Mild Conditions for Copper-Catalyzed N-Arylation of Imidazoles

Huaming Chen,[a] Deping Wang,[b,c] Xianyang Wang,[d] Wenlong Huang,*[a] Qian Cai,[b] Ke Ding*[b]

[a] China Pharmaceutical University, # 24 Tongjiaxiang, Nanjing 210009, P. R. of China
E-mail: ydhuangwenlong@126.com

[b] Key Laboratory of Regenerative Biology and Institute of Chemical Biology, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou International Business Incubator D-10, Guangzhou Science Park, Guangzhou 510663, P. R. of China
Fax +86(20)32290606.; E-mail: ding_ke@gibh.ac.cn

[c] Graduate School of the Chinese Academy of Sciences, Chinese Academy of Sciences, 19AYuquan Road, Beijing 100049, P. R. of China

[d] Jiangsu Provincial Institute of Materia Medica, Nanjing University of Technology, 5 Xinmofan Road, Nanjing 210009, P. R. of China

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Abstract: An efficient copper(I) bromide catalyzed N-arylation of azoles with a variety of aromatic bromides and iodides under mild conditions is reported. This reaction displayed great functional group compatibility and excellent reactive selectivity.

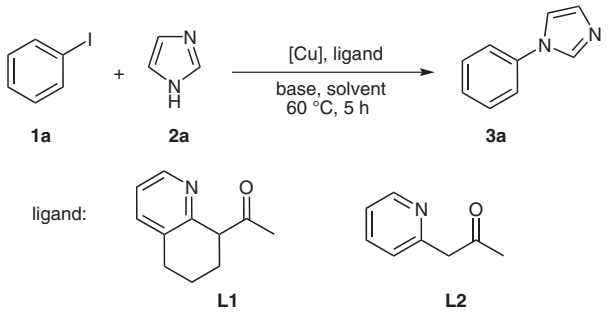
Key words: copper, aryl halides, imidazoles, azoles, N-arylation

N-Arylimidazoles represent an attractive class of chemicals that are widely used in the preparation of agrochemicals, pharmaceuticals, biological active compounds, and N-heterocyclic carbene chemistry.[1,2] Classical synthetic methods for these compounds included nucleophilic aromatic substitution of active aryl halides with imidazole and Ullmann-type coupling reactions etc.[3] However, these methods suffer from several drawbacks such as harsh reaction conditions (>200 °C) and/or the use of stoichiometric amounts of copper.[4] Much progress has been achieved over the last few decades in copper-catalyzed C–N bond formation.[3] Employing different mono- and bidentate chelators as effective ancillary ligands, *N*-arylimidazoles were successfully produced under lower temperatures (100–150 °C) in 24–40 hours.[5] Most recently, a ligand-free N-arylation of imidazoles from aryl iodides was also reported at 35–40 °C in 40 hours.[6] Nevertheless, a new strategy for the assembly of *N*-arylimidazoles under mild conditions, especially at lower temperatures and with shorter reaction times, remains highly desirable.

Recently, we identified pyridin-2-yl β-ketones as new efficient supporting ligands for copper-catalyzed coupling reactions of aliphatic amines, ammonia, and phenols with aryl halides under mild conditions.[7] Herein we report the efficient N-arylation of azoles with a variety of aromatic bromides and iodides under the catalysis of a combination of copper(I) bromide/pyridin-2-yl β-ketone.

Initially, we chose the coupling of iodobenzene (**1a**) with 1*H*-imidazole (**2a**) as a model to optimize the reaction conditions. As shown in Table 1, the yield of **3a** was poor, less than 10%, when the reaction was carried out in the ab-

Table 1 Optimization of the Reaction Conditions for the N-Arylation of 1*H*-Imidazole (**2a**) with Iodobenzene (**1a**)[a]



Entry	Base	Solvent	[Cu]	Yield (%)
1	Cs_2CO_3	DMSO	CuBr	<10[b]
2	Cs_2CO_3	DMSO	–	<10
3	Cs_2CO_3	DMSO	CuBr	50[c]
4	Cs_2CO_3	DMSO	CuBr	95
5	Cs_2CO_3	DMSO	CuBr	85[d]
6	Cs_2CO_3	DMSO	CuI	95
7	Cs_2CO_3	DMSO	CuCl	66
8	Cs_2CO_3	MeCN	CuBr	17
9	Cs_2CO_3	*i*-PrOH	CuBr	11
10	Cs_2CO_3	H_2O	CuBr	0
11	Cs_2CO_3	DMF	CuBr	93
12	Na_2CO_3	DMSO	CuBr	65
13	K_2CO_3	DMSO	CuBr	38
14	NaOH	DMSO	CuBr	85
15	Et_3N	DMSO	CuBr	8

[a] Reaction conditions: PhI (**1a**, 1.0 mmol), 1*H*-imidazole (**2a**, 1.2 mmol), [Cu] (5 mmol%), **L1** (10 mmol%) (unless otherwise noted), base (2.0 mmol), solvent (1.0 mL), 60 °C, N_2, 5 h.
[b] Without ligand.
[c] **L1** (5 mmol%) was used.
[d] **L2** (10 mmol%) was used.

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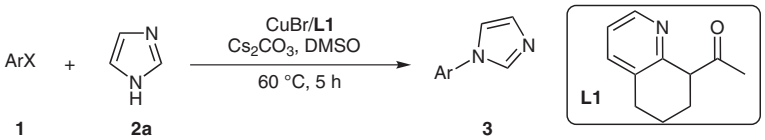
sence of ligand or copper at 60 °C (Table 1, entries 1 and 2). However, when 5 mmol% copper(I) bromide and 5 mmol% 1-(5,6,7,8-tetrahydroquinolin-8-yl)ethanone (**L1**) were employed, **3a** was produced in moderate yield (Table 1, entry 3). The isolated yield of **3a** improved significantly (~95%) when 10 mmol% of supporting ligand **L1** was utilized. The results also revealed that the simplest and commercially available pyridin-2-yl β-ketone analogue, 1-pyridin-2-ylpropan-2-one (**L2**), also successfully promoted the coupling reaction with a slightly lower yield (Table 1, entry 5). Other conditions, such as copper sources, solvents, and bases, were also screened. The results indicated that optimal combination of 5 mmol% copper(I) bromide, 10 mmol% **L1**, and 2.0 equivalents of cesium carbonate in dimethyl sulfoxide (1.0 mL).

Table 2 Copper(I) Bromide/**L1**-Catalyzed N-Arylation of 1*H*-Imidazole (**2a**) with Aryl and Heteroaryl Halides **1**[a]



1 **2a** **3**

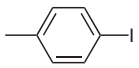
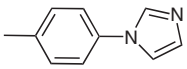
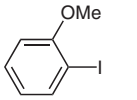
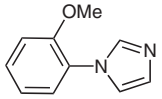
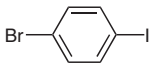
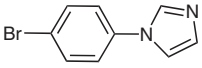
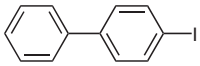
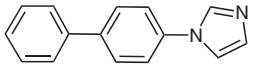
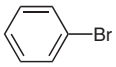
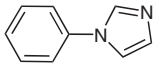
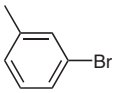
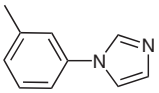
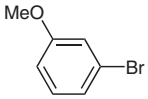
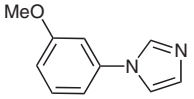
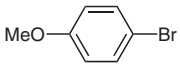
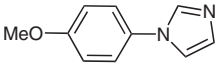
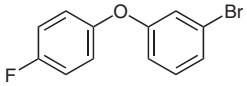
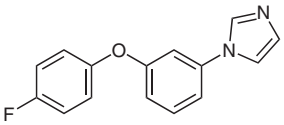
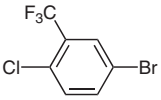
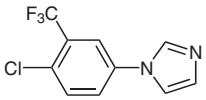
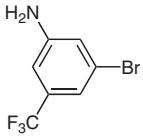
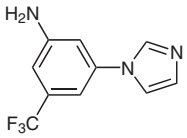
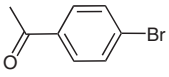
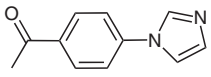
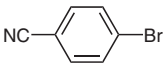
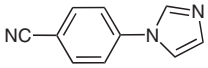
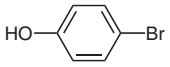
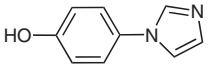
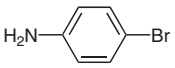
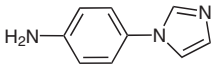
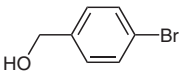
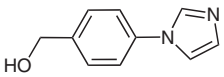
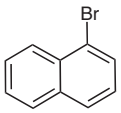
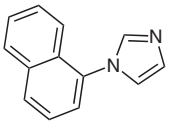
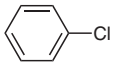
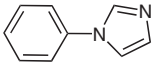
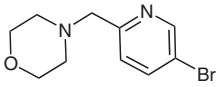
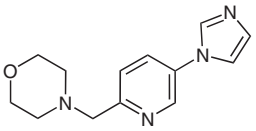
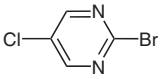
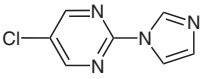
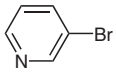
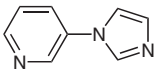
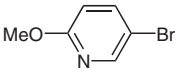
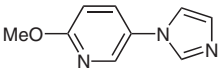
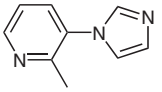
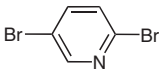
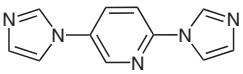
Entry	Ar-X	Product	Yield (%)
1		**3b** 	83
2		**3c** 	78
3		**3d** 	91
4		**3e** 	89
5		**3a** 	86
6		**3f** 	82
7		**3g** 	80
8		**3h** 	82
9		**3i** 	86
10		**3j** 	95
11		**3k** 	86[b]
12		**3l** 	92
13		**3m** 	88

Table 2 Copper(I) Bromide/**L1**-Catalyzed N-Arylation of 1*H*-Imidazole (**2a**) with Aryl and Heteroaryl Halides **1**[a] (continued)

1 **2a** **3**

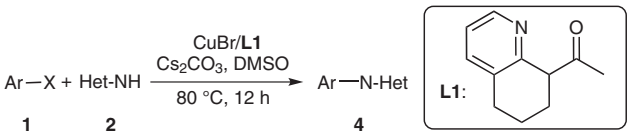
Entry	Ar-X	Product	Yield (%)
14		**3n** 	72[b]
15		**3o** 	81[b]
16		**3p** 	80[b]
17		**3q** 	92
18		**3a** 	0
19		**3r** 	78
20		**3s** 	76
21		**3t** 	77
22		**3u** 	80
23		**3v** 	73
24		**3w** 	75[c]

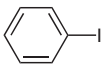
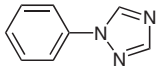
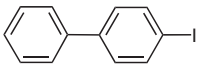
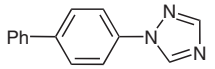
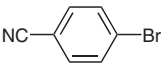
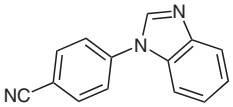
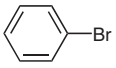
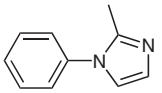
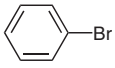
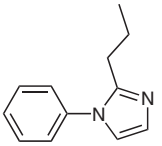
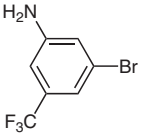
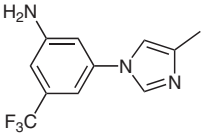
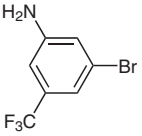
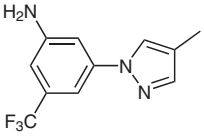
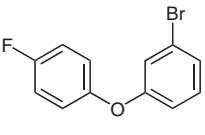
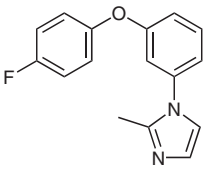
[a] Reaction conditions: Ar-X **1** (1.0 mmol), 1*H*-imidazole (**2a**, 1.2 mmol), CuBr (5 mmol%), **L1** (10 mmol%), Cs_2CO_3 (2.0 mmol), DMSO (1.0 mL), 60 °C, N_2, 5 h.
[b] 120 °C, 12 h.
[c] Performed with 2.0 mmol of imidazole.

The scope of the copper(I) bromide/**L1**-catalyzed N-arylation of 1*H*-imidazole (**2a**) was explored by using a variety of aryl iodides and aryl bromides **1** under the optimized conditions. As summarized in Table 2, the results showed that all the tested aryl iodides coupled with 1*H*-imidazole (**2a**) to afford the desired products **3b–e** with satisfactory yields (entries 1–4). For aryl bromides, the catalyst system efficiently promoted the coupling reactions in most cases. The results also indicated that electron-withdrawing groups in the aryl bromide substrates benefited the coupling reaction to give the products **3j**,**l**,**m** in excellent yields (Table 2, entries 10, 12, and 13). The coupling reactions were also successfully performed using electron-rich substrates, such as 3-bromotoluene, 3-bromoanisole, and 4-bromoanisole, giving **3f–h** in good yields (Table 2, entries 6–8). Furthermore, the copper(I) bromide/**L1** system was well tolerated by multiple functional groups such as ketones, nitriles, free amines, and free hydroxy groups (Table 2, entries 11–16). Although this protocol did not work well for electron-rich aryl chlorides (i.e., chlorobenzene, Table 2, entry 18) even if the reactions were carried out at high temperatures (120 °C) with longer reaction time, the catalyst system significantly improved the reaction efficiency of electron-deficient aryl

chlorides with 1*H*-imidazole (**2a**). For example, coupling of 1-chloro-4-nitrobenzene with 1*H*-imidazole (**2a**) at 100 °C in the absence of **L1** gave 1-(4-nitrophenyl)-1*H*-imidazole in only 41% yield, but addition of 10% **L1** at 100 °C gave the product in a dramatically improved 81% yield (results not shown). Utilizing 4-chlorobenzonitrile as the substrate with 1*H*-imidazole (**2a**) gave **3m** in 75% isolated yield (results not shown).

Table 3 Copper(I) Bromide/**L1**-Catalyzed N-Arylation of Azoles with Aryl Halides[a]



Entry	Ar-X	Product	Yield (%)
1		**4a** 	83[b]
2		**4b** 	83[b]
3		**4c** 	86
4		**4d** 	78
5		**4e** 	65
6		**4f** 	81[c,d]
7		**4g** 	88[c]
8		**4h** 	78

[a] Reaction conditions: Ar-X **1** (1.0 mmol), Het-NH **2** (1.2 mmol), CuBr (5 mmol%), **L1** (10 mmol%), Cs_2CO_3 (2.0 mmol), DMSO (1.0 mL), 80 °C, N_2, 12 h.
[b] 60 °C.
[c] 120 °C.
[d] The regioselectivity (19:1) was determined by GC-MS analysis and the major pure product was isolated by recrystallization.

The N-arylation of imidazole with various halopyridines and halopyrimidines was also performed with great success. Almost all the halopyridines and halopyrimidines coupled with 1*H*-imidazole (**2a**) to give **3r–w** in excellent or good yields under the optimized conditions (Table 2, entries 19–24). In addition, the double-coupling product **3w** was obtained when 2,5-dibromopyridine was reacted with 1*H*-imidazole (**2a**) (Table 2, entry 24).

To further expand the scope of this methodology, the catalytic system was applied to other nitrogen-containing heterocycles **2**. We were pleased to find that most of azoles **2** coupled with aryl halides **1** to afford the corresponding products **4** in good yields (Table 3), but that slightly higher reaction temperatures (80 °C) and longer reaction times (12 h) were required. It should be noted that sterically hindered 2-methyl-1*H*-imidazole and 2-propyl-1*H*-imidazole gave the desired coupling products **4d**,**e**,**h** in good yields (Table 3, entries 4, 5, and 8). Aryl bromides bearing a free amino group could successfully undergo selective N-arylation of 4-methyl-1*H*-imidazole and 4-methyl-1*H*-pyrazole to assemble the corresponding products **4f**,**g** in 81% and 88% yields, respectively (Table 3, entries 6 and 7). In addition, excellent N1 regioselectivity (19:1) for the coupling of 4-methyl-1*H*-imidazole was observed (Table 3, entry 6).

In summary, we have successfully developed an efficient copper(I) bromide/**L1** catalyst system for the N-arylation of azoles with a variety of aromatic bromides and iodides. Employing this catalytic system, *N*-arylazoles can be synthesized under much milder conditions (60–80 °C, 5–12 h). Also, this new protocol displays great functional groups compatibility and excellent reactive selectivity. Our effort may provide an attractive addition to the copper-catalyzed synthesis of *N*-arylazoles.

All reactions were carried out in 5-mL sealed tubes, under a pure and dry argon atmosphere. Solvents, base and all other materials were used commercially without further purification. **L1**, **L2** were prepared as previously described.[7a] All new compounds are indicated as such: **3i**, **3j**, **3k**, **3r**, **3s**, **3v**, **3w**, **4e**, **4g**, **4h**; for all known compounds, adequate characterization was obtained by ^{1}H NMR spectroscopy and mass spectrometry. NMR spectra were recorded at 20 °C on a 300 or 400 MHz spectrometer working respectively at 300 or 400 MHz for ^{1}H, at 75 or 100 MHz for ^{13}C.

Arylazoles 3 and 4; General Procedure

A sealed tube equipped with a Teflon valve was charged with a magnetic stir bar, CuBr (7 mg, 0.05 mmol, 5 mol%), Cs_2CO_3 (650 mg, 2 mmol) and any remaining solids (azoles **2** and/or aryl halides **1**). The tube was evacuated and backfilled with N_2 (3 ×). Under a counter flow of N_2, azole **2** (1.2 mmol, if liquid), aryl halide **1** (1 mmol, if liquid), DMSO (1.0 mL), and **L1** (18 mg, 0.10 mmol, 10 mol%) were added by syringe. The tube was evacuated and again backfilled with N_2 (3 ×) and sealed. The mixture was heated to the indicated temperature for the required time period. After cooling to r.t., the mixture was diluted with EtOAc (25 mL), passed through a fritted glass filter to remove the inorganic salts and the filtrate was washed by H_2O, brine, then removed under vacuum. The residue was purified by column chromatography (silica gel) and the product was dried under high vacuum (at least 1 h).

1-Phenyl-1*H*-imidazole (3a)[5e]
^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.28 (s, 1 H), 7.76 (t, 1 H), 7.67 (q, *J* = 5.8 Hz, 2 H), 7.53 (t, 2 H), 7.37 (t, 1 H), 7.14 (s, 1 H).

MS: *m*/*z* = 144.

1-(4-Tolyl)-1*H*-imidazole (3b)[5t]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.19 (s, 1 H), 7.69 (s, 1 H), 7.52 (d, *J* = 6.8 Hz, 2 H), 7.31 (d, *J* = 7.2 Hz, 2 H), 7.09 (s, 1 H), 2.34 (s, 3 H).

MS: *m*/*z* = 158.

1-(2-Methoxyphenyl)-1*H*-imidazole (3c)[6]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.89 (s, 1 H), 7.40 (t, *J* = 7.5 Hz, 3 H), 7.25 (d, *J* = 8.5 Hz, 1 H), 7.07 (t, *J* = 7.5 Hz, 2 H), 3.82 (s, 3 H).

MS: *m*/*z* = 174.

1-(4-Bromophenyl)-1*H*-imidazole (3d)[5e]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.28 (s, 1 H), 7.84 (s, 1 H), 7.72 (d, *J* = 9.0 Hz, 2 H), 7.63 (d, *J* = 9.0 Hz, 2 H), 7.11 (s, 1 H).

MS: *m*/*z* = 223.

1-Biphenyl-4-yl-1*H*-imidazole (3e)[5i]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.33 (s, 1 H), 7.81 (m, 3 H), 7.74 (m, 4 H), 7.49 (m, 2 H), 7.39 (t, *J* = 7.3 Hz, 1 H), 7.13 (s, 1 H).

MS: *m*/*z* = 220.

1-(3-Tolyl)-1*H*-imidazole (3f)[5r]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.23 (s, 1 H), 7.73 (s, 1 H), 7.49 (s, 1 H), 7.39 (t, 2 H), 7.18 (t, *J* = 7.0 Hz, 1 H), 7.10 (s, 1 H), 2.38 (s, 3 H).

MS: *m*/*z* = 158.

1-(3-Methoxyphenyl)-1*H*-imidazole (3g)[5r]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.29 (s, 1 H), 7.77 (s, 1 H), 7.42 (t, *J* = 8.5 Hz, 1 H), 7.22 (t, 2 H), 7.11 (s, 1 H), 6.94 (q, 1 H), 3.84 (s, 3 H).

MS: *m*/*z* = 174.

1-(4-Methoxyphenyl)-1*H*-imidazole (3h)[6]
^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.12 (s, 1 H), 7.64 (s, 1 H), 7.55 (d, *J* = 8.8 Hz, 2 H), 7.06 (d, *J* = 8.8 Hz, 3 H), 3.80 (s, 3 H).

MS: *m*/*z* = 174.

1-[3-(4-Fluorophenoxy)phenyl]-1*H*-imidazole (3i)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.30 (s, 1 H), 7.78 (s, 1 H), 7.45 (m, 3 H), 7.28 (m, 2 H), 7.15 (m, 2 H), 7.10 (s, 1 H), 6.88 (t, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.0, 159.2, 157.8, 151.7, 138.6, 135.5, 131.0, 130.4, 123.4, 121.3, 121.2, 120.3, 118.1, 116.8, 116.5, 116.4, 115.6, 114.9, 111.0.

MS: *m*/*z* = 254.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{12}FN_2O$: 255.0928; found: 255.0936.

1-[4-Chloro-3-(trifluoromethyl)phenyl]-1*H*-imidazole (3j)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.42 (s, 1 H), 8.12 (d, 1 H), 8.02 (m, 1 H), 7.90 (m, 2 H), 7.15 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.0, 135.5, 133.1, 131.4, 131.2, 130.4, 127.5, 125.4, 123.9, 120.75, 120.67, 120.61, 120.54, 120.29, 118.1.

MS: *m*/*z* = 246.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{10}H_7ClF_3N_2$: 247.0244; found: 247.0240.

3-(1*H*-Imidazol-1-yl)-5-(trifluoromethyl)aniline (3k)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.20 (br, 1 H), 7.72 (br, 1 H), 7.10 (s, 1 H), 7.01 (s, 1 H), 6.97 (s, 1 H), 6.84 (s, 1 H), 5.89 (s, 2 H).

MS: *m*/*z* = 227.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{10}H_7ClF_3N_2$: 228.0743; found: 228.0748.

1-[4-(1*H*-Imidazol-1-yl)phenyl]ethanone (3l)[5t]
^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.48 (s, 1 H), 8.15 (d, *J* = 8.8 Hz, 2 H), 7.94 (s, 1 H), 7.90 (d, *J* = 8.8 Hz, 2 H), 7.22 (s, 1 H), 2.67 (s, 3 H).

MS: *m*/*z* = 186.

4-(1*H*-Imidazol-1-yl)benzonitrile (3m)[5t]
^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.43 (s, 1 H), 7.97 (d, *J* = 8.8 Hz, 2 H), 7.88 (d, *J* = 8.8 Hz, 3 H), 7.15 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 140.57, 136.25, 134.67, 130.99, 120.95, 118.81, 118.21, 109.53.

MS: *m*/*z* = 169.

4-(1*H*-Imidazol-1-yl)phenol (3n)[5t]
^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.81 (br, 1 H), 8.15 (s, 1 H), 7.60 (s, 1 H), 7.39 (d, *J* = 8.8 Hz, 2 H), 7.11 (s, 1 H), 6.85 (d, *J* = 8.8 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 157.03, 143.02, 129.24, 129.06, 122.86, 119.21, 116.57.

MS: *m*/*z* = 160.

4-(1*H*-Imidazol-1-yl)aniline (3o)[5t]
^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.95 (br, 1 H), 7.47 (s, 1 H), 7.23–7.19 (m, 2 H), 7.01 (s, 1 H), 6.67–6.63 (m, 2 H), 5.24 (br, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 148.42, 135.81, 129.47, 126.72, 122.45, 118.90, 114.73.

MS: *m*/*z* = 159.

[4-(1*H*-Imidazol-1-yl)phenyl]methanol (3p)[6]
^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.21 (s, 1 H), 7.70 (s, 1 H), 7.57 (d, *J* = 8.8 Hz, 2 H), 7.42 (d, *J* = 8.4 Hz, 2 H), 7.09 (s, 1 H), 5.32 (t, *J* = 6.0 Hz, 1 H), 4.52 (d, *J* = 6.0 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 141.74, 135.95, 135.90, 130.17, 128.24, 120.55, 118.52, 115.48, 62.71.

MS: *m*/*z* = 174.

1-Naphthalen-1-yl-1*H*-imidazole (3q)[5e]
^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.15 (d, 2 H), 8.00 (s, 1 H), 7.66 (m, 1 H), 7.60 (m, 2 H), 7.56 (m, 2 H), 7.50 (m, 1 H), 7.20 (s, 1 H).

MS: *m*/*z* = 194.

4-{[5-(1*H*-Imidazol-1-yl)pyridin-2-yl]methyl}morpholine (3r)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.85 (d, 1 H), 8.31 (s, 1 H), 8.07 (dd, *J* = 7.2, 3.6 Hz, 1 H), 7.81 (s, 1 H), 7.60 (m, 1 H), 7.15 (s, 1 H), 3.64 (s, 2 H), 3.60 (m, 4 H), 2.45 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.8, 142.2, 135.5, 132.6, 130.9, 129.4, 123.8, 118.1, 66.8, 64.2, 53.7.

MS: *m*/*z* = 244.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{17}N_4O$: 245.1397; found: 245.1392.

5-Chloro-2-(1*H*-imidazol-1-yl)pyrimidine (3s)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.00 (s, 2 H), 8.56 (s, 1 H), 7.93 (s, 1 H), 7.16 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 190.5, 157.1, 136.3, 131.0, 116.6, 106.3.

MS: *m*/*z* = 180.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_7H_6ClN_4$: 181.0276; found: 181.0279.

3-(1*H*-Imidazol-1-yl)pyridine (3t)[5u]
^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.96 (d, *J* = 3.2 Hz, 1 H), 8.57 (q, 1 H), 8.35 (s, 1 H), 8.11 (m, 1 H), 7.84 (s, 1 H), 7.57 (m, 1 H), 7.16 (s, 1 H).

MS: *m*/*z* = 145.

5-(1*H*-Imidazol-1-yl)-2-methoxypyridine (3u)[5u]
^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.48 (d, *J* = 4.0 Hz, 1 H), 8.17 (s, 1 H), 8.01 (dd, *J* = 8.0, 4.0 Hz, 1 H), 7.68 (s, 1 H), 7.11 (s, 1 H), 6.98 (d, *J* = 11.6 Hz, 1 H), 3.90 (s, 3 H).

MS: *m*/*z* = 175.

3-(1*H*-Imidazol-1-yl)-2-methylpyridine (3v)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.56 (m, 1 H), 7.90 (s, 1 H), 7.75 (m, 1 H), 7.67 (s, 1 H), 7.43 (m, 1 H), 7.13 (s, 1 H), 2.36 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.6, 149.4, 137.3, 133.9, 132.8, 130.0, 121.7, 120.3, 40.9.

MS: *m*/*z* = 159.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_9H_{10}N_3$: 160.0869; found: 160.0871.

2,5-Bis(1*H*-imidazol-1-yl)pyridine (3w)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.87 (d, *J* = 3.6 Hz, 1 H), 8.58 (s, 1 H), 8.38 (s, 1 H), 8.34 (d, *J* = 3.6 Hz, 1 H), 8.00 (m, 2 H), 7.88 (s, 1 H), 7.16 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.1, 142.1, 135.5, 135.0, 132.4, 132.1, 131.4, 131.2, 118.1, 116.1, 112.8.

MS: *m*/*z* = 211.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{10}N_5$: 212.0931; found: 212.0933.

1-Phenyl-1*H*-1,2,4-triazole (4a)[5r]
H NMR (300 MHz, DMSO-d_6): δ = 9.30 (s, 1 H), 8.24 (s, 1 H), 7.88 (m, 2 H), 7.58 (m, 2 H), 7.43 (t, *J* = 7.2 Hz, 1 H).

MS: *m*/*z* = 145.

1-Biphenyl-4-yl-1*H*-1,2,4-triazole (4b)[8b]
^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.36 (s, 1 H), 8.27 (s, 1 H), 7.95–7.98 (d, *J* = 8.9 Hz, 2 H), 7.85–7.89 (d, *J* = 8.8 Hz, 2 H), 7.73–7.76 (t, *J* = 7.2 Hz, 2 H), 7.47–7.53 (t, *J* = 7.8 Hz, 2 H), 7.38–7.43 (t, *J* = 7.3 Hz, 1 H).

MS: *m*/*z* = 221.

4-(1*H*-Benzoimidazol-1-yl)benzonitrile (4c)[5s]
^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.65 (s, 1 H), 8.06 (d, *J* = 8.4 Hz, 2 H), 7.90 (d, *J* = 8.8 Hz, 2 H), 7.79–7.77 (m, 1 H), 7.71–7.68 (m, 1 H), 7.36–7.31 (m, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 144.43, 143.57, 140.20, 134.75, 132.77, 124.45, 124.30, 123.54, 120.62, 118.77, 111.35, 110.30.

MS: *m*/*z* = 219.

2-Methyl-1-phenyl-1*H*-imidazole (4d)[5r]
^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.54 (m, 2 H), 7.45 (m, 3 H), 7.27 (s, 1 H), 6.92 (s, 1 H), 2.28 (s, 3 H).

MS: *m*/*z* = 158.

1-Phenyl-2-propyl-1*H*-imidazole (4e)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.51–7.56 (m, 3 H), 7.41–7.48 (m, 2 H), 7.23 (s, 1 H), 6.94 (s, 1 H), 2.50–2.58 (m, 2 H), 1.53–1.60 (m, 2 H), 0.78–0.81 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.5, 137.9, 129.3, 128.2, 127.5, 125.8, 120.6, 28.9, 21.4, 13.7.

MS: *m*/*z* = 186.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{15}N_2$: 187.1230; found: 187.1233.

3-(4-Methyl-1*H*-imidazol-1-yl)-5-(trifluoromethyl)aniline (4f)[8a]
^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.06 (d, *J* = 0.8 Hz, 1 H), 7.35 (s, 1 H), 6.97 (s, 1 H), 6.94 (s, 1 H), 6.82 (s, 1 H), 5.87 (s, 2 H), 2.15 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 151.29, 138.89, 135.17, 135.81, 131.50, 125.81, 123.10, 114.62, 108.32, 103.69, 103.65, 13.97.

MS: *m*/*z* = 241.

3-(4-Methyl-1*H*-pyrazol-1-yl)-5-(trifluoromethyl)aniline (4g)
^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.22 (s, 1 H), 7.54 (s, 1 H), 7.24 (s, 1 H), 7.14 (s, 1 H), 6.74 (s, 1 H), 5.82 (s, 2 H), 2.08 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 151.05, 142.17, 141.58, 131.73, 131.42, 131.11, 130.80, 126.63, 125.98, 123.27, 118.30, 107.50, 107.46, 106.38, 101.55, 101.50, 9.13.

MS: *m*/*z* = 241.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{14}FN_2O$: 242.0900; found: 242.0908.

1-[3-(4-Fluorophenoxy)phenyl]-2-methyl-1*H*-imidazole (4h)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.48–7.54 (t, *J* = 7.8 Hz, 1 H), 7.26–7.30 (m, 3 H), 7.20–7.25 (m, 3 H), 7.14–7.19 (m, 1 H), 6.99–7.06 (m, 1 H), 6.89 (s, 1 H), 2.28 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 161.0, 158.8, 157.8, 151.73, 151.7, 144.5, 139.3, 130.5, 127.8, 121.30, 121.25, 121.19, 120.5, 119.7, 117.1, 116.8, 116.5, 114.8, 13.8.

MS: *m*/*z* = 268.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{14}FN_2O$: 269.1085; found: 269.1094.

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