.6, 132.8, 132.7, 131.4, 131.3, 131.2, 130.6, 125.2, 125.1, 122.7, 122.6, 121.7, 121.5, 120.7, 120.1, 116.5, 116.3, 113.9; GC−MS m/z 289 (M^+). Anal. Calcd for $C_{18}H_{12}FN_3$: C, 74.73; H, 4.18; N, 14.52. Found: C, 74.65; H, 4.18; N, 14.42.

1-(2-Pyridyl)-3-(3-chlorophenyl)imidazo[1,5-*a*]pyridine (2i): 88% (method A, ketone/aldehyde/NH_4OAc = 1:1.5:4, molar ratio); yellow solid; mp 130−131 °C (EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 8.67 (1H, d, J = 9.0 Hz), 8.58 (1H, d, J = 4.5 Hz), 8.18 (2H, d, J = 7.0 Hz), 7.82 (1H, s), 7.68 (2H, t, J = 7.5 Hz), 7.44−7.37 (2H, m), 7.06 (1H, t, J = 6.5 Hz), 6.89 (1H, dd, J = 9.0 Hz), 6.64 (1H, t, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 155.1, 149.2, 136.7, 136.5, 135.3, 132.1, 131.2, 130.7, 130.5, 129.1, 128.6, 126.3, 122.2, 121.6, 121.5, 120.9, 120.2, 114.6; GC−MS m/z 306 (M^+). Anal. Calcd for $C_{18}H_{12}ClN_3$: C, 70.71; H, 3.96; N, 13.74. Found: C, 70.92; H, 3.99; N, 13.71.

1-(2-Pyridyl)-3-(3-nitrophenyl)imidazo[1,5-*a*]pyridine (2j): 90% (method A, ketone/aldehyde/NH_4OAc = 1:2:5, molar ratio); red solid; mp 185−186 °C (HOAc/ethanol); ^{1}H NMR (DMSO-d_6) δ 8.61−8.57 (4H, m), 8.31 (1H, d, J = 8.0 Hz), 8.26 (1H, d, J = 8.0 Hz), 8.10 (1H, d, J = 8.0 Hz), 7.83−7.79 (2H, m), 7.15 (1H, t, J = 7.0 Hz), 7.09 (1H, t, J = 7.0 Hz), 6.88 (1H, t, J = 7.0 Hz); ^{13}C NMR (DMSO-d_6) δ 154.9, 149.8, 149.0, 137.4, 135.9, 134.5, 131.8, 131.4, 131.0, 130.7, 123.8, 123.5, 123.3, 123.2, 121.6, 121.5, 120.0, 115.7; GC−MS m/z 316 (M^+). Anal. Calcd for $C_{18}H_{12}N_4O_2$: C, 68.35; H, 3.82; N, 17.71. Found: C, 68.32; H, 3.82; N, 17.66.

1-(2-Pyridyl)-3-(2-furyl)imidazo[1,5-*a*]pyridine (2k): 52% (method B, ketone/aldehyde/NH_4OAc = 1:2:4, molar ratio); yellow solid; flash silica column: EtOAc/hexanes = 1/3 (v/v); mp 123−124 °C (EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 8.66 (1H, d, J = 9.0 Hz), 8.60 (1H, d, J = 7.0 Hz), 8.57 (1H, d, J = 4.5 Hz), 8.19 (1H, d, J = 8.0 Hz), 7.67 (1H, t, J = 8.0 Hz), 7.55 (1H, s), 7.07−7.02 (2H, m), 6.90 (1H, t, J = 8.0 Hz), 6.69 (1H, t, J = 7.0 Hz), 6.56 (1H, s); ^{13}C NMR ($CDCl_3$) δ 154.7, 149.0, 146.1, 142.3, 136.3, 130.09, 130.1, 129.9, 123.0, 121.7, 121.3, 120.7, 120.1, 114.5, 111.7, 108.8; GC−MS m/z 261 (M^+). Anal. Calcd for $C_{16}H_{11}N_3O$: C, 73.55; H, 4.24; N, 16.08. Found: C, 73.63; H, 4.28; N, 15.91.

1-(2-Pyridyl)-3-(3-furyl)imidazo[1,5-*a*]pyridine (2l): 55% (method B, ketone/aldehyde/NH_4OAc = 1:2:4, molar ratio); yellow solid; flash silica column: EtOAc/hexanes = 1/3 (v/v); mp 103−104 °C (EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 8.64 (1H, d, J = 9.0 Hz), 8.57 (1H, d, J = 4.5 Hz), 8.17 (1H, d, J = 8.0 Hz), 8.01 (1H, d, J = 7.0 Hz), 7.96 (1H, s), 7.67 (1H, t, J = 8.0 Hz), 7.56 (1H, s), 7.04 (1H, t, J = 6.5 Hz), 6.95 (1H, s), 6.87 (1H, t, J = 8.0 Hz), 6.66 (1H, t, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 155.1, 149.2, 143.8, 140.7, 136.5, 131.6, 130.6, 130.2, 122.1, 121.9, 120.9, 120.7, 120.1, 116.5, 114.3, 110.3; GC−MS m/z 261 (M^+). Anal. Calcd for $C_{16}H_{11}N_3O$: C, 73.55; H, 4.24; N, 16.08. Found: C, 73.64; H, 4.26; N, 16.05.

1-(2-Pyridyl)-3-(2-thienyl)imidazo[1,5-*a*]pyridine (2m): 53% (method B, ketone/aldehyde/NH_4OAc = 1:2:5, molar ratio); yellow solid; mp 131−132 °C (EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 8.67 (1H, d, J = 9.0 Hz), 8.57 (1H, d, J = 4.5 Hz), 8.28 (1H, d, J = 7.0 Hz), 8.20 (1H, d, J = 8.0 Hz), 7.67 (1H, t, J = 8.0 Hz), 7.51 (1H, s), 7.40 (1H, d, J = 4.5 Hz), 7.16 (1H, m), 7.05 (1H, t, J = 6.5 Hz), 6.88 (1H, t, J = 8.0 Hz), 6.68 (1H, t, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 155.0, 149.2, 136.5, 132.8, 132.3, 130.9, 130.6, 127.9, 126.6, 125.7, 122.2, 122.1, 121.3, 120.9, 120.3, 114.7; GC−MS m/z 277 (M^+). Anal. Calcd for $C_{16}H_{11}N_3S$: C, 69.29; H, 4.00; N, 15.15. Found: C, 69.38; H, 3.95; N, 15.21.

1,3-Di(2-pyridyl)imidazo[1,5-*a*]pyridine (2n): 12% (method B, ketone/aldehyde/NH_4OAc = 1:2:5, molar ratio); yellow solid; flash column: EtOAc/hexanes = 1/5; mp 151−152 °C (EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 9.98 (1H, d, J = 7.0 Hz), 8.73 (1H, d, J = 9.0 Hz), 8.60 (2H, s), 8.43 (1H, d, J = 8.0 Hz), 8.25 (1H, d, J = 8.0 Hz), 7.77−7.68 (2H, m), 7.21−7.15 (1H, m), 7.09−6.99 (2H, m), 6.78 (1H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 155.1, 151.2, 149.1, 148.3, 136.7, 136.5, 135.1, 131.9, 126.5, 122.6, 122.4, 122.0, 121.2, 120.8, 120.3, 114.5; GC−MS m/z 272 (M^+). Anal. Calcd for $C_{17}H_{12}N_4$: C,74.98; H, 4.44; N, 20.58. Found: C, 74.86; H, 4.50; N, 20.58.

1-(2-Pyridyl)-3-(4-diphenylaminophenyl)imidazo[1,5-*a*]pyridine (2o): 84% (method B, ketone/aldehyde/NH_4OAc = 1:2:5, molar ratio); yellow solid; mp 154−155 °C (HOAc/EtOAc); ^{1}H NMR (DMSO-d_6) δ 8.54 (2H, m), 8.41 (1H, m), 8.05 (1H, m), 7.73 (3H, m), 7.30 (4H, m), 7.06 (10H, m), 6.76 (1H, m); ^{13}C NMR ($CDCl_3$) δ 155.0, 151.2, 149.1, 148.3, 136.7, 136.6, 135.2, 131.9, 130.7, 126.5, 122.6, 122.4, 122.0, 121.2, 120.8, 120.3, 114.6; GC−MS m/z 438 (M^+). Anal. Calcd for $C_{30}H_{22}N_4$: C, 82.17; H, 5.06; N, 12.78. Found: C, 82.23; H, 5.04; N, 12.62.

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