Copper-Catalyzed Tandem C–N Bond Formation Reaction: Selective Synthesis of 2-(Trifluoromethyl)benzimidazoles

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Abstract: A highly practical method for the synthesis of fluorinated benzimidazoles was developed by CuI/TMEDA-catalyzed cross-coupling reaction of *N*-(2-haloaryl)trifluoroacetimidoyl chlorides with primary amines. The present double amination process tolerates the presence of Cl, Br, or I substituent at the 2-position of the phenyl group.

Key words: copper, double amination, *N*-(2-haloaryl)trifluoroacetimidoyl chlorides, primary amines, benzimidazoles

Benzimidazole derivatives are known as an important class compounds due to their wide range of biological activities.[1] Heterocycles containing a benzimidazole scaffold were reported as drug leads (such as polymerase inhibitor)[2] and commercial pharmaceutical products (such as telmisartan),[3] and were also widely used in fungicides, herbicides, and other veterinary applications.[4] It is well known that the trifluoromethyl group has a great effect on biological activity and often confers significant changes in chemical and physical properties.[5] The introduction of a trifluoromethyl group into benzimidazole resulted in compounds with a broad spectrum of insecticidal and herbicidal activities.[6] Consequently, a number of methods have been reported for the synthesis of trifluoromethyl-containing benzimidazole derivatives.[7] The classical methods for these compounds involve the direct trifluoromethylation of benzimidazoles[8] and the condensation of *o*-phenylenediamine[9] or *o*-nitroaniline[10] with trifluoroacetic acid or trifluoroacetic anhydride. Uneyama's group,[11] for example, has described the preparation of 2-(trifluoromethyl)benzimidazoles by electrochemical oxidative intramolecular cyclization of N,N′-disubstituted trifluoroethanimidamides. In an attempt to expand the diversity of the available starting materials, Ma and co-workers[12] prepared N-substituted 2-(trifluoromethyl)benzimidazoles by a Cu-catalyzed cascade aryl amination/condensation process of 2-iodo(bromo)trifluoroacetanilides with primary amines. Herein, we wish to report a new process for the formation of N-substituted 2-(trifluoromethyl)benzimidazoles via tandem amination reactions of *N*-(2-haloaryl)trifluoroacetimidoyl chlorides with primary amines.

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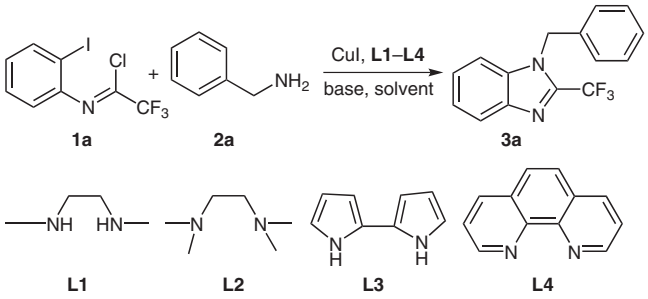
Transition metal catalyzed C–N bond formation has been an area of intensive research during the past decade.[13] Pioneering work has been reported concerning the palladium-[14] or copper-[15] catalyzed N-arylation and alkenylation coupling reactions. In 2007, Buchwald[16] developed a copper-catalyzed tandem C–N bond forming reaction of 1,4-diiodo(dibromo)-1,3-dienes with *tert*-butyl carbamate to prepare pyrroles and heteroarylpyrroles. Inspired by the aforementioned work, we envisioned whether *N*-(2-haloaryl)trifluoroacetimidoyl chlorides could undergo double amination reaction with primary amines to construct N-substituted 2-(trifluoromethyl)benzimidazole framework by the similar tandem amination reaction strategy.

With this idea in mind, we examined the double amination reaction of *N*-(2-iodophenyl)trifluoroacetimidoyl chloride (**1a**), which can be conveniently prepared from 2-iodoaniline and trifluoroacetic acid.[17] A variety of ligands, bases and solvents were examined to optimize the reaction conditions, and the results are summarized in Table 1. Initially, a suitable ligand was screened for the reaction of substrate **1a** with benzylamine (**2a**), CuI and Cs_2CO_3 in toluene at 110 °C (entries 1–5). To our delight, *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (**L2**) gave the best results among the four ligands **L1**–**L4** tested, and the corresponding fluorinated benzimidazole **3a** was obtained in 98% yield (entry 3). We found that the amount of **L2** affected the reaction, and the yield of **3a** was reduced sharply to 46% in the presence of 10 mol% of **L2**. Subsequently, the effect of base was tested (entries 3 and 7–9). The results indicated that the choice of base also played a crucial role in the reaction because the formation of **3a** through elimination of HX presumably requires the strong basicity.[18] Thus, Cs_2CO_3 was found to provide the best results. Switching to mild bases, such as K_2CO_3, K_3PO_4, or triethylamine, resulted in low yields (entries 7–9). Finally, a series of other solvents, including DMF, THF, dioxane, and MeCN were evaluated and found to be less effective than toluene (entries 10–13).

With the optimized conditions in hand, we next explored the scope and generality of this coupling reaction. A range of *N*-(2-halophenyl)trifluoroacetimidoyl chlorides and primary amines were used to investigate the synthesis of N-substituted 2-(trifluoromethyl)benzimidazoles. The results are summarized in Table 2. These results demonstrated that a variety of *N*-(2-halophenyl)trifluoroacetimidoyl chlorides were compatible with these reaction conditions. Interestingly, the less expensive and more

Table 1 Optimization of Double Amination of *N*-(2-Iodophenyl)trifluoroacetimidoyl Chloride[a]

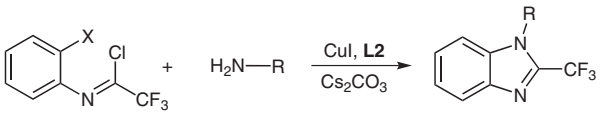


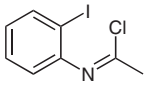
Entry	Ligand/mol%	Base	Solvent	Yield (%)[b]
1	none	Cs_2CO_3	toluene	19
2	**L1**/20	Cs_2CO_3	toluene	57
3	**L2**/20	Cs_2CO_3	toluene	98
4	**L3**/20	Cs_2CO_3	toluene	64
5	**L4**/20	Cs_2CO_3	toluene	76
6	**L2**/10	Cs_2CO_3	toluene	46
7	**L2**/20	Et_3N	toluene	trace
8	**L2**/20	K_2CO_3	toluene	64
9	**L2**/20	K_3PO_4	toluene	48
10	**L2**/20	Cs_2CO_3	DMF	68
11[c]	**L2**/20	Cs_2CO_3	THF	78
12	**L2**/20	Cs_2CO_3	dioxane	26
13[d]	**L2**/20	Cs_2CO_3	MeCN	19

[a] Reactions were carried out with 1.0 mmol of **1a**, 1.2 mmol of **2a**, 0.1 mmol of CuI, 2.0 mmol of base, 0.1–0.2 mmol of ligand in 3 mL of solvent in a sealed tube at 110 °C for 8 h.
[b] Isolated yield.
[c] At 65 °C.
[d] At 80 °C.

available aryl chlorides can also be converted into the corresponding benzimidazoles. As shown in Table 2, *N*-(2-chlorophenyl)-, *N*-(2-bromophenyl)- and *N*-(2-iodophenyl)trifluoroacetimidoyl chlorides ran smoothly in this procedure and afforded the corresponding benzimidazoles in good to excellent yields. It is well known that the reactivity of aryl iodides is higher than that of aryl bromides and aryl chlorides in the coupling reaction, and the elimination of HI is easier than that of HBr and HCl in the amination of haloarenes. However, less active aryl bromides and aryl chlorides can be also transformed to the corresponding benzimidazoles in this Cu-catalyzed double amination reaction, albeit aryl bromides and aryl chlorides afforded lower yields of products (entries 17–20). It is worth noting that the strong electron-withdrawing ability of trifluoromethyl is essential to this double amination reaction. Without the activation of C–Cl bond by trifluoromethyl, the corresponding benzimidazole could not be obtained. For example, the amination took place only at the

Table 2 Synthesis of 2-(Trifluoromethyl)benzimidazoles[a]



Entry	**1**, X =	**2**, R =	Product **3**	Yield (%)[b]
1	I (**1a**)	$PhCH_2$ (**2a**)	**3a**	98
2	I (**1a**)	4-$MeOC_6H_4CH_2$ (**2b**)	**3b**	89
3	I (**1a**)	4-$MeC_6H_4CH_2$ (**2c**)	**3c**	95
4	I (**1a**)	4-$ClC_6H_4CH_2$ (**2d**)	**3d**	83
5	I (**1a**)	2-$ClC_6H_4CH_2$ (**2e**)	**3e**	89
6	I (**1a**)	4-$FC_6H_4CH_2$ (**2f**)	**3f**	93
7	I (**1a**)	2-$FC_6H_4CH_2$ (**2g**)	**3g**	88
8	I (**1a**)	PhCHMe (**2h**)	**3h**	98
9	I (**1a**)	$MeCH_2CH_2CH_2$ (**2i**)	**3i**	79
10	I (**1a**)	4-MeC_6H_4 (**2j**)	**3j**	82
11	I (**1a**)	2-MeC_6H_4 (**2k**)	**3k**	76
12	I (**1a**)	4-$MeOC_6H_4$ (**2l**)	**3l**	86
13	I (**1a**)	3-$MeOC_6H_4$ (**2m**)	**3m**	73
14	I (**1a**)	2-$MeOC_6H_4$ (**2n**)	**3n**	70
15	I (**1a**)	4-ClC_6H_4 (**2o**)	**3o**	92
16	I (**1a**)	4-$NO_2C_6H_4$ (**2p**)	**3p**	62
17	Br (**1b**)	$PhCH_2$ (**2a**)	**3a**	89
18	Br (**1b**)	4-MeC_6H_4 (**2j**)	**3j**	77
19	Cl (**1c**)	$PhCH_2$ (**2a**)	**3a**	76
20	Cl (**1c**)	4-MeC_6H_4 (**2j**)	**3j**	70
21	 (**1d**)	$PhCH_2$ (**2a**)	–	0

[a] Reactions were carried out with 1.0 mmol of **1**, 1.2 mmol of amine, 0.1 mmol of CuI, 2.0 mmol of Cs_2CO_3, 0.2 mmol of TMEDA in 3 mL of toluene in a sealed tube at 110 °C for 8 h.
[b] Isolated yield.

C–I bond when *N*-(2-iodophenyl)acetimidoyl chloride (**1d**) was treated with benzylamine (**2a**) under the standard conditions, without the formation of any benzimidazole product (entries 21).

As listed in Table 2, both aromatic and aliphatic amines were suitable substrates for this tandem amination reaction. It should be noted that electronic effects of the substituent in the primary amine have significant influence on the yields. In general, aromatic amines (Table 2, entries

10–16) afforded higher yields than aliphatic amines (Table 2, entries 1–9). In comparison with aromatic amines bearing an electron-donating group on the phenyl ring (e.g., methyl or methoxy group), electron-deficient 4-nitrobenzeneamine reduced the reaction yield significantly (Table 2, entry 16). In addition, the yields were influenced slightly by the different position of the substituent on the phenyl ring in aromatic amines. Thus, low yields were observed for aromatic amines bearing an *ortho*-substituent (Table 2, entries 11 and 14) which might be due to the steric hindrance of the substrate. All compounds **3** were identified by ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and IR spectroscopy as well as MS, and the structures were unambiguously confirmed by the X-ray single-crystal diffraction analysis of **3l** (Figure 1).[19]

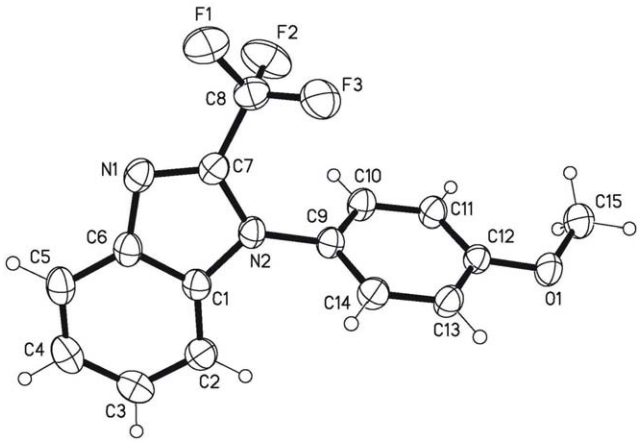


Figure 1 ORTEP diagram of the single crystal X-ray structure of compound **3l**

In conclusion, we have successfully developed a highly practical method to synthesize N-substituted 2-(trifluoromethyl)benzimidazoles by CuI/TMEDA (**L2**) catalyzed coupling reaction of *N*-(2-haloaryl)trifluoroacetimidoyl chlorides with primary amines. It is worth noting that *N*-(2-chlorophenyl)-, *N*-(2-bromophenyl)-, and *N*-(2-iodophenyl)trifluoroacetimidoyl chlorides can participate smoothly in the amination reaction. The tandem process allows the assembly of a wide range of N-substituted 2-(trifluoromethyl)benzimidazoles by changing different aromatic primary amines or aliphatic primary amines.

Chemicals were either purchased from commercial vendors or purified by standard techniques. Petroleum ether used refers to the fraction boiling at 60–90 °C. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker Avance 300 (300 M Hz) spectrometer using TMS as the internal standard. ^{19}F NMR spectra were recorded in $CDCl_3$ on a Bruker Avance 300 (282.2 MHz) spectrometer using CF_3CO_2H as the external standard. All chemical shifts (δ) were expressed in parts per million, and coupling constants (*J*) were given in Hertz. All reactions were conducted under N_2 using standard Schlenk techniques. Column chromatography was performed using EM silica gel 60 (300–400 mesh).

N-Substituted 2-(Trifluoromethyl)benzimidazoles 3 from *N*-(2-Halophenyl)acetimidoyl Chlorides 1; General Procedure

A flame-dried Schlenk tube with a magnetic stirring bar was charged with *N*-(2-halophenyl)trifluoroacetimidoyl chloride **1** (1.0 mmol), primary amine **2** (1.2 mmol), CuI (19.1 mg, 0.1 mmol), Cs_2CO_3 (650 mg, 2.0 mmol), *N,N,N′,N′*-tetramethylethylenediamine (**L2**; 23.2 mg, 0.2 mmol), and toluene (3 mL). The reaction vessel was fitted with a rubber septum and the system was evacuated and back-filled with N_2. The reaction mixture was stirred for 30 min at r.t., and then heated at 110 °C for 8 h. The mixture was cooled to r.t. and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography on a silica gel column using EtOAc–petroleum ether (1:10) as eluent to give the product **3**.

1-Benzyl-2-(trifluoromethyl)-1*H*-benzo[*d*]imidazole (3a)[12]

Yellowish solid; mp 75–76 °C.

IR (KBr): 3061, 2924, 1593, 1521, 1479, 1428, 1361, 1278, 1188, 747, 693 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.89–7.92 (m, 1 H), 7.29–7.38 (m, 6 H), 7.11 (m, 2 H), 5.52 (s, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 48.6, 111.3, 119.3 (q, $J_{C,F}$ = 270.1 Hz), 121.9, 124.0, 125.7, 126.5, 128.4, 129.2, 135.0, 135.8, 141.1 (q, $J_{C,F}$ = 38.0 Hz), 141.4.

^{19}F NMR ($CDCl_3$): δ = –61.53.

MS (ESI): *m*/*z* = 277 (M + H$^+$).

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{11}F_3N_2$ + Na ([M + Na]$^+$): 299.0767; found: 299.0763.

1-(4-Methoxybenzyl)-2-(trifluoromethyl)-1*H*-benzo[*d*]imidazole (3b)

Yellowish solid; mp 80–81 °C.

IR (KBr): 3017, 2941, 1613, 1515, 1466, 1424, 1342, 1265, 1183, 1137, 825, 751 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.88–7.91 (m, 1 H), 7.29–7.35 (m, 3 H), 7.06 (d, *J* = 8.7 Hz, 2 H), 6.83 (d, *J* = 8.7 Hz, 2 H), 5.45 (s, 2 H), 3.75 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 48.3, 55.4, 111.4, 114.6, 119.4 (q, $J_{C,F}$ = 270.1 Hz), 121.8, 123.9, 125.7, 127.1, 128.0, 135.8, 140.9 (q, $J_{C,F}$ = 38.0 Hz), 141.5, 159.7.

^{19}F NMR ($CDCl_3$): δ = –61.65.

MS (ESI): *m*/*z* = 307 (M + H$^+$).

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{13}F_3N_2O$ + Na ([M + Na]$^+$): 329.0872; found: 329.0874.

1-(4-Methylbenzyl)-2-(trifluoromethyl)-1*H*-benzo[*d*]imidazole (3c)

Yellowish solid; mp 65–66 °C.

IR (KBr): 3057, 2963, 1592, 1520, 1477, 1428, 1355, 1278, 1181, 1125, 800, 748 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.89–7.92 (m, 1 H), 7.28–7.36 (m, 3 H), 7.12 (d, *J* = 8.0 Hz, 2 H), 7.01 (d, *J* = 8.0 Hz, 2 H), 5.49 (s, 2 H), 2.31 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.3, 48.6, 111.4, 119.4 (q, $J_{C,F}$ = 270.1 Hz), 121.9, 124.0, 125.7, 126.6, 129.9, 132.1, 135.9, 138.3, 141.1 (q, $J_{C,F}$ = 38.0 Hz), 141.5.

^{19}F NMR ($CDCl_3$): δ = –61.57.

MS (ESI): *m*/*z* = 291 (M+ H$^+$).

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{14}F_3N_2$ ([M + H]$^+$): 291.1104; found: 291.1105.

1-(4-Chlorobenzyl)-2-(trifluoromethyl)-1*H*-benzo[*d*]imidazole (3d)
Yellowish oil.

IR (neat): 2948, 1666, 1522, 1453, 1278, 1119, 1017, 806, 748 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.90–7.93 (m, 1 H), 7.34–7.39 (m, 2 H), 7.24–7.31 (m, 3 H), 7.03 (d, *J* = 8.4 Hz, 2 H), 5.50 (s, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 48.0, 111.1, 119.3 (q, $J_{C,F}$ = 270.1 Hz), 122.1, 126.0, 127.9, 128.8, 129.5, 133.6, 134.5, 138.8, 141.0 (q, $J_{C,F}$ = 38.0 Hz), 141.4.

^{19}F NMR ($CDCl_3$): δ = –61.72.

MS (ESI): *m*/*z* = 311 (M + H^+).

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{11}ClF_3N_2$ ([M + $H]^+$): 311.0557; found: 311.0555.

1-(2-Chlorobenzyl)-2-(trifluoromethyl)-1*H*-benzo[*d*]imidazole (3e)
Yellowish oil.

IR (neat): 3065, 2929, 1678, 1593, 1525, 1465, 1426, 1347, 1278, 1198, 1097, 909, 738 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.92–7.95 (m, 1 H), 7.43–7.47 (m, 1 H), 7.35–7.39 (m, 2 H), 7.22–7.34 (m, 2 H), 7.07–7.20 (m, 1 H), 6.44 (d, *J* = 7.5 Hz, 1 H), 5.63 (s, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.0, 111.0, 119.3 (q, $J_{C,F}$ = 270.1 Hz), 122.0, 124.2, 126.0, 126.7, 127.6, 129.5, 129.9, 132.2, 132.7, 135.7, 141.3 (q, $J_{C,F}$ = 38.0 Hz), 141.5.

^{19}F NMR ($CDCl_3$): δ = –61.83.

MS (ESI): *m*/*z* = 311 (M + H^+).

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{11}ClF_3N_2$ ([M + $H]^+$): 311.0557; found: 311.0557.

1-(4-Fluorobenzyl)-2-(trifluoromethyl)-1*H*-benzo[*d*]imidazole (3f)
Yellowish solid; mp 62–63 °C.

IR (KBr): 3070, 2949, 1606, 1514, 1467, 1423, 1388, 1193, 1128, 845, 751 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.88–7.91 (m, 1 H), 7.33–7.37 (m, 2 H), 7.25–7.28 (m, 1 H), 7.06–7.10 (m, 2 H), 6.95–7.01 (m, 2 H), 5.48 (s, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 47.9, 111.1, 116.0, 116.3, 119.3 (q, $J_{C,F}$ = 270.1 Hz), 121.9, 125.8, 128.3, 130.9, 135.7, 140.9 (q, $J_{C,F}$ = 38.0 Hz), 141.4, 162.7 (d, $J_{C,F}$ = 249.9 Hz).

^{19}F NMR ($CDCl_3$): δ = –61.51, –113.47.

MS (ESI): *m*/*z* = 295 (M + H^+).

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{11}F_4N_2$ ([M + $H]^+$): 295.0853; found: 295.0859.

1-(2-Fluorobenzyl)-2-(trifluoromethyl)-1*H*-benzo[*d*]imidazole (3g)
Yellowish solid; mp 63–64 °C.

IR (KBr): 3059, 2951, 1589, 1526, 1472, 1429, 1359, 1279, 1175, 1127, 841, 751 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.89–7.92 (m, 1 H), 7.33–7.37 (m, 4 H), 7.26–7.30 (m, 1 H), 6.98–7.13 (m, 1 H), 6.73 (m, 1 H), 5.58 (s, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 42.2 (dq, $J_{C,F}$ = 4.3 Hz, 7.5 Hz), 110.9, 115.7, 115.9, 119.3 (q, $J_{C,F}$ = 270.1 Hz), 121.9, 122.4, 124.9, 125.9, 127.8, 130.2, 135.6, 140.5 (q, $J_{C,F}$ = 38.0 Hz), 141.3, 159.9 (d, $J_{C,F}$ = 249.9 Hz).

^{19}F NMR ($CDCl_3$): δ = –61.68, –118.22.

MS (ESI): *m*/*z* = 295 (M + H^+).

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{11}F_4N_2$ ([M + $H]^+$): 295.0853; found: 295.0853.

1-(1-Phenylethyl)-2-(trifluoromethyl)-1*H*-benzo[*d*]imidazole (3h)
Yellowish oil.

IR (neat): 3062, 2989, 1587, 1524, 1453, 1422, 1280, 1257, 1177, 1125, 747, 699 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 8.1 Hz, 1 H), 7.24–7.39 (m, 6 H), 7.14 (m, 1 H), 6.97 (d, *J* = 8.1 Hz, 1 H), 6.03 (q, *J* = 7.4 Hz, 1 H), 2.02 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.4, 55.0, 113.4, 119.7 (q, $J_{C,F}$ = 270.1 Hz), 122.0, 123.5, 125.1, 126.6, 128.4, 129.1, 134.0, 138.4, 140.9 (q, $J_{C,F}$ = 38.0 Hz), 142.1.

^{19}F NMR ($CDCl_3$): δ = –61.87.

MS (ESI): *m*/*z* = 291 (M + H^+).

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{13}F_3N_2$ + Na ([M + $Na]^+$): 313.0923,.found: 313.0920.

1-Butyl-2-(trifluoromethyl)-1*H*-benzo[*d*]imidazole (3i)[20]
Yellowish oil.

IR (neat): 3058, 2963, 1590, 1520, 1477, 1457, 1366, 1266, 1196, 1130, 1096, 746 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.84–7.87 (m, 1 H), 7.30–7.43 (m, 3 H), 4.27 (t, *J* = 7.8 Hz, 2 H), 1.78 (tt, *J* = 15.6, 7.8 Hz, 2 H), 1.35–1.45 (qt, *J* = 15.6, 7.3 Hz, 2 H), 0.96 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.7, 20.1, 32.2, 45.2, 110.8, 119.5 (q, $J_{C,F}$ = 270.1 Hz), 121.8, 123.7, 125.4, 135.6, 140.7 (q, $J_{C,F}$ = 38.0 Hz), 141.4.

^{19}F NMR ($CDCl_3$): δ = –61.92.

MS (ESI): *m*/*z* = 243 (M + H^+).

HRMS (ESI): *m*/*z* calcd for $C_{12}H_{14}F_3N_2$ ([M + $H]^+$) 243.1104; found: 243.1102.

1-*p*-Tolyl-2-(trifluoromethyl)-1*H*-benzo[*d*]imidazole (3j)
Yellowish oil.

IR (neat): 3041, 2932, 1591, 1517, 1452, 1420, 1334, 1288, 1264, 1137, 846, 747 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.92–7.95 (m, 1 H), 7.36–7.41 (m, 4 H), 7.25–7.31 (m, 2 H), 7.14–7.17 (m, 1 H), 2.49 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5, 111.5, 119.2 (q, $J_{C,F}$ = 270.1 Hz), 121.6, 126.0, 127.5, 128.7, 130.6, 132.1, 133.2, 138.9, 140.6 (q, $J_{C,F}$ = 38.0 Hz), 141.5.

^{19}F NMR ($CDCl_3$): δ = –60.52.

MS (ESI): *m*/*z* = 277 (M + H^+).

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{12}F_3N_2$ ([M + $H]^+$): 277.0947; found: 277.0945.

1-*o*-Tolyl-2-(trifluoromethyl)-1*H*-benzo[*d*]imidazole (3k)
Yellowish oil.

IR (neat): 3059, 2928, 1590, 1524, 1498, 1456, 1417, 1289, 1263, 1203, 1139, 912, 721 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.94–7.97 (m, 1 H), 7.29–7.52 (m, 6 H), 6.99 (d, *J* = 7.4 Hz, 1 H), 1.96 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.2, 111.3, 119.1 (q, $J_{C,F}$ = 270.1 Hz), 121.8, 124.2, 126.1, 127.4, 128.8, 130.6, 131.5, 133.4, 136.7, 136.9, 140.5 (q, $J_{C,F}$ = 38.0 Hz), 141.0.

^{19}F NMR ($CDCl_3$): δ = –60.61.

MS (ESI): *m/z* = 277 ($M + H^+$).

HRMS (ESI): *m/z* calcd for $C_{15}H_{12}F_3N_2$ ($[M + H]^+$): 277.0947; found: 277.0944.

1-(4-Methoxyphenyl)-2-(trifluoromethyl)-1*H*-benzo[*d*]imidazole (3l)[11a]
Yellowish solid; mp 90–91 °C.

IR (KBr): 2972, 1610, 1514, 1453, 1419, 1296, 1254, 1205, 1180, 1138, 1026, 850, 680 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.91–7.92 (m, 1 H), 7.32–7.40 (m, 4 H), 7.14–7.16 (m, 1 H), 7.05–7.08 (m, 2 H), 3.89 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.8, 111.4, 115.1, 119.2 (q, $J_{C,F}$ = 270.1 Hz), 121.6, 124.2, 125.9, 127.1, 128.9, 137.8, 141.1 (q, $J_{C,F}$ = 38.0 Hz), 142.0, 160.7.

^{19}F NMR ($CDCl_3$): δ = –60.45.

MS (ESI): *m/z* = 293 ($M + H^+$).

HRMS (ESI): *m/z* calcd for $C_{15}H_{12}F_3N_2O$ ($[M + H]^+$): 293.0896, found: 293.0896.

1-(3-Methoxyphenyl)-2-(trifluoromethyl)-1*H*-benzo[*d*]imidazole (3m)
Yellowish oil.

IR (neat): 2941, 1602, 1525, 1493, 1461, 1290, 1267, 1240, 1207, 1006, 853, 695 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.90–7.93 (m, 1 H), 7.35–7.48 (m, 3 H), 6.93–7.10 (m, 4 H), 3.83 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.8, 111.5, 113.3, 115.8, 119.1 (q, $J_{C,F}$ = 270.1 Hz), 119.7, 121.6, 124.5, 126.0, 130.7, 135.6, 137.3, 140.8 (q, $J_{C,F}$ = 38.0 Hz), 141.2, 160.7.

^{19}F NMR ($CDCl_3$): δ = –60.54.

MS (ESI): *m/z* = 293 ($M + H^+$).

HRMS (ESI): *m/z* calcd for $C_{15}H_{12}F_3N_2O$ ($[M + H]^+$): 293.0896; found: 293.0894.

1-(2-Methoxyphenyl)-2-(trifluoromethyl)-1*H*-benzo[*d*]imidazole (3n)
Yellowish oil.

IR (neat): 2943, 1599, 1511, 1463, 1421, 1257, 1143, 1025, 911, 644 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 7.2 Hz, 1 H), 7.52 (m, 1 H), 7.30–7.39 (m, 3 H), 7.04–7.13 (m, 3 H), 3.69 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.9, 111.4, 112.4, 119.1 (q, $J_{C,F}$ = 270.1 Hz), 121.0, 121.5, 123.2, 123.9, 125.7, 129.5, 131.8, 137.3, 141.2 (q, $J_{C,F}$ = 38.0 Hz), 141.9, 155.7.

^{19}F NMR ($CDCl_3$): δ = –60.69.

MS (ESI): *m/z* = 293 ($M + H^+$).

HRMS (ESI): *m/z* calcd for $C_{15}H_{12}F_3N_2O$ ($[M + H]^+$): 293.0896; found: 293.0893.

1-(4-Chlorophenyl)-2-(trifluoromethyl)-1*H*-benzo[*d*]imidazole (3o)
Yellowish solid; mp 73–74 °C.

IR (KBr): 3058, 1608, 1527, 1495, 1452, 1418, 1265, 1138, 1087, 981, 751 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.90–7.93 (m, 1 H), 7.54–7.57 (m, 2 H), 7.34–7.41 (m, 4 H), 7.11–7.14 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 111.2, 119.0 (q, $J_{C,F}$ = 270.1 Hz), 121.8, 124.5, 126.3, 129.0, 130.4, 133.2, 136.4, 137.3, 140.9 (q, $J_{C,F}$ = 38.0 Hz), 141.2.

^{19}F NMR ($CDCl_3$): δ = –60.71.

MS (ESI): *m/z* = 297 ($M + H^+$).

HRMS (ESI): *m/z* calcd for $C_{14}H_9ClF_3N_2$ ($[M + H]^+$): 297.0401; found: 297.0402.

1-(4-Nitrophenyl)-2-(trifluoromethyl)-1*H*-benzo[*d*]imidazole (3p)
Yellowish solid; mp 107–108 °C.

IR (KBr): 2924, 1594, 1528, 1498, 1453, 1349, 1293, 1263, 1157, 915, 695 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.49 (m, 2 H), 7.96–7.97 (m, 1 H), 7.67 (d, *J* = 8.7 Hz, 2 H), 7.44–7.47 (m, 2 H), 7.15–7.18 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 110.8, 119.0 (q, $J_{C,F}$ = 270.1 Hz), 122.2, 125.0, 125.6, 126.8, 128.8, 136.9, 140.2, 140.7 (q, $J_{C,F}$ = 38.0 Hz), 141.2, 148.8.

^{19}F NMR ($CDCl_3$): δ = –60.74.

MS (ESI): *m/z* = 308 ($M + H^+$).

HRMS (ESI): *m/z* calcd for $C_{14}H_9F_3N_3O_2$ ($[M + H]^+$): 308.0641; found: 308.0647.

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