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PAPER

General and efficient method for direct *N*-monomethylation of aromatic primary amines with methanol†

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The direct *N*-monomethylation of aromatic primary amines, including arylamines, arylsulfonamides and amino-azoles, using methanol as a methylating agent has been accomplished in the presence of a $[Cp^*IrCl_2]_2$/NaOH system. From both synthetic and environmental points of view, the reaction is highly attractive because of low catalyst loading, broad substrate scope and excellent selectivities.

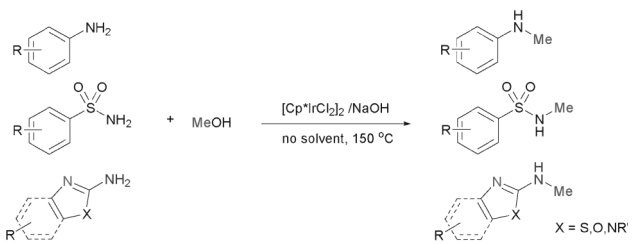
Introduction

The direct *N*-monomethylation of primary arylamines, one of the most important organic reactions, is widely utilized for the synthesis of numerous natural products, pharmaceuticals and fine chemicals.[1] Traditionally, the transformation is performed using highly toxic and hazardous methyl halide or dimethyl sulfate as methylating agents in the presence of bases. In the past several years, dimethyl carbonate (DMC) and other alkyl methyl carbonates were also used as green methylating agents for the *N*-monomethylation of primary arylamines in the presence of a large amount of zeolites as catalysts (the weight ratio of zeolites and primary amines is over 1 : 2).[2] As mentioned above, these procedures inevitably suffer from the generation of *N*,*N*-dimethyl amines as side products due to the resulting *N*-methyl amines being more nucleophilic than the starting primary arylamines in the process of the reactions.

Recently, much attention has been focused on the *N*-alkylation of amines with alcohols as environmentally benign alkylating agents instead of alkyl halides based on the "hydrogen autotransfer (or hydrogen-borrowing) process",[3] using iridium,[4] ruthenium[5] or other transition metal catalysts.[6] In this process, alcohols are first dehydrogenated to form aldehydes, followed by the condensation of the resulting aldehydes with amines to afford imine intermediates, which are hydrogenated to give the final *N*-alkylated products. The methodology is attractive because of high atom efficiency and the formation of water as the only side product. As a result, several groups explored transition metal-catalyzed *N*-methylation of primary arylamines with methanol.[7] However, these procedures suffer from a lack of selectivity towards the *N*-monomethylation[7a] or are highly restricted in the scope of substrates.[7b] It was also speculated that a relatively high energy is required for the dehydrogenation of methanol compared with higher alcohols such as ethanol (ΔH = +84 *vs.* +68 kJ mol^{-1}, respectively).[8] Therefore, the development of a simple, efficient and versatile system for the *N*-monomethylation of primary arylamines with methanol is still an extreme challenge. Very recently, Krische and co-workers reported the direct C–C coupling of allenes with activated methanol catalyzed by an iridium complex.[9] We also reported the regioselective *N*-alkylation of amino-thiazoles[10a,b] and amino-imidazoles[10c] with alcohols catalyzed by transition metal/base systems. Encouraged by their research and as part of our continuing interest in exploring selective *N*-alkylation reactions, we herein wish to describe our efforts towards the direct *N*-monomethylation of primary arylamines using methanol as a methylating agent catalyzed by a $[Cp^*IrCl_2]_2$/NaOH system.[11] Further, the direct *N*-monomethylation of arylsulfonamides and regioselective *N*-monomthylation of amino-azoles with methanol was explored for the first time (Scheme 1).

Results and discussion

The 4-chloroaniline **1a** was chosen as a model substrate to explore the feasibility of the reaction. In an initial experiment, the reaction of **1a** (2 mmol) with methanol **2** (1 ml) was carried out in the presence of commercially available $[Cp^*IrCl_2]_2$ (Cp^* = pentamethylcyclopentadienyl) (0.1 mol%) at 150 °C for 12h and no conversion was observed (Table 1, entry 1). When K_2CO_3 or K_3PO_4 (1.0 equiv.) was used as an additive, reactions afforded the *N*-monomethylated product **3a** with 38% and 46% yields,



Scheme 1 *N*-Monomethylation of aromatic primary amines.

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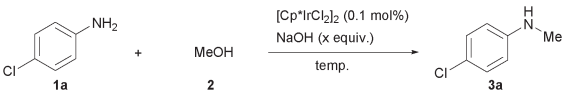
Table 1 *N*-Methylation of 4-chloroaniline **1a** with **2** under various conditions[a]



Entry	Base	Equiv.	Temp (°C)	Yield[b] (%)
1	—	1.0	150	0
2	K_2CO_3	1.0	150	38
3	K_3PO_4	1.0	150	46
4	**NaOH**	**1.0**	**150**	**96**
5	KOH	1.0	150	94
6	NaO*t*Bu	1.0	150	96
7	NaOH	0.5	150	72
8	NaOH	0.2	150	63
9	NaOH	1.0	130	85
10	NaOH	1.0	100	56

[a] Reaction conditions: 2 mmol **1a**, 0.1 mol% $[Cp^*IrCl_2]_2$, *x* equiv. base, 1 ml methanol, 150 °C, 12 h. [b] Isolated yield.

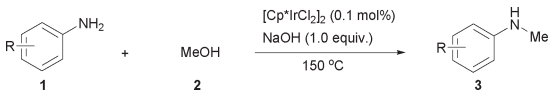
respectively (entries 2–3). Surprisingly, the product **3a** could be obtained with almost quantitative yield in the presence of a strong base such as NaOH, KOH or NaO*t*Bu (entries 4–6).

Among them, NaOH was selected as the base for further research. Attempts to decrease the reaction temperature and reduce the amount of NaOH resulted in relatively low yields (entries 7–10). It was also found that no reaction took place in the individual presence of NaOH.

To expand the scope of the reaction, the *N*-methylation of a variety of arylamines with methanol was examined under the above optimal conditions (Table 1, entry 4) and the results are outlined in Table 2. Reactions of other anilines bearing one or two halide atoms, such as 3-chloro **1b**, 4-bromo **1c**, 4-iodo **1d** and 3,5-difluoro **1e** afforded the desired products **3b–e** with 73–90% yields (Table 2, entries 1–4). Anilines bearing an electron-withdrawing group, such as 4-methylsulfonyl **1f** and 4-trifluoromethoxy **1g**, were converted to the corresponding products **3f** and **3g** with 94% and 96% yields, respectively (entries 5–6). Further, the *N*-methylation of anilines containing an electron-donating group, such as 4-methyl **1h**, 3-chloro-4-methyl **1i**, and 3-methoxy **1j**, afforded the desired products **3h–3j** with 71–96% yields (entries 7–9). The 2-naphthylamine **1k** was also proven to be a suitable substrate and the corresponding product **3k** was obtained with 88% yield (entry 10). In the case of heteroanilines, such as aminopyridines **1l–m** and aminopyrazine **1n**, reactions afforded the desired products **3l–n** with 90–94% yields (entries 11–13).

The *N*-methylation of a series of arylsulfonamides **4** with methanol was then investigated. As shown in Table 3, reactions of benzenesulfonamides bearing a halide atom **4a** and **4b** afforded the desired products **5a** and **5b** with 91% and 87% yields, respectively (Table 3, entries 1–2). The *N*-methylation of benzenesulfonamides bearing an electron-withdrawing group **4c** and **4d** gave the corresponding products **5c** and **5d** with 90% and 96% yields, respectively (entries 3–4). Further, the desired products **5e–g** were obtained with 92–96% yields when benzenesulfonamides bearing an electron-donating group **4e–g** were utilized as substrates (entries 5–7). Transformations of benzenesulfonamide **4h** and naphthalenesulfonamide **4i** afforded the desired products **5h** and **5i** with 97% and 87% yields, respectively (entries 8–9).

Table 2 *N*-Methylation of arylamines **1** with **2**[a]



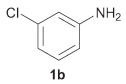
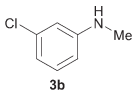
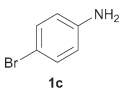
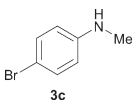
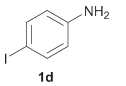
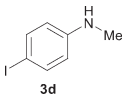
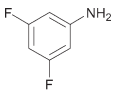
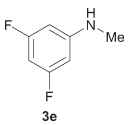
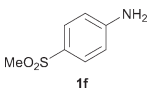
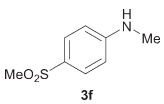
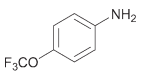
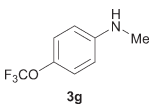
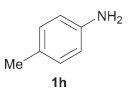
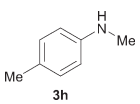
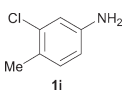
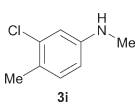
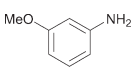
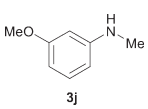
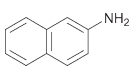
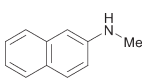
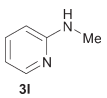
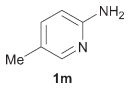
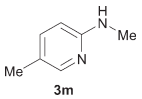
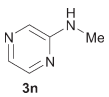
Entry	Arylamine	Product	Yield[b] (%)
1	 1b	 3b	90
2	 1c	 3c	88[c]
3	 1d	 3d	73
4	 1e	 3e	87
5	 1f	 3f	94
6	 1g	 3g	96
7	 1h	 3h	71[c]
8	 1i	 3i	96
9	 1j	 3j	73[d]
10	 1k	 3k	88[c]
11	 1l	 3l	94[c]

Table 2 (*Continued*)

12	 1m	 3m	93
13	 1n	 3n	90

[a] Reaction conditions: 2 mmol arylamine, 0.1 mol% $[Cp^*IrCl_2]_2$, 1.0 equiv. NaOH, 1 ml methanol, 150 °C, 12 h. [b] Isolated yield. [c] 2.0 equiv. NaOH. [d] 2.0 equiv. NaO*t*Bu.

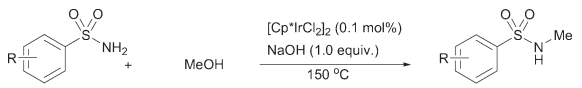
It was well documented that the *N*-alkylation of amino-azoles with alkyl halides,[12] including methyl halides,[12e,g–h] afforded the *N*-endosubstituted 3-alkyl-2-iminoazolines as products because the endocyclic nitrogen is more basic than the exocyclic one (Scheme 2, left). However, it was found that only *N*-exosubstituted products were obtained in the *N*-methylation of amino-azoles using methanol as the methylating agent (Scheme 2, right). The reaction of 2-aminobenzothiazole **6a** with **2** in the presence of $[Cp^*IrCl_2]_2$ (0.4 mol%) and NaOH (1.0 equiv.) was carried out for 12 h to afford 2-(*N*-methylamino)benzothiazole **7a** with 93% yield (Table 4, entry 1). Similarly, 2-aminobenzothiazoles bearing an electron-donating group **6b–d** or electron-withdrawing group **6e** were successfully converted to give the corresponding products **7b–e** with 88–95% yields (entries 2–5). High yields were also obtained in reactions of 2-aminobenzothiazoles containing a halide atom **6f–g** (entries 6–7). Further, reactions of non-benzo-fused 2-aminothiazoles **6h** and **6i** afforded the desired products **7h** and **7i** with 90% and 93% yields, respectively (entries 8–9). As amino-oxazole **6j** was used as the substrate, the corresponding product **7j** was obtained with 87% yield (entry 10). The *N*-methylation was also applied to amino-imidazoles **6k–m**, giving the desired products **7k–m** with 90–94% products (entries 11–13).

In all cases, apart from the desired *N*-monomethylated products, no *N*,*N*-dimethylated products were detected by ^1H NMR of the crude reaction mixture, although an excess amount of methanol was used. In addition, no 3-methyl-2-iminoazoline isomers were observed in the *N*-methylation of amino-azoles.

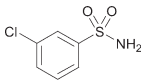
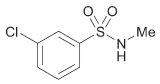
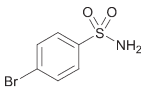
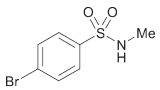
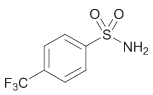
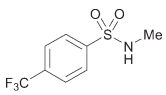
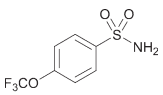
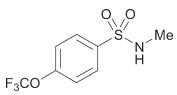
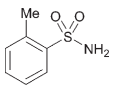
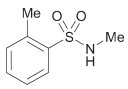
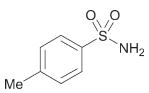
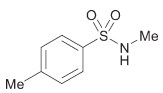
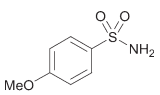
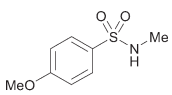
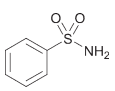
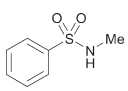
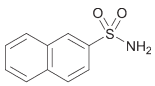
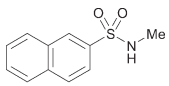
To understand the excellent selectivities towards *N*-monomethylation of this reaction, the *N*-methylation of the *N*-methylamine with methanol was then investigated. As shown in Scheme 3, the reaction of 4-chloro-*N*-methylbenzenamine **3a** with **2** was carried out for 12 h and no conversion was detected, indicating that the $[Cp^*IrCl_2]_2$/NaOH system is only effective for the conversion of aromatic primary amines to the corresponding *N*-monomethylated products.

Based on the experimental results and the "hydrogen autotransfer (or hydrogen-borrowing) process",[3,4] the possible mechanism for the *N*-monomethylation reaction was proposed in Scheme 4. The methanol was first dehydrogenated to form the formaldehyde coordinated with the iridium hydride species **B** in the presence of base,[13] followed by the condensation of the resulting **B** with the aromatic primary amine affording the imine coordinated with iridium hydride species **C**. Further, the addition of iridium hydride into the C=N bond of the imines gave the amido-iridium species **D**. Finally, the *N*-monomethylated product was released and the catalytically active alkoxo iridium species **A** were generated *via* an amido-alkoxo exchange reaction between **D**

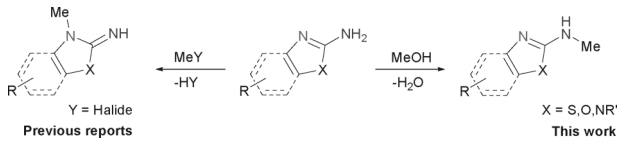
Table 3 *N*-Methylation of arylsulfonamides **4** with **2**[a]



4 2 5

Entry	Arylsulfonamide	Product	Yield[b] (%)
1	 4a	 5a	91
2	 4b	 5b	87
3	 4c	 5c	90
4	 4d	 5d	96
5	 4e	 5e	92
6	 4f	 5f	96
7	 4g	 5g	95
8	 4h	 5h	97
9	 4i	 5i	87[c]

[a] Reaction conditions: 2 mmol arylsulfonamide, 0.1 mol% $[Cp^*IrCl_2]_2$, 1.0 equiv. NaOH, 1 ml methanol, 150 °C, 12 h. [b] Isolated yield. [c] 1.5 ml NMP (1-methyl-2-pyrrolidone) was used as the solvent.



Scheme 2 Regioselective *N*-methylation of amino-azoles.

and methanol.[14] The regioselective formation of 2-(*N*-methylamino)azole may be attributed to the exocylic nitrogen being favored over the endocyclic one in the condensation step of the amino-azoles with the resulting formaldehyde.[10]

Conclusions

We have demonstrated a simple, efficient and versatile system for the direct *N*-monomethylation of aromatic primary amines, including arylamines, arylsulfonmides and amino-azoles, with methanol as the methylating agent. From both synthetic and environmental points of view, the iridium-catalyzed reaction is highly attractive because of low catalyst loading, broad substrate scope and excellent selectivities. Further studies to expand the application of the synthetic strategy are currently underway.

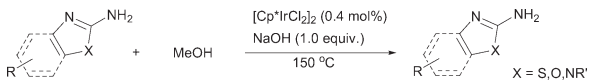
Experimental section

General experimental details

Infrared spectra were recorded on a Nicolet iS10 FT-IR spectrometer. High-resolution mass spectra (HRMS) were obtained on a HPLC-Q-Tof MS(Micro) spectrometer and are reported as *m/z* (relative intensity). Accurate masses are reported for the molecular ion $[M+H]^+$. Melting points were measured on a X-6 micro-melting apparatus (Beijing Tech Instrument Co., Ltd). Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded at 500 MHz using a Bruker Avance 500 spectrometer. Chemical shifts are reported in delta (δ) units, parts per million (ppm) downfield from trimethylsilane or ppm relative to the center of the singlet at 7.26 ppm for $CDCl_3$. Coupling constants as *J* values are reported in Hertz (Hz), and the splitting patterns were designated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; b, broad. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded at 125 MHz using a Bruker Avance 500 spectrometer. Chemical shifts are reported in delta (δ) units, ppm relative to the center of the triplet at 77.0 ppm for $CDCl_3$. ^{13}C NMR spectra were routinely run with broadband decoupling. Reactions tubes were purchased from Beijing Synthware Glass Inc. All reactions were run under an atmosphere of nitrogen, unless otherwise indicated. Analytical thin-layer chromatography (TLC) was carried out using 0.2 mm commercial silica gel plates.

General procedure for direct *N*-monomethylation of arylamines or sulfonamides with methanol. To an oven-dried, nitrogen purged 20 ml Schlenk tube were added arylamines or sulfonamides (2.0 mmol), methanol (1 ml), $[Cp^*IrCl_2]_2$ (0.002 mmol, 0.1 mol%) and NaOH (2 mmol, 1.0 equiv.). The resulting mixture was heated at 150 °C for 12 h, followed by the mixture of the reaction being allowed to cool to ambient temperature. The mixture of the reaction was concentrated in *vacuo* and purified

Table 4 *N*-Methylation of amino-azoles **6** with **2**[a]



6 2 7

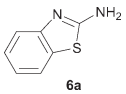
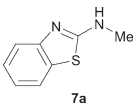
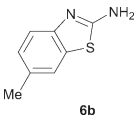
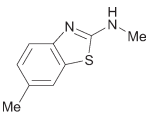
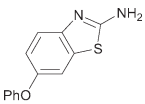
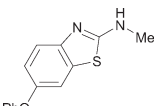
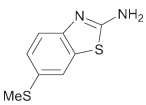
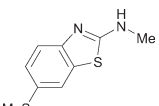
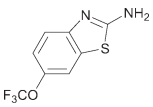
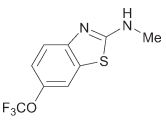
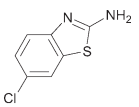
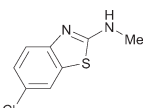
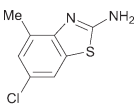
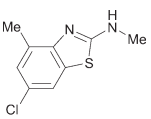
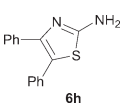
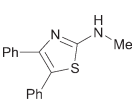
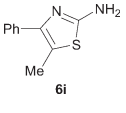
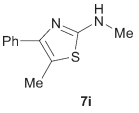
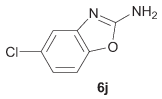
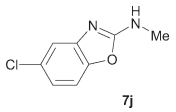
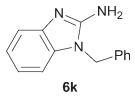
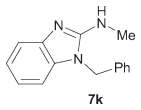
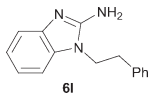
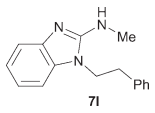
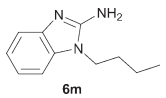
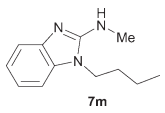
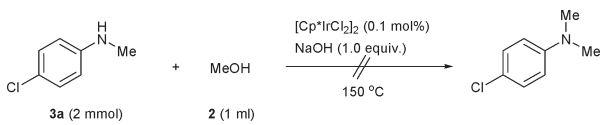
Entry	Arylamine	Product	Yield[b] (%)
1	 **6a**	 **7a**	93
2	 **6b**	 **7b**	95
3	 **6c**	 **7c**	88
4	 **6d**	 **7d**	90
5	 **6e**	 **7e**	92
6	 **6f**	 **7f**	94
7	 **6g**	 **7g**	91
8	 **6h**	 **7h**	90
9	 **6i**	 **7i**	93

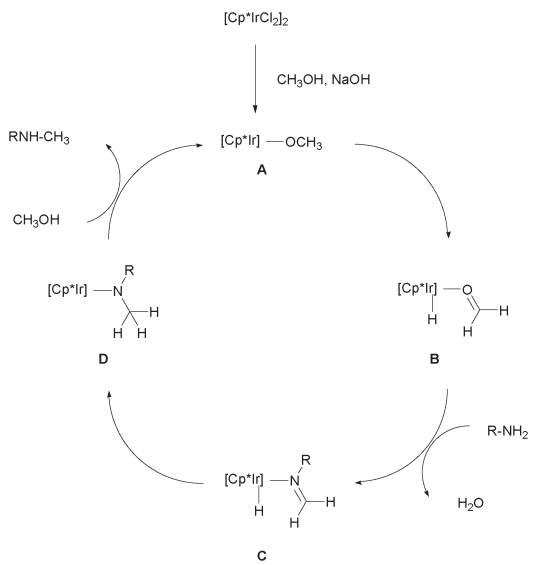
Table 4 (*Continued*)

10	 6j	87  7j
11	 6k	94  7k
12	 6l	90  7l
13	 6m	92  7m

[a] Reaction conditions: 0.5 mmol amino-azole, 0.4 mol% $[Cp^*IrCl_2]_2$, 1.0 equiv. NaOH, 1 ml methanol, 150 °C, 12 h. [b] Isolated yield.



Scheme 3 Reaction of *N*-methylamine **3a** with **2**.



Scheme 4 Possible mechanism.

by flash column chromatography with hexane/ethyl acetate to afford the corresponding product.

General procedure for direct *N*-monomethylation of amino-azoles with methanol. To an oven-dried, nitrogen purged 20 ml Schlenk tube were added amino-azole (0.5 mmol), methanol (1 ml), $[Cp^*IrCl_2]_2$ (0.002 mmol, 0.4 mol%) and NaOH (0.5 mmol, 1.0 equiv.). The resulting mixture was heated at 150 °C for 12 h, followed by the mixture of the reaction being allowed to cool to ambient temperature. The mixture of the reaction was concentrated in *vacuo* and purified by flash column chromatography with hexane/ethyl acetate to afford the corresponding product.

4-Chloro-*N*-methylbenzenamine (3a)[15]. Oil, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (d, J = 8.8 Hz, 2H, ArH), 6.51 (d, J = 8.8 Hz, 2H, ArH), 3.69 (br s, 1H, NH), 2.79 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 128.8, 121.5, 113.3, 30.6.

3-Chloro-*N*-methylbenzenamine (3b)[15]. Oil, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.06 (t, J = 8.1 Hz, 1H, ArH), 6.65 (d, J = 7.9 Hz, 1H, ArH), 6.55 (s, 1H, ArH), 6.45 (dd, J = 8.3 Hz and 2.3 Hz, 1H, ArH), 3.76 (br s, 1H, NH), 2.79 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.3, 134.9, 130.0, 116.8, 111.8, 110.7, 30.4.

4-Bromo-*N*-methylbenzenamine (3c)[16]. Oil, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, J = 8.9 Hz, 2H, ArH), 6.46 (d, J = 8.9 Hz, 2H, ArH), 3.70 (br s, 1H, NH), 2.79 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.1, 131.7, 113.8, 108.5, 30.5.

4-Iodo-*N*-methylbenzenamine (3d)[17]. Oil, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, J = 8.8 Hz, 2H, ArH), 6.39 (d, J = 8.8 Hz, 2H, ArH), 3.73 (br s, 1H, NH), 2.80 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.8, 137.7, 114.6, 77.7, 30.5.

3,5-Difluoro-*N*-methylbenzenamine (3e)[18]. Oil, ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.14–6.10 (m, 1H, ArH), 6.08–6.05 (m, 2H, ArH), 3.94 (br s, 1H, NH), 2.79 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.2 (dd, $J_{C\text{-}F}$ = 242.1 Hz and 16.0 Hz), 151.5 (t, $J_{C\text{-}F}$ = 13.2 Hz), 95.0–94.8 (m), 92.0 (t, $J_{C\text{-}F}$ = 26.1 Hz), 30.4.

***N*-Methyl-4-(methylsulfonyl)benzenamine (3f)[19].** mp 125–126 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, J = 8.6 Hz, 2H, ArH), 6.61 (d, J = 8.6 Hz, 2H, ArH), 4.39 (br s, 1H, NH), 3.00 (s, 3H, CH_3), 2.89 (d, J = 5.0 Hz, 3H, CH_3N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.2, 129.1, 126.8, 111.3, 45.0, 29.9.

***N*-Methyl-4-(trifluoromethoxy)benzenamine (3g)[20].** Oil, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (d, J = 8.3 Hz, 2H, ArH), 6.54 (d, J = 8.9 Hz, 2H, ArH), 3.76 (br s, 1H, NH), 2.81(s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.1, 140.4, 122.3, 120.8 (q, $J_{C\text{-}F}$ = 253.4 Hz), 112.5, 30.7.

***N*,4-Dimethylbenzenamine (3h)[15].** Oil, ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 (d, J = 8.2 Hz, 2H, ArH), 6.54 (d, J = 8.3 Hz, 2H, ArH), 2.80 (s, 3H, CH_3N), 2.23 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.1, 129.6, 126.4, 112.6, 31.0, 20.3.

3-Chloro-*N*,4-dimethylbenzenamine (3i)[21]. Oil, ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 (d, J = 8.3 Hz, 1H, ArH), 6.60 (d, J = 2.5 Hz, 1H, ArH), 6.41 (dd, J = 8.2 Hz and 2.5 Hz, 1H, ArH), 3.60 (br s, 1H, NH), 2.78 (s, 3H, CH_3N), 2.24 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.4, 134.7, 131.1, 123.8, 112.4, 111.2, 30.7, 18.7.

3-Methoxy-*N*-methylbenzenamine (3j)[22]. Oil, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (t, J = 8.0 Hz, 1H, ArH), 6.27 (dd, J = 8.0 Hz and 2.3 Hz, 1H, ArH), 6.23 (dd, J = 8.0 Hz and 2.1 Hz, 1H, ArH), 6.15 (t, J = 2.2 Hz, 1H, ArH), 3.71 (br s, 1H, NH), 3.77 (s, 3H, OCH_3), 2.81 (s, 3H, NCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.7, 150.7, 129.8, 105.5, 102.2, 98.2, 54.9, 30.5.

***N*-Methylnaphthalen-1-amine (3k)[15].** Oil, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67–7.60 (m, 3H, ArH), 7.36 (t, J = 7.6 Hz, 1H, ArH), 7.19 (t, J = 7.3 Hz, 1H, ArH), 6.87 (dd, J = 8.5 Hz and 2.5 Hz, 1H, ArH), 6.79 (d, J = 2.5 Hz, 1H, ArH), 3.86 (br s, 1H, NH), 2.92 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.0, 135.3, 128.8, 127.6, 127.5, 126.3, 125.9, 121.9, 117.9, 103.7, 30.7

***N*-Methylpyridin-2-amine (3l)[23].** Oil, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, J = 5.1 Hz, 1H, ArH), 7.42 (t, J = 7.9 Hz, 1H, ArH), 6.56 (t, J = 5.9 Hz, 1H, ArH), 6.37 (d, J = 8.5 Hz, 1H, ArH), 4.65 (br s, 1H, NH), 2.90 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.5, 147.8, 137.3, 112.4, 106.0, 28.9.

***N*,5-Dimethylpyridin-2-amine (3m)[24].** Oil, ^{1}H NMR (500 MHz, $CDCl_3$) 7.90 (s, 1H, ArH), 7.26 (d, J = 8.0 Hz, 1H, ArH), 6.32 (d, J = 8.5 Hz, 1H, ArH), 4.46 (br s, 1H, NH), 2.88 (s, 3H, CH_3N), 2.16 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) 157.7, 147.3, 138.3, 121.1, 105.7, 29.1, 17.1.

***N*-Methylpyrazin-2-amine (3n)[25].** Oil, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (s, 1H, ArH), 7.89 (s, 1H, ArH), 7.79 (s, 1H, ArH), 4.82 (br s, 1H, NH), 2.97 (d, J = 5.2 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.2, 141.7, 132.0, 131.7, 28.0.

3-Chloro-*N*-methylbenzenesulfonamide (5a)[26]. mp 44–45 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (s, 1H, ArH), 7.75 (d, J = 7.5 Hz, 1H, ArH), 7.56 (d, J = 7.5 Hz, 1H, ArH), 7.48 (t, J = 7.7 Hz, 1H, ArH), 4.53 (br s, 1H, NH), 2.69 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.5, 135.2, 132.8, 130.4, 127.2, 125.2, 29.2.

4-Bromo-*N*-methylbenzenesulfonamide (5b)[27]. mp 74–75 °C (lit.[27] mp 76–77 °C); ^{1}H NMR (500 MHz, $CDCl_3$) 7.73 (d, J = 8.3 Hz, 2H, ArH), 7.67 (d, J = 8.4 Hz, 2H, ArH), 4.47 (br s, 1H, NH), 2.67 (d, J = 4.3 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) 137.8, 132.3, 128.7, 127.6, 29.2.

***N*-Methyl-4-(trifluoromethyl)benzenesulfonamide (5c).** mp 76–78 °C; ^{1}H NMR (500 MHz, $CDCl_3$) 8.00 (d, J = 8.2 Hz, 2H, ArH), 7.80 (d, J = 8.3 Hz, 2H, ArH), 4.57 (br s, 1H, NH), 2.71 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.5, 134.5 (q, $J_{C\text{-}F}$ = 32.9 Hz), 127.7, 126.3 (q, $J_{C\text{-}F}$ = 3.6 Hz), 123.2 (q, $J_{C\text{-}F}$ = 271.5 Hz), 29.2; HRMS-EI (70 eV) m/z calcd for $C_8H_8NO_2F_3NaS$ $[M+Na]^+$ 262.0126, found 262.0131.

***N*-Methyl-4-(trifluoromethoxy)benzenesulfonamide (5d).** Oil, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (dt, J = 9.2 Hz and 2.4 Hz, 2H, ArH), 7.36 (d, J = 8.2 Hz, 2H, ArH), 4.57 (q, J = 5.0 Hz, 1H, NH), 2.69 (d, J = 5.4 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.1 (d, $J_{C\text{-}F}$ = 1.8 Hz), 137.2, 129.3, 120.2 (q, $J_{C\text{-}F}$ = 257.7 Hz), 29.2; HRMS-EI (70 eV) m/z calcd for $C_8H_8NO_3F_3NaS$ $[M+Na]^+$ 278.0075, found 278.0077.

***N*,2-Dimethylbenzenesulfonamide (5e)[28].** mp 70–72 °C; ^{1}H NMR (500 MHz, $CDCl_3$) 7.96 (d, J = 8.1 Hz, 1H, ArH), 7.46 (t, J = 7.3 Hz, 1H, ArH), 7.33 (t, J = 6.4 Hz, 2H, ArH), 4.47 (br s, 1H, NH), 2.64–2.63 (m, 6H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.0, 136.7, 132.7, 132.5, 129.6, 126.0, 28.9, 20.2.

***N*,4-Dimethylbenzenesulfonamide (5f)[29].** mp 75–76 °C; ^{1}H NMR (500 MHz, $CDCl_3$) 7.75 (d, J = 8.2 Hz, 2H, ArH), 7.32 (d, J = 8.1 Hz, 2H, ArH), 4.46 (br s, 1H, NH), 2.64 (d, J = 5.5 Hz, 3H, CH_3N), 2.43 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.4, 135.7, 129.6, 127.2, 29.2, 21.4.

4-Methoxy-*N*-methylbenzenesulfonamide (5g)[30]. mp 94–95 °C (lit.[30] mp 96–98.5 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, J = 8.6 Hz, 2H, ArH), 6.99 (d, J = 8.6 Hz, 2H, ArH), 4.43 (br s, 1H, NH), 3.87 (s, 3H, CH_3O), 2.63 (d, J = 5.4 Hz, 3H, CH_3N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.8, 130.2, 129.2, 114.2, 55.5, 29.1.

***N*-Methylbenzenesulfonamide (5h)[31].** Oil, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, J = 7.9 Hz, 2H, ArH), 7.59 (t, J = 7.4 Hz, 1H, ArH), 7.53 (t, J = 7.6 Hz, 2H, ArH), 4.60 (br s, 1H, NH), 2.66 (d, J = 5.1 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.7, 132.6, 129.0, 127.1, 29.1.

***N*-Methylnaphthalene-2-sulfonamide (5i)[32].** mp 107–108 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.44 (s, 1H, ArH), 7.97 (d, J = 8.6 Hz, 2H, ArH), 7.91 (d, J = 8.2 Hz, 1H, ArH), 7.84 (d, J = 8.6 Hz, 1H, ArH), 7.65 (t, J = 7.2 Hz, 1H, ArH), 7.61 (t, J = 7.1 Hz, 1H, ArH), 4.59 (br s, 1H, NH), 2.69 (d, J = 5.4 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.4, 134.7, 132.0, 129.4, 129.1, 128.7, 128.6, 127.8, 127.4, 122.2, 29.2.

***N*-Methylbenzo[d]thiazol-2-amine (7a)[33].** mp 155–156 °C (lit.[33] mp 141–142 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, J = 7.6 Hz, 1H, ArH), 7.53 (d, J = 8.0 Hz, 1H, ArH), 7.29 (t, J = 7.5 Hz, 1H, ArH), 7.08 (t, J = 7.5 Hz, 1H, ArH), 5.86 (br s, 1H, NH), 3.10 (s, 3H, CH_3N); ^{13}C NMR (125MHz, $CDCl_3$) δ 168.9, 152.4, 130.2, 125.9, 121.2, 120.8, 118.5, 31.6.

***N*,6-Dimethylbenzo[d]thiazol-2-amine (7b)[34].** mp 155–156 °C (lit.[34] mp 153 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43–7.40 (m, 2H, ArH), 7.09 (d, J = 7.8 Hz, 1H, ArH), 5.85 (br s, 1H, NH), 3.08 (s, 3H, CH_3N), 2.38 (s, 3H, CH_3); ^{13}C NMR (125MHz, $CDCl_3$) δ 168.1, 150.3, 131.0, 130.4, 127.0, 120.8, 118.2, 31.6, 21.1.

***N*-Methyl-6-phenoxybenzo[d]thiazol-2-amine (7c).** mp 158–159 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, J = 8.6 Hz, 1H, ArH), 7.31 (t, J = 7.9 Hz, 2H, ArH), 7.26 (s, 1H, ArH), 7.06 (t, J = 7.3 Hz, 1H, ArH), 7.01 (dd, J = 8.6 Hz and 2.2 Hz, 1H, ArH), 6.98 (d, J = 7.9 Hz, 2H, ArH), 5.49 (br s, 1H, NH), 3.10 (s, 3H, CH_3N); ^{13}C NMR (125MHz, $CDCl_3$) δ 168.1, 158.2, 151.4, 148.8, 131.2, 129.6, 122.6, 119.1, 118.3, 117.9, 111.9, 31.6; HRMS-EI (70 eV) m/z calcd for $C_{14}H_{13}N_2OS$ $[M+H]^+$ 257.0749, found 257.0747.

***N*-Methyl-6-(methylthio)benzo[d]thiazol-2-amine (7d).** mp 155–156 °C; ^{1}H NMR (500 MHz, $CDCl_3$) 7.56 (s, 1H, ArH),7.45 (d, J

= 8.3 Hz, 1H, ArH), 7.27 (d, J = 9.5 Hz, 1H, ArH), 5.72 (br s, 1H, NH), 3.10 (s, 3H, CH_3N), 2.50 (s, 3H, CH_3S); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.6, 150.9, 131.2, 130.1, 127.0, 120.7, 118.8, 31.6, 18.0; HRMS-EI (70 eV) m/z calcd for $C_9H_{11}N_2S_2$ $[M+H]^+$ 211.0364, found 211.0358.

***N*-Methyl-6-(trifluoromethoxy)benzo[d]thiazol-2-amine (7e)[35].** mp 158–160 °C (lit.[35] mp 162 °C); ^1H NMR (500 MHz, $CDCl_3$) δ 7.51–7.47 (m, 2H, ArH), 7.16 (d, J = 8.1 Hz, 1H, ArH), 5.62 (br s, 1H, NH), 3.11 (s, 3H, CH_3N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.1, 151.3, 143.5, 131.1, 120.6 (quart, $J_{C\text{-}F}$ = 255.1 Hz), 119.7, 118.9, 114.0, 31.7.

6-Chloro-*N*-methylbenzo[d]thiazol-2-amine (7f)[36]. mp 216–217 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, J = 2.0 Hz, 1H, ArH), 7.43 (d, J = 8.7 Hz, 1H, ArH), 7.25 (dd, J = 8.7 Hz and 2.0 Hz, 1H, ArH), 5.52 (br s, 1H, NH), 3.11 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.4, 151.2, 131.7, 126.7, 126.4, 120.5, 119.5, 31.7.

6-Chloro-*N*,4-dimethylbenzo[d]thiazol-2-amine (7g). mp 163–165 °C; ^1H NMR (500 MHz, $CDCl_3$) 7.41 (d, J = 2.0 Hz, 1H, ArH), 7.09 (s, 1H, ArH), 5.46 (br s, 1H, NH), 3.07 (s, 3H, CH_3N), 2.52 (s, 3H, CH_3); ^{13}C NMR (125MHz, $CDCL_3$) δ 168.1, 150.2, 131.0, 129.5, 127.0, 126.0, 117.9, 31.9, 18.2. HRMS-EI (70 eV) m/z calcd for $C_9H_{10}N_2SCl$ $[M+H]^+$ 213.0253, found 213.0258.

***N*-Methyl-4,5-diphenylthiazol-2-amine (7h)[37].** mp 191–192 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, J = 6.6 Hz, 2H, ArH), 7.28–7.20 (m, 8H, ArH), 5.96 (br s, NH, 1H), 2.90 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.0, 146.2, 135.6, 133.0, 129.2, 129.0, 128.5, 128.2, 127.5, 126.9, 120.2, 32.1.

***N*,5-Dimethyl-4-phenylthiazol-2-amine (7i)[37].** mp 125–126 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, J = 7.9 Hz, 2H, ArH), 7.39 (t, J = 7.5 Hz, 2H, ArH), 7.29 (t, J = 7.4 Hz, 1H, ArH), 5.47 (br s, 1H, NH), 2.90 (s, 3H, NCH_3), 2.40 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.7, 146.5, 135.5, 128.5, 128.2, 127.1, 115.3, 32.1, 12.4.

5-Chloro-*N*-methylbenzo[d]oxazol-2-amine (7j)[38]. mp 111–112 °C (lit.[38] mp 156–158 °C); ^1H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, J = 1.8 Hz, 1H, ArH), 7.14 (d, J = 8.4 Hz, 1H, ArH), 6.99 (dd, J = 8.5 Hz and 1.9 Hz, 1H, ArH), 5.26 (br s, 1H, NH), 3.12 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.6, 147.2, 144.2, 129.3, 120.7, 116.3, 109.3, 29.4.

1-Benzyl-*N*-methyl-1*H*-benzo[d]imidazol-2-amine (7k)[39]. ^1H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, J = 7.8 Hz, 1H, ArH), 7.35–7.28 (m, 3H, ArH), 7.15–7.12 (m, 3H, ArH), 7.08–7.03 (m, 2H, ArH), 5.08 (s, 2H, CH_2N), 4.01 (br s, 1H, NH), 3.07 (d, J = 4.6 Hz, 3H, CH_3N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.1, 142.2, 135.4, 134.9, 129.1, 128.0, 126.3, 121.3, 119.7, 116.5, 107.2, 45.5, 30.0.

***N*-Methyl-1-phenethyl-1*H*-benzo[d]imidazol-2-amine (7l).** ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, J = 7.7 Hz, 1H, ArH), 7.32–7.25 (m, 3H, ArH), 7.13 (t, J = 7.0 Hz, 1H, ArH), 7.08–7.05 (m, 4H, ArH), 4.08 (t, J = 6.7 Hz, 2H, CH_2N), 3.22 (br s, 1H, NH), 3.02 (t, J = 6.6 Hz, 2H, CH_2), 2.80 (d, J = 5.0 Hz, 3H, CH_3N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.2, 142.3, 138.3, 134.1, 129.0, 128.8, 127.1, 121.2, 119.5, 116.5, 107.0, 44.4, 35.3, 30.0; HRMS-EI (70 eV) m/z calcd for $C_{16}H_{18}N_3$ $[M+H]^+$ 252.1501, found 252.1502.

1-Butyl-*N*-methyl-1*H*-benzo[d]imidazol-2-amine (7m). ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, J = 7.7 Hz, 1H, ArH), 7.11–7.03 (m, 3H, ArH), 4.12 (br s, 1H, NH), 3.84 (t, J = 7.1 Hz, 2H, CH_2N), 3.17 (d, J = 4.4 Hz, 3H, CH_3N), 1.72 (quint, J = 7.5 Hz, 2H, CH_2), 1.39 (sext, J = 7.5 Hz, 2H, CH_2), 0.95 (t, J = 7.3 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.7, 142.2, 134.6, 121.0, 119.4, 116.4, 107.2, 42.1, 31.0, 30.1, 20.2, 13.7; HRMS-EI (70 eV) m/z calcd for $C_{12}H_{18}N_3$ $[M+H]^+$ 204.1501, found 204.1504.

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