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Nickel-Catalyzed Intramolecular Desulfitative C−N Coupling: Synthesis of Aromatic Amines

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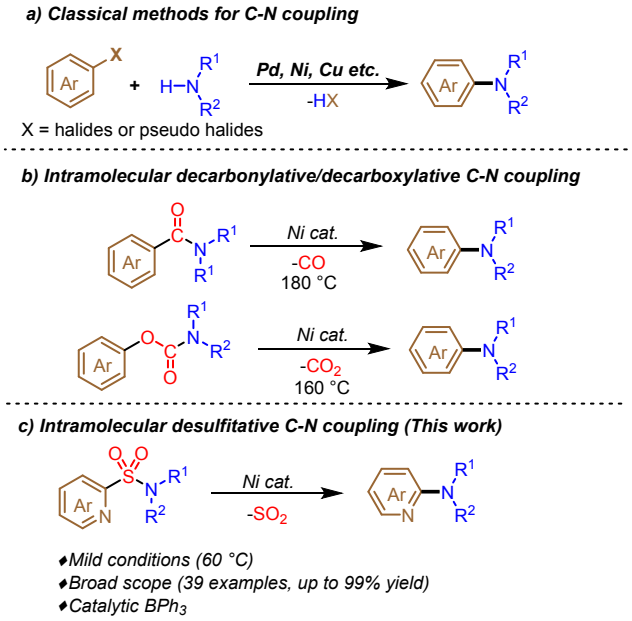
ABSTRACT: A nickel-catalyzed intramolecular C−N coupling reaction via SO_2 extrusion is presented. The use of a catalytic amount of BPh_3 allows the transformation to take place under much milder conditions (60 °C) compared to previously reported C−N coupling reactions by CO or CO_2 extrusion (160−180 °C). In addition, this method displays good functional group tolerance and versatility as it can be applied to the synthesis of dialkyl aryl amines, alkyl diaryl amines, and triaryl amines. The robustness of the desulfitative C−N coupling is demonstrated with three high-yielding gram-scale reactions.

Aromatic amines are important building blocks in organic synthesis and they are present in numerous natural products,[1] bioactive compounds,[2] pharmaceuticals,[3] and polymers[4]. Therefore, the preparation of aromatic amines is an important task which has attracted significant attention in the past decades. Common synthetic routes include direct nucleophilic substitution and cross-coupling reactions between amines and aryl halides such as palladium- and nickel-catalyzed Buchwald-Hartwig aminations[5] and copper-catalyzed Ullmann reactions[6] (Scheme 1a).



Scheme 1. Strategies for C-N coupling reactions.

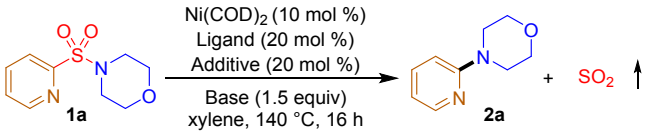
Bond formation via gas extrusion followed by intramolecular recombination is considered atom-economic, since the only byproduct is a small gaseous molecule.[7] During the last decade significant progress has been achieved for these intramolecular coupling reactions via CO and CO_2 extrusion. For CO extrusion, the formation of a range of different bonds have been reported (C−X; X = C, O, N, P, S, Cl)[7b-7d, 8] while only C−N coupling via CO_2 extrusion[9] has been developed. Albeit intramolecular C−N coupling reactions via both CO and CO_2 extrusion has been achieved, both transformations require harsh conditions with elevated temperatures (Scheme 1b).

Recently, coupling reactions via SO_2 extrusion has started to gain attention. Since 2017, a few groups have reported intermolecular desulfitative coupling reactions for C−C bond formation.[10] Subsequently, Yorimitsu and Wei independently reported nickel-catalyzed intramolecular C−C coupling reactions of sulfones via SO_2 extrusion.[11] Recently, we reported both a nickel- and a palladium-catalyzed intramolecular desulfitative C−O coupling of sulfonates.[12] Despite these efforts there are still no examples of transition-metal-catalyzed intramolecular C−N bond forming reactions by SO_2 extrusion.[13] Herein, we report the first example of such a transformation. We demonstrate that C−N bond formation by SO_2 extrusion from sulfonamides can be performed under much milder conditions than the previously reported C−N coupling reactions via CO or CO_2 extrusion.

Inspired by many of the inter- and intramolecular desulfitative coupling reactions, we initiated our study with a substrate containing a pyridyl group as a potential directing group.[10-12] Importantly, pyridines are pivotal in medicinal chemistry. Our initial investigation employed 4-(pyridin-2-ylsulfonyl)morpholine (**1a**) as substrate, 10 mol % $Ni(COD)_2$ as catalyst, 1.5 equiv KO*t*Bu as base, and xylene as solvent at 140 °C (Table 1). However, the desulfitative product 4-(pyridin-2-yl)morpholine (**2a**) was not detected after 16 h (entry 1). The addition of monodentate phosphine ligands (PPh_3, PCy_3, or XPhos) or bidentate phosphine ligand (DPPP, BINAP, DPEPhos, or XantPhos) did not improve the reaction outcome (entries 2-3). When bidentate nitrogen ligands were used, compound **2a** was produced in up to 6% yield (entries 4-5). The use of NHC ligands (IPr·HCl, SIPr·HCl, and IMes·HCl) significantly improved the yield of this desulfinative C−N coupling, and among of them IPr·HCl showed the best performance (entries 6-8). Nonetheless, the yield of **2a** was still moderate. We envisaged that the addition of a Lewis acid could aid activating the substrate either by binding to the pyridine nitrogen or to the sulfonyl group. To our delight, a catalytic amount of the Lewis acid, BPh_3, improved the yield to 47% (entry 9). The use of $B(C_6F_5)_3$ as additive led to inhibition of product formation, while other boron- or metal-based Lewis acids only led to minor changes in yield compared to the additive-free conditions (entries 10-18). A subsequent screening of other *tert*-butoxide bases than KO*t*Bu revealed as small improvement with NaO*t*Bu (entries 19-20). To our surprise, lowering the reaction temperature would suppress the decomposition of **1a** and lead to a significant increase in yield leading to 78% yield of **2a** (entry 21). NaO*t*Bu still showed the best performance among *tert*-butoxide bases at 60 °C (entries 21-23). Finally, control experiments revealed that the catalyst and ligand

are necessary for this desulfitative C−N coupling reaction (entries 24-27).

Table 1. Optimization of Reaction Conditions for the Desulfitative C−N Coupling.[a]

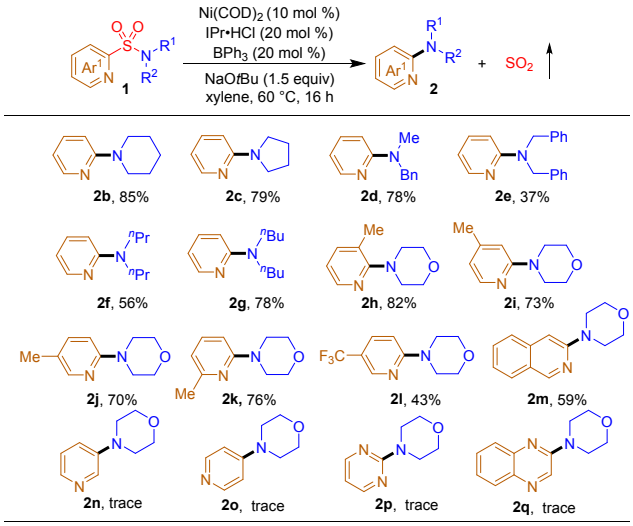


entry	ligand	additive	base	yield of **2a**[b] (%)
1	-	-	KO*t*Bu	0
2	monodentate phosphines[b]	-	KO*t*Bu	0
3	bidentate phosphines[c]	-	KO*t*Bu	0
4	2,2'-bipyridine	-	KO*t*Bu	6
5	1,10-phenanthroline	-	KO*t*Bu	trace
6	IPr·HCl	-	KO*t*Bu	30
7	SIPr·HCl	-	KO*t*Bu	25
8	IMes·HCl	-	KO*t*Bu	27
9	IPr·HCl	BPh_3	KO*t*Bu	47
10	IPr·HCl	$B(C_6F_5)_3$	KO*t*Bu	0
11	IPr·HCl	$PhB(OH)_2$	KO*t*Bu	40
12	IPr·HCl	$B(OH)_3$	KO*t*Bu	34
13	IPr·HCl	$B(OPh)_3$	KO*t*Bu	26
14	IPr·HCl	$FeCl_3$	KO*t*Bu	32
15	IPr·HCl	$MgCl_2$	KO*t*Bu	33
16	IPr·HCl	$CuCl_2$	KO*t*Bu	24
17	IPr·HCl	$CuBr_2$	KO*t*Bu	26
18	IPr·HCl	$AlCl_3$	KO*t*Bu	24
19	IPr·HCl	BPh_3	NaO*t*Bu	59
20	IPr·HCl	BPh_3	LiO*t*Bu	35
21[e]	IPr·HCl	BPh_3	NaO*t*Bu	81 (78)[f]
22[e]	IPr·HCl	BPh_3	KO*t*Bu	49
23[e]	IPr·HCl	BPh_3	LiO*t*Bu	61
24[e]	IPr·HCl		NaO*t*Bu	67
25[e,g]	IPr·HCl	BPh_3	NaO*t*Bu	0
26[e,h]	-	BPh_3	NaO*t*Bu	0
27[e,i]	-	BPh_3	NaO*t*Bu	0

[a] Reactions in this table were performed under an Ar atmosphere at 0.2 mmol scale. Yields were determined by GC using dodecane as an internal standard. [b] GC yield using dodecane as an internal standard. [c] Monodentate phosphine ligands: PPh_3, PCy_3, and XPhos. [d] Bidentate phosphine ligands: DPPP, BINAP, DPEPhos, and XantPhos. [e] At 60 °C. [f] Product yield in parenthesis. [g] In the absence of $Ni(COD)_2$. [h] In the absence of IPr·HCl. [i] In the absence of $Ni(COD)_2$ and IPr·HCl.

With satisfactory reaction conditions established, we set out to examine the scope of the reaction. First, a variety of dialkyl-substituted sulfonamides were evaluated (Table 2). Both sulfonamides bearing cyclic and acyclic amines can be successfully employed (**2b**-**2g**), leading to high yields in most cases. In order to evaluate the influence of steric and electronic effects on the pyridine moiety, 3-, 4-, 5-, and 6-methylpyridyl substrates were examined (**2h**-**2k**) as well as a substrate bearing a 3-trifluoromethyl substituent (**2l**). The consistently good yields for the different methyl-substituted pyridines, even in the 3-position, indicate minimal influence of the steric effect from the methyl group on the reaction outcome. In contrast, the strongly electron-withdrawing CF_3-group decreases the yield suggesting that electronic effects do play a role. In addition to pyridine substrates, an isoquinoline sulfonamide also produced a good yield of the SO_2 extrusion product (**2m**). Lastly, some unsuccessful heteroaromatic sulfonamides were concluded in Table 2. (**2n-2q**)

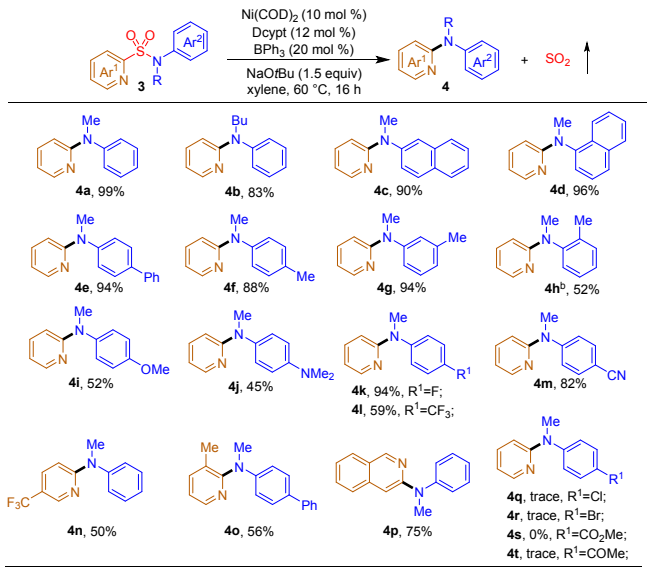
Table 2. Substrate Scope of Dialkyl Sulfonamides.[a]



[a] The reactions were set up on 0.2 mmol scale.

Next, we examined if the method could be applied to alkyl aryl substituted sulfonamides (Table 3). Indeed, under the standard conditions (Table 1, entry 21), phenylmethylpyridine (**4a**) was obtained in 75% yield. By changing the ligand to 3,4-bis(dicyclohexylphosphino)thiophene (Dcypt), the yield of **4a** increased to 99%.[14] Continuing with Dcypt as ligand, a range of different alkyl aryl substituted sulfonamides were examined. An N-butyl substituted sulfonamide afforded the aryl amine in good yield (**4b**). Also, substrates with various electron-neutral aromatic rings led to high yields of the desulfinated product (**4c**-**4e**). Sulfonamides containing different methyl-substituted phenylamines were also examined (**4f**-**4h**). While *meta*- and *para*-methyl substituents are well-tolerated, an *ortho*-methyl substituent leads to a lower yield. This contrasts with the limited steric effect observed for the methyl-substituents on the pyridine moiety when morpholine sulfonamides were used. Substrates bearing functional groups such as ether, amine, fluoride, trifluoromethyl, and nitrile also afforded the desulfinated product (**4i**-**4m**). The trend in terms of yield seems to suggest that strongly electron-donating and electron-withdrawing substituents decrease the yield, while functional groups with moderate electronic features lead to high yields. On the pyridine moiety, both 5-CF_3 (**4n**) and 3-Me (**4o**) substituents were tolerated. In addition, an isoquinoline substituted sulfonamides led to the formation of **4p** in 75% yield. Due to the competition between the C−halide (halide = Cl and Br) and S−N bond cleavage, these sulfonamides produced the corresponding products (**4r** and **4s**) in trace yields. Ester and ketone substituted sulfonamides were not subjected to the standard conditions (**4s** and **4t**), leading to the decomposition of the starting materials.

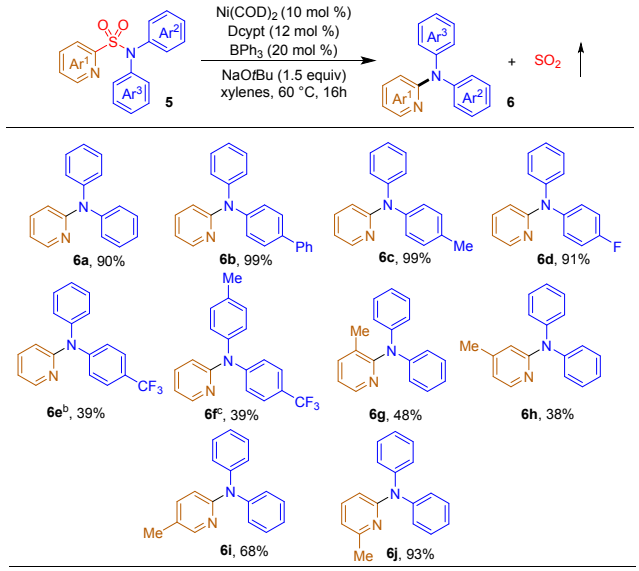
Table 3. Substrate Scope of Alkyl Aryl Sulfonamides.[a]



[a] The reactions were set up on 0.2 mmol scale. [b] 80 °C.

Finally, we investigated the desulfitative C−N coupling reaction for diaryl substituted sulfonamides (Table 4). When diphenyl substituted sulfonamide **5a** was subjected to the reaction conditions with Dcypt as ligand, the desulfitative product **6a** was isolated in 90% yield. Other diaryl substituted sulfonamides were also investigated. Similar to the trend observed for alkyl aryl sulfonamides, substrates containing substituents that are only moderately electron-donating/withdrawing produce the highest yields (**6b-6f**). Methyl substituents on the pyridine moiety was also tolerated (**6g-6j**). However, due to the steric bulk of the diarylamine moiety, the best yields are obtained when the methyl group is located away from the amine.

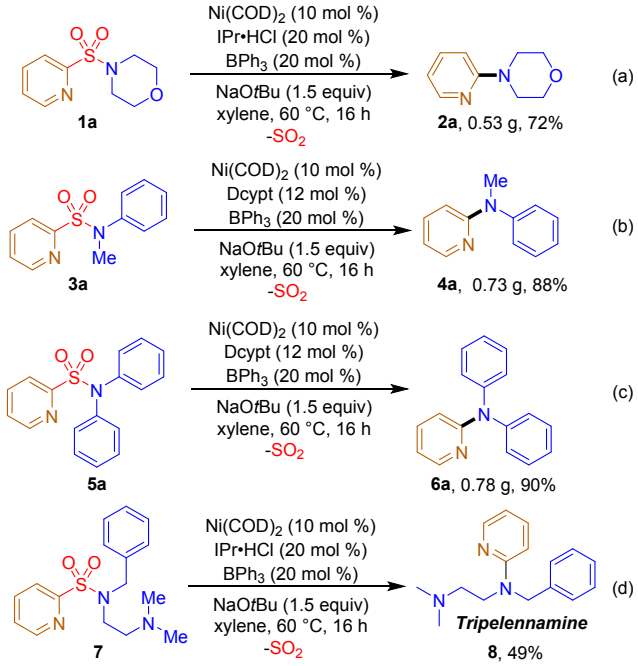
Table 4. Substrate Scope of Diaryl Sulfonamides.[a]



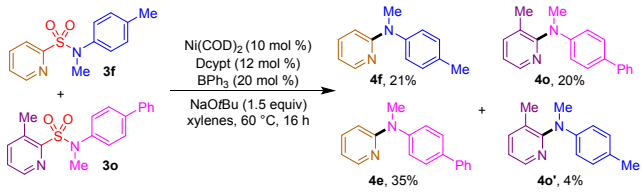
[a] The reactions were set up on 0.2 mmol scale. [b] 100 °C. [c] 80 °C.

Having established the generality of the developed desulfitative C−N coupling, we set out to investigate the scalability of the method. Encouragingly, on a 4.5 mmol scale, sulfonamide **1a** produced the desired amine **2a** in 72% yield (Scheme 2a). Similarly, the use of two other sulfonamides also led to high yields on gram-scale (Scheme 2b and 2c). In all three cases, the yields are very close to those obtained on 0.2 mmol scale, thus indicating the robustness of the method toward scaling up. Finally, we demonstrated the relevance of the desulfitative C−N coupling for medicinal chemistry with the synthesis of the antihistamine, tripelennamine (Scheme 2d). Cross-over experiment between **3f** and **3o** was set up and four amines were detected, which indicated that this reaction might proceed via both intra- and intermolecular pathway. (Scheme 3)

Scheme 2. Three Examples of Gram Scale Desulfitative C−N Coupling Reactions (a-c) and an Example of Application for Medicinal Chemistry (d).

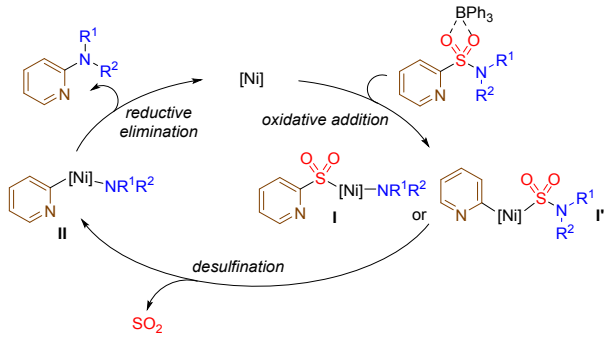


Scheme 3. Cross-over experiment between 3f and 3o.[a]



Based on the results above and previous studies, we propose a mechanistic hypothesis (Scheme 4).[7b, 8e, 9-11] Initially, low-valent nickel undergo oxidative addition into either the S−N or S−C bond of the sulfonamide forming intermediate **I** or **I'**. We hypothesize that the pyridine moiety serves as directing group for nickel since no product is formed when 4-(pyridin-3-ylsulfonyl)morpholine or 4-(pyridin-4-ylsulfonyl)morpholine are used as substrates. From intermediate **I/I'**, SO_2 can be released, and a subsequent reductive elimination from **II** affords the aryl amine product and regenerates the low-valent nickel catalyst. The beneficial role of BPh_3 is unclear at this point. Potentially, it could aid the oxidative addition by coordination to the sulfonyl moiety, aid the desulfination, and/or aid the reductive elimination by coordination to pyridine.

Scheme 4. Proposed Mechanism.



In summary, we have developed the first nickel-catalyzed intramolecular desulfitative C–N coupling reaction. The transformation proceeds at much lower temperature than the analogous reactions via CO or CO_2 extrusion. The scope is broad as the method can be used for synthesis of dialkyl aryl amines, alkyl diaryl amines, and triaryl amines. The results provide new perspectives for sulfonamides as functional handles for aryl amine synthesis.

Experimental Section

General Experimental Information: Unless otherwise noted, all reagents were obtained from commercial suppliers and used as received. Unless otherwise noted, all catalytic reactions were set up in an argon atmosphere glovebox (Vigor, SGI800-750TS-F). Unless otherwise noted, the substrates and reagents for catalytic reactions were degassed and stored in the glovebox. All work-up and purification procedures were carried out with reagent-grade solvents in air. Thin Layer Chromatography analyses were performed on silica gel coated glass plates (0.25 mm) with fluorescence indicator UV254. For detection of spots, irradiation of UV light at 254 nm or staining reagent using phosphomolybdic acid solution was used. Flash column chromatography was conducted with silica gel 60 (particle size 230–400 mesh, Huanghai) at room temperature and under elevated pressure. Gas chromatography (GC) analysis was conducted on a Shimadzu GC-2030 instrument equipped with a Rtx-5 column (30 m × 0.25 mm) with dodecane as an internal standard. GC-MS analysis was conducted on an Agilent 5977B GC/MSD instrument equipped with a HP-5MS UI column (30 m × 0.25 mm). Melting points were measured with a micro melting point apparatus. ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 MHz and at 101 MHz(or 151 MHz), respectively in $CDCl_3$ at room temperature. ^{1}H NMR was reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet), coupling constant (*J* values) in Hz and integration. Chemical shifts (δ) were reported with respect to the corresponding solvent residual peak at 7.26 ppm for $CDCl_3$ for ^{1}H NMR. ^{13}C NMR spectra (^{1}H-broadband decoupled) were reported in ppm using the central peak of $CDCl_3$ (77.16 ppm). High-resolution mass spectrometric measurements were provided by the Department of The State Key Laboratory of Biotherapy, Sichuan University. The molecular ion $[M+H]^+$ and $[M+Na]^+$ are given in m/z units.

General Procedure for the Synthesis of Pyridine-2-Sulfonamides

Synthesis of pyridylsulfonyl chloride: Pyridylsulfonyl chloride were synthesized according to procedures reported in the literature[15]. 2-mercaptopyridine (2.22 g, 20 mmol) was dissolved in conc. H_2SO_4 (56 mL) and cooled in ice bath. NaClO (roughly 5% NaClO, 220mL) was added dropwise to the solution. The resulting mixture was stirred for 15 min at 0 °C before it was extracted with CH_2Cl_2(3 × 30 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated to afford 2-pyridylsulfonyl chloride as a pale-yellow oil. The compound is relatively unstable at room temperature and the crude product was used without further purification in the next step.

Synthesis of pyridine-2-sulfonamides: [Method A][16] General procedure for compounds 1a-1c, 1f, 1g. To a solution of pyridylsulfonyl chloride (5 mmol) in CH_2Cl_2 (15 mL) was added amine (3.0 equiv, 15 mmol) in ice bath. The resulting mixture was allowed to reach room temperature and stirred at room temperature overnight. The reaction mixture was quenched with water, extracted with CH_2Cl_2 (3 × 30 mL) and dried over Na_2SO_4. After filtration, the solvent was removed by evaporation at reduced pressure. The residue was purified *via* flash column chromatography to give the desired product.

[Method B][17] General procedure for compounds 1d, 1e, 7. 4 M solution of aq.K_2CO_3 (8 mL) was added to a solution of 4 mmol amine and 4.8 mmol pyridine-2-sulfonyl chloride in ether (8 mL), the resulting mixture was stirred vigorously for 1-6 h at 0°C. After completion, Separating the aqueous phase and the organic phase, and the aqueous phase was then extracted with CH_2Cl_2 (3 × 20 mL), dried over Na_2SO_4. After filtration, the solution was evaporated to dryness under reduced pressure. The residue was purified *via* flash column chromatography to give the desired product.

[Method C][15] General procedure for compounds 1h-1m, 3a-3p. To a solution of amine (5.0 mmol) and pyridine (1.5 equiv, 7.5 mmol) in THF (50 mL) at 0°C, 2-pyridylsulfonyl chloride (1.5 equiv, 7.5 mmol) was added slowly. The resulting mixture was allowed to reach room temperature and stirred at room temperature overnight. The mixture was quenched with saturated aq. NH_4Cl solution (10 mL) and extracted with EtOAc (3 × 20 mL). The combined organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash chromatography to afford the desired product.

[Method D][18] General Procedure for Compounds 5a-5j. To a solution of amine (5 mmol) in THF (50 mL), cooled to 0°C and under nitrogen atmosphere, were successively added pyridine (1.8 equiv, 9 mmol) and a solution of 2-pyridylsulfonyl chloride (6 mmol, 1.2 equiv) in THF (2 mL). The resulting solution was allowed to reach room temperature and it was stirred overnight (precipitate was formed). The precipitate was removed by filtration. To the filtrate was added water (20 mL), the mixture was evaporated under reduced pressure to remove the THF. The resulting suspension was filtered to obtain a white solid, the solid was filtered, washed with toluene and dried under vacuum. The solid (sulfonamide) was used without further purification in the next step. A solution of sulfonamide(1 equiv), triarylbismuth (2 equiv), anhydrous $Cu(OAc)_2$ (1.5 equiv), pyridine (1.5 equiv) in CH_2Cl_2 (2.5 mL/mmol of substrate) was stirred at room temperature overnight. The crude reaction mixture was preabsorbed on silica gel and concentrated *in vacuo*. The residue was purified by flash column chromatography to afford the desired product.

General Procedure for the Synthesis of Compounds 2a-2m: In the glovebox, alkyl sulfonamide (0.2 mmol), $Ni(COD)_2$ (10 mol%, 5.5 mg), IPr·HCl (20 mol%, 17.0 mg), BPh_3 (20 mol %, 9.7 mg), and NaO*t*Bu (2.0 equiv, 38.5 mg) were added into an oven-dried 4 ml vial with a magnetic stirring bar, followed by addition of xylenes (1.0 mL). The vial was sealed and removed out of the glovebox and heated to 60 °C in heating block. After 16 h, the vial was cooled to room temperature. The mixture was concentrated *in vacuo* and the residue was purified by flash column chromatography to give the desired product.

4-(pyridin-2-yl)morpholine (2a). Isolated as pale-yellow oil using petroleum ether/ethyl acetate (5:1) as eluent (25.9 mg, yield 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23-8.17 (m, 1H), 7.52-7.46 (m, 1H), 6.67-6.61 (m, 2H), 3.82 (t, *J* = 4.8 Hz, 4H), 3.49 (t, *J* = 4.8 Hz, 4H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.6, 148.0, 137.5,

113.8, 107.0, 66.8, 45.6. HRMS (ESI-TOF) *m/z* calculated for $C_9H_{12}N_2O$ $[M+H]^+$: 165.1022, found: 165.1026.

2-(piperidin-1-yl)pyridine (2b). Isolated as pale-yellow oil using petroleum ether/dichloromethane (20:1) as eluent (27.4 mg, yield 85%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.19-8.14 (m, 1H), 7.47-7.40 (m, 1H), 6.64 (d, *J* = 8.6 Hz, 1H), 6.58-6.50 (m, 1H), 3.55-3.50 (m, 4H), 1.66-1.61 (m, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.7, 147.9, 137.3, 112.4, 107.1, 46.4, 25.5, 24.7. HRMS (ESI-TOF) *m/z* calculated for $C_{10}H_{14}N_2$ $[M+H]^+$: 163.1230, found: 163.1233.

2-(pyrrolidin-1-yl)pyridine (2c). Isolated as pale-yellow oil using petroleum ether/ethyl acetate (5:1) as eluent (23.4 mg, yield 79%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.17-8.11 (m, 1H), 7.44-7.38 (m, 1H), 6.52-6.47 (m, 1H), 6.34 (d, *J* = 8.4 Hz, 1H), 3.46-3.42 (m, 4H), 2.02-1.95 (m, 4H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 157.3, 148.1, 136.9, 111.0, 106.5, 46.7, 25.5. HRMS (ESI-TOF) *m/z* calculated for $C_9H_{12}N_2$ $[M+H]^+$: 149.1073, found: 149.1077.

***N*-benzyl-*N*-methylpyridin-2-amine (2d).** Isolated as pale-yellow oil using petroleum ether/ethyl acetate (5:1) as eluent (30.9 mg, yield 78%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.24-8.15 (m, 1H), 7.46-7.41 (m, 1H), 7.33-7.28 (m, 2H), 7.26-7.20 (m, 3H), 6.59-6.54 (m, 1H), 6.51 (d, *J* = 8.4 Hz, 1H), 4.80 (s, 2H), 3.08 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.7, 147.7, 138.6, 137.5, 128.6, 127.0, 126.9, 111.8, 105.9, 53.3, 36.3. HRMS (ESI-TOF) *m/z* calculated for $C_{13}H_{14}N_2$ $[M+H]^+$: 199.1230, found: 199.1232.

***N*,*N*-dibenzylpyridin-2-amine (2e).** Isolated as a pale-yellow oil using petroleum ether/diethyl ether (100:1) as eluent (20.3 mg, yield 37%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.23-8.13 (m, 1H), 7.37-7.32 (m, 1H), 7.31-7.24 (m, 4H), 7.23-7.18 (m, 6H), 6.58-6.51 (m, 1H), 6.47-6.39 (m, 1H), 4.77 (s, 4H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.8, 148.1, 138.6, 137.6, 128.7, 127.2, 127.1, 112.4, 106.1, 51.0. HRMS (ESI-TOF) *m/z* calculated for $C_{19}H_{18}N_2$ $[M+H]^+$: 275.1543, found: 275.1544.

***N*,*N*-dipropylpyridin-2-amine (2f).** Isolated as yellow oil using petroleum ether/ethyl acetate (50:1) as eluent (19.9 mg, yield 56%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.14-8.09 (m, 1H), 7.46-7.35 (m, 1H), 6.49-6.40 (m, 2H), 3.39 (t, *J* =7.6 Hz, 4H), 1.66-1.58 (m, 4H), 0.93 (t, *J* = 7.6 Hz, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.0, 148.0, 136.9, 110.7, 105.6, 50.5, 20.8, 11.5. HRMS (ESI-TOF) *m/z* calculated for $C_{11}H_{18}N_2$ $[M+H]^+$: 179.1543, found: 179.1546.

***N*,*N*-dibutylpyridin-2-amine (2g).** Isolated as white syrup liquid using petroleum ether/ethyl acetate (50:1) as eluent (32.1 mg, yield 78%).^1H NMR (400 MHz, $CDCl_3$) δ 8.14-8.10 (m, 1H), 7.40-7.35 (m, 1H), 6.47-6.40 (m, 2H), 3.45-3.40 (m, 4H), 1.61-1.53 (m, 4H), 1.39-1.31 (m, 4H), 0.95 (t, *J* = 7.2 Hz, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 157.9, 148.0, 136.9, 110.6, 105.5, 48.4, 29.8, 20.4, 14.1. HRMS (ESI-TOF) *m/z* calculated for $C_{13}H_{22}N_2$ $[M+H]^+$: 207.1856, found: 207.1861.

4-(3-methylpyridin-2-yl)morpholine (2h). Isolated as a pale-yellow oil using petroleum ether/diethyl ether (20:1) as eluent (29.2 mg, yield 82%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.20-8.14 (m, 1H), 7.44-7.40 (m, 1H), 6.87 (dd, *J* = 7.2, 4.8 Hz, 1H), 3.85 (t, *J* = 4.8 Hz, 4H), 3.15 (t, *J* = 4.8 Hz, 4H), 2.28 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 161.5, 145.4, 139.6, 125.0, 118.3, 67.3, 50.2, 18.5. HRMS (ESI-TOF) *m/z* calculated for $C_{10}H_{14}N_2O$ $[M+H]^+$: 179.1179, found: 179.1179.

4-(4-methylpyridin-2-yl)morpholine (2i). Isolated as a pale-yellow oil using petroleum ether/diethyl ether (15:1) as eluent (26.0 mg, yield 73%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 5.2 Hz, 1H), 6.51 (d, *J* = 5.2 Hz, 1H), 6.45 (s, 1H), 3.81 (t, *J* = 4.8 Hz, 4H), 3.48 (t, *J* = 4.8 Hz, 4H), 2.27 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.0, 148.7, 147.7, 115.5, 107.6, 66.9, 45.9, 21.5. HRMS (ESI-TOF) *m/z* calculated for $C_{10}H_{14}N_2O$ $[M+H]^+$: 179.1179, found: 179.1185.

4-(5-methylpyridin-2-yl)morpholine (2j). Isolated as a pale-yellow oil using petroleum ether/diethyl ether (20:1) as eluent (25.0 mg, yield 70%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.06-8.00 (m, 1H), 7.33 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.57 (d, *J* = 8.8 Hz, 1H), 3.82 (t, *J* = 4.8 Hz, 4H), 3.43 (t, *J* = 4.8 Hz, 4H), 2.20 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.3, 147.8, 138.6, 123.1, 107.0, 66.9, 46.3, 17.5. HRMS (ESI-TOF) *m/z* calculated for $C_{10}H_{14}N_2O$ $[M+H]^+$: 179.1179, found: 179,1181.

4-(6-methylpyridin-2-yl)morpholine (2k). Isolated as yellow oil using petroleum ether/ethyl acetate (10:1) as eluent (27.1 mg, yield 76%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 8.4, 7.6 Hz, 1H), 6.53 (d, *J* = 7.2 Hz, 1H), 6.42 (d, *J* = 8.4 Hz, 1H), 3.82 (t, *J* = 4.8 Hz, 4H), 3.49 (t, *J* = 4.8 Hz, 4H), 2.41 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.3, 156.8, 137.9, 113.2, 103.6, 66.9, 45.8, 24.5. HRMS (ESI-TOF) *m/z* calculated for $C_{10}H_{14}N_2O$ $[M+H]^+$: 179.1179, found: 179.1186.

4-(5-(trifluoromethyl)pyridin-2-yl)morpholine (2l). Isolated as a pale-yellow oil using petroleum ether/diethyl ether (20:1) as eluent (20 mg, yield 43%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.48-8.36 (m, 1H), 7.65 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.63 (d, *J* = 9.2 Hz, 1H), 3.81 (t, *J* = 4.8 Hz, 4H), 3.60 (t, *J* = 4.8 Hz, 4H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -61.22 . $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 160.7, 145.9(q, *J* = 4.2 Hz), 134.7(q, *J* = 2.7 Hz), δ 124.7 (q, *J* = 270.1 Hz), 115.9 (q, *J* = 33.0 Hz), 105.7, 66.7, 45.2. HRMS (ESI-TOF) *m/z* calculated for $C_{10}H_{11}F_3N_2O$ $[M+H]^+$: 233.0896, found: 233.0900.

4-(isoquinolin-3-yl)morpholine (2m). Isolated as a pale-yellow oil using petroleum ether/diethyl ether (20:1) as eluent (25.3 mg, yield 59%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.95 (s, 1H), 7.80 (d, *J* = 8.4 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.55-7.46 (m, 1H), 7.33-7.25 (m, 1H), 6.77 (s, 1H), 3.90 (t, *J* = 4.8 Hz, 4H), 3.55 (t, *J* = 4.8 Hz, 4H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 157.0, 151.4, 138.8, 130.5, 127.8, 125.5, 124.1, 123.7, 99.1, 67.0, 46.8. HRMS (ESI-TOF) *m/z* calculated for $C_{13}H_{14}N_2O$ $[M+H]^+$: 215.1179, found: 215.1179.

General Procedure for Compounds 4a-4p, 6a-6j: In the glovebox, aryl pyridine sulfonamide (0.2 mmol), $Ni(COD)_2$ (10 mol%, 5.5 mg), dcypt (12 mol%, 11.5 mg), BPh_3 (20 mol %, 9.7 mg), and NaO*t*Bu (1.5 equiv, 28.8 mg) were added into an oven-dried 4 ml vial with a magnetic stirring bar, followed by addition of xylenes (1.0 mL). The vial was sealed and removed out of the glovebox and heated to 60 °C in heating block for 16 h. After cooling the reaction mixture to room temperature, the mixture was concentrated *in vacuo* and the residue was purified by flash column chromatography to give the desired product.

***N*-methyl-*N*-phenylpyridin-2-amine (4a).** Isolated as pale-yellow syrup liquid using petroleum ether/dichloromethane (1:5) as eluent (36.5 mg, yield 99%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.27-8.20 (m, 1H), 7.44-7.37 (m, 2H), 7.34-7.28 (m, 1H), 7.28-7.25 (m, 2H), 7.24-7.19 (m, 1H), 6.65-6.58 (m, 1H), 6.53 (d, *J* = 8.4 Hz, 1H), 3.49 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.8, 147.7, 146.8, 136.6, 129.7, 126.3, 125.5, 113.1, 109.2, 38.4. HRMS (ESI-TOF) *m/z* calculated for $C_{12}H_{12}N_2$ $[M+H]^+$: 185.1073, found: 185.1076.

***N*-butyl-*N*-phenylpyridin-2-amine (4b).** Isolated as pale-yellow oil using petroleum ether/dichloromethane (1:1) as eluent (37.4 mg, yield 83%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.21-8.15 (m, 1H), 7.44-7.38 (m, 2H), 7.28-7.22 (m, 4H), 6.58-6.53 (m, 1H), 6.35 (d, *J* = 8.4 Hz, 1H), 3.95 (t, *J* = 7.6 Hz, 2H), 1.67-1.58 (m, 2H), 1.41-1.31 (m, 2H), 0.91 (t, *J* = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.6, 147.6, 145.6, 136.6, 129.8, 127.7, 125.8, 112.7, 109.1, 49.9, 30.2, 20.2, 14.0. HRMS (ESI-TOF) *m/z* calculated for $C_{15}H_{18}N_2$ $[M+H]^+$: 227.1543, found: 227.1546.

***N*-methyl-*N*-(naphthalen-2-yl)pyridin-2-amine (4c).** Isolated as white syrup liquid using petroleum ether/diethyl ether (30:1) as

eluent (42.2 mg, yield 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33-8.24 (m, 1H), 7.90-7.81 (m, 2H), 7.78 (d, *J* = 7.4 Hz, 1H), 7.69 (d, *J* = 2.4 Hz, 1H), 7.53-7.44 (m, 2H), 7.41 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.37-7.28 (m, 1H), 6.71-6.56 (m, 2H), 3.60 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.9, 147.9, 144.4, 136.9, 134.5, 131.4, 129.5, 127.8, 127.5, 126.5, 125.6, 125.4, 123.3, 113.6, 109.7, 38.7. HRMS (ESI-TOF) *m/z* calculated for $C_{16}H_{14}N_2$ $[M+H]^+$: 235.1230, found: 235.1234.

***N*-methyl-*N*-(naphthalen-1-yl)pyridin-2-amine (4d).** Isolated as yellow oil using petroleum ether/ethyl acetate (10:1) as eluent (45.1 mg, yield 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28-8.22 (m, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.56-7.49 (m, 2H), 7.48-7.41 (m, 2H), 7.22-7.15 (m, 1H), 6.62-6.54 (m, 1H), 6.02 (d, *J* = 8.4 Hz, 1H), 3.57 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz , $CDCl_3$) δ 159.4, 147.5, 143.0, 136.7, 135.2, 131.0, 128.6, 127.6, 126.7, 126.5, 126.4, 125.9, 123.4, 112.5, 108.7, 38.5. HRMS (ESI-TOF) *m/z* calculated for $C_{16}H_{14}N_2$ $[M+H]^+$: 235.1230, found: 235.1235.

***N*-([1,1'-biphenyl]-4-yl)-*N*-methylpyridin-2-amine (4e).** Isolated as a pale-yellow oil using petroleum ether/diethyl ether (10:1) as eluent (48.9 mg, yield 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27-8.21 (m, 1H), 7.66-7.59 (m, 4H), 7.50-7.41 (m, 2H), 7.39-7.31 (m, 4H), 6.69-6.61 (m, 2H), 3.52 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.8, 147.9, 146.2, 140.6, 138.1, 136.8, 128.9, 128.4, 127.3, 127.0, 126.3, 113.5, 109.6, 38.5. HRMS (ESI-TOF) *m/z* calculated for $C_{18}H_{16}N_2$ $[M+H]^+$: 261.1386, found: 261.1389.

***N*-methyl-*N*-(*p*-tolyl)pyridin-2-amine (4f).** Isolated as pale-yellow oil using petroleum ether/dichloromethane (1:5) as eluent (34.9 mg, yield 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20-8.14 (m, 1H), 7.29-7.23 (m, 1H), 7.21-7.16 (m, 2H), 7.15-7.08 (m, 2H), 6.59-6.52 (m, 1H), 6.48-6.42 (m, 1H), 3.43 (s, 3H), 2.35 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.8, 147.4, 144.1, 136.7, 135.5, 130.4, 126.5, 112.7, 109.0, 38.6, 21.0. HRMS (ESI-TOF) *m/z* calculated for $C_{13}H_{14}N_2$ $[M+H]^+$:199.1230, found: 199.1238.

***N*-methyl-*N*-(*m*-tolyl)pyridin-2-amine (4g).** Isolated as pale-yellow oil using petroleum ether/dichloromethane (1:5) as eluent (37.3 mg, yield 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20-8.16 (m, 1H), 7.29-7.22 (m, 2H), 7.06-6.99 (m, 3H), 6.58-6.54 (m, 1H), 6.48 (d, *J* = 8.4 Hz, 1H), 3.43 (s, 3H), 2.33 (s, 3H).^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.9, 147.7, 146.8, 139.7, 136.5, 129.5, 127.0, 126.3, 123.4, 112.9, 109.2, 38.4, 21.4. HRMS (ESI-TOF) *m/z* calculated for $C_{13}H_{14}N_2$ $[M+H]^+$: 199.1230, found: 199.1232.

***N*-methyl-*N*-(*o*-tolyl)pyridin-2-amine (4h).** Prepared by general procedure B at 80°C, isolated as yellow oil using petroleum ether/dichloromethane (1:1) as eluent (20.6 mg, yield 52%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23-8.18 (m, 1H), 7.33-7.22 (m, 4H), 7.20-7.15 (m, 1H), 6.58-6.53 (m, 1H), 6.05 (d, *J* = 8.8 Hz, 1H), 3.40 (s, 3H), 2.15 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.4, 147.5, 144.7, 136.9, 136.8, 131.5, 128.6, 127.7, 127.3, 112.1, 107.9, 37.4, 17.7. HRMS (ESI-TOF) *m/z* calculated for $C_{13}H_{14}N_2$ $[M+H]^+$: 199.1230, found: 199.1237.

***N*-(4-methoxyphenyl)-*N*-methylpyridin-2-amine (4i).** Isolated as a pale-yellow oil using petroleum ether/diethyl ether (100:1) as eluent (22.3 mg, yield 52%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15-8.09 (m, 1H), 7.24-7.16 (m, 1H), 7.13-7.05 (m, 2H), 6.91-6.82 (m, 2H), 6.53-6.45 (m, 1H), 6.30 (d, *J* = 8.8 Hz, 1H), 3.75 (s, 3H), 3.35 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.3, 157.8, 147.7, 139.8, 136.7, 128.4, 115.2, 112.6, 108.7, 55.6, 38.8. HRMS (ESI-TOF) *m/z* calculated for $C_{13}H_{14}N_2O$ $[M+H]^+$: 215.1179, found: 215.1187.

***N*^{1},*N*^{1},*N*^{4}-trimethyl-*N*^{4}-(pyridin-2-yl)benzene-1,4-diamine (4j).** Isolated as a white solid using petroleum ether/diethyl ether (50:1) as eluent (20.5 mg, yield 45%, mp 91–92 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23-8.15 (m, 1H), 7.28-7.22 (m, 1H), 7.15-7.07 (m, 2H), 6.80-6.73 (m, 2H), 6.56-6.49 (m, 1H), 6.37 (d, *J* = 8.8 Hz, 1H), 3.42 (s, 3H),_2.98(s, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.5, 149.1, 147.4, 136.6, 135.9, 128.1, 113.7, 112.1, 108.8, 40.9, 38.9. HRMS (ESI-TOF) *m/z* calculated for $C_{14}H_{17}N_3$ $[M+H]^+$: 228.1495, found: 228.1496.

***N*-(4-fluorophenyl)-*N*-methylpyridin-2-amine (4k).** Isolated as pale-yellow oil using petroleum ether/dichloromethane (1:5) as eluent (38.0 mg, yield 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27-8.17 (m, 1H), 7.34-7.29 (m, 1H), 7.25-7.19 (m, 2H), 7.13-7.06 (m, 2H), 6.64-6.58 (m, 1H), 6.42 (d, *J* = 8.4 Hz, 1H), 3.44 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.37. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.4 (d, *J* = 246.0 Hz), 158.9, 147.8, 142.9 (d, *J* = 3.1 Hz), 136.7, 128.4 (d, *J* = 8.4 Hz), 116.6 (d, *J* = 22.6 Hz), 113.1, 108.6, 38.6. HRMS (ESI-TOF) *m/z* calculated for $C_{12}H_{11}FN_2$ $[M+H]^+$: 203.0979, found: 203.0980.

***N*-methyl-*N*-(4-(trifluoromethyl)phenyl)pyridin-2-amine (4l).** Isolated as a pale-yellow oil using petroleum ether/diethyl ether (100:1) as eluent (29.8 mg, yield 59%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32-8.25 (m, 1H), 7.65-7.55 (m, 2H), 7.49-7.39 (m, 1H), 7.37-7.30 (m, 2H), 6.79 (d, *J* = 8.4 Hz, 1H), 6.77-6.73 (m, 1H), 3.52 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.09. ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 158.2, 150.1, 148.3, 137.3, 126.7 (q, *J* = 3.5 Hz), 125.8 (q, *J* = 32.7 Hz), 124.4 (q, *J* = 271.4 Hz), 123.9, 115.3, 111.0, 38.3. HRMS (ESI-TOF) *m/z* calculated for $C_{13}H_{11}F_3N_2$ $[M+H]^+$: 253.0947, found: 253.0951.

4-(methyl(pyridin-2-yl)amino)benzonitrile (4m). Isolated as a pale-yellow oil using petroleum ether/diethyl ether (15:1) as eluent (34.3 mg, yield 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36-8.28 (m, 1H), 7.59-7.56 (m, 1H), 7.56-7.50 (m, 2H), 7.26-7.21 (m, 2H), 6.95 (d, *J* = 8.4 Hz, 1H), 6.90-6.82 (m, 1H), 3.52 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.8, 150.8, 148.6, 137.6, 133.4, 121.4, 119.4, 117.1, 113.3, 104.9, 38.0. HRMS (ESI-TOF) *m/z* calculated for $C_{13}H_{11}N_3$ $[M+H]^+$: 210.1026, found: 210.1032.

***N*-methyl-*N*-phenyl-5-(trifluoromethyl)pyridin-2-amine (4n).** Isolated as a pale-yellow oil using petroleum ether/diethyl ether (100:1) as eluent (25.2 mg, yield 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49-8.38 (m, 1H), 7.46-7.39 (m, 3H), 7.31-7.26 (m, 1H), 7.26-7.21 (m, 2H), 6.43 (d, *J* = 8.8 Hz, 1H), 3.49 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -61.19. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.4, 145.70, 145.68 (q, *J* = 3.9 Hz), 133.6 (q, *J* = 3.1 Hz), 130.2, 127.0, 126.9, 124.8 (q, *J* = 271.2 Hz), 115.5 (q, *J* = 33.0 Hz), 107.9, 38.8. HRMS (ESI-TOF) *m/z* calculated for $C_{13}H_{11}F_3N_2$ $[M+H]^+$: 253.0947, found: 253.0950.

***N*-([1,1'-biphenyl]-4-yl)-*N*,3-dimethylpyridin-2-amine (4o).** Isolated as a pale-yellow oil using petroleum ether/diethyl ether (50:1) as eluent (30.7 mg, yield 56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.59-7.52 (m, 2H), 7.51-7.45 (m, 3H), 7.43-7.35 (m, 2H), 7.31-7.26 (m, 1H), 7.02 (dd, *J* = 7.6, 4.8 Hz, 1H), 6.84-6.76 (m, 2H), 3.46 (s, 3H), 2.02 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.5, 148.1, 146.7, 141.0, 139.9, 133.2, 128.8, 128.3, 127.8, 126.64, 126.61, 119.8, 118.2, 39.6, 18.8. HRMS (ESI-TOF) *m/z* calculated for $C_{19}H_{18}N_2$ $[M+H]^+$: 275.1543, found: 275.1541.

***N*-methyl-*N*-phenylisoquinolin-3-amine (4p).** Isolated as a pale-yellow oil using petroleum ether/diethyl ether (50:1) as eluent (35.1 mg, yield 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.41-7.36 (m, 2H), 7.36-7.30 (m, 2H), 7.27-7.21 (m, 2H), 7.19-7.14 (m, 1H), 7.14-7.07 (m, 1H), 6.75 (s, 1H), 3.50 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 155.9, 151.3, 147.7, 138.6, 130.3, 129.7, 127.7, 125.3, 125.2, 124.6, 123.8, 123.4, 101.6, 38.9. HRMS (ESI-TOF) *m/z* calculated for $C_{16}H_{14}N_2$ $[M+H]^+$: 235.1230, found: 235.1238.

***N*,*N*-diphenylpyridin-2-amine (6a).** Isolated as pale-yellow solid using petroleum ether/ethyl acetate (30:1) as eluent (44.3 mg,

yield 90%, mp 94–95 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26-8.22 (m, 1H), 7.48-7.41 (m, 1H), 7.36-7.29 (m, 4H), 7.23-7.17 (m, 4H), 7.16-7.12 (m, 2H), 6.82-6.74 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.0, 148.3, 146.1, 137.3, 129.4, 126.3, 124.5, 116.1, 113.9. HRMS (ESI-TOF) *m/z* calculated for $C_{17}H_{14}N_2$ $[M+H]^+$: 247.1230, found: 247.1235.

***N*-([1,1'-biphenyl]-4-yl)-*N*-phenylpyridin-2-amine (6b).** Isolated as white solid using petroleum ether/ethyl acetate (50:1) as eluent (63.7 mg, yield 99%, mp 106–108 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28-8.26 (m, 1H), 7.63-7.52 (m, 4H), 7.51-7.40 (m, 3H), 7.39-7.29 (m, 3H), 7.27-7.22 (m, 4H), 7.20-7.14 (m, 1H), 6.83-6.75 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.9, 148.3, 146.0, 145.4, 140.7, 137.4, 137.1, 129.5, 128.7, 128.0, 127.0, 126.9, 126.5, 126.1, 124.8, 116.3, 114.1. HRMS (ESI-TOF) *m/z* calculated for $C_{23}H_{18}N_2$ $[M+H]^+$: 323.1543, found: 323.1543.

***N*-phenyl-*N*-(*p*-tolyl)pyridin-2-amine (6c).** Isolated as pale-yellow oil using petroleum ether/ethyl acetate (20:1) as eluent (51.5 mg, yield 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25-8.21 (m, 1H), 7.46-7.39 (m, 1H), 7.35-7.28 (m, 2H), 7.23-7.18 (m, 2H), 7.18-7.08 (m, 5H), 6.81-6.71 (m, 2H), 2.36 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.1, 148.2, 146.2, 143.5, 137.3, 134.5, 130.2, 129.3, 126.7, 126.0, 124.3, 115.8, 113.4, 21.0. HRMS (ESI-TOF) *m/z* calculated for $C_{18}H_{16}N_2$ $[M+H]^+$: 261.1386, found: 261.1384.

***N*-(4-fluorophenyl)-*N*-phenylpyridin-2-amine (6d).** Isolated as white syrup liquid using petroleum ether/ethyl acetate (20:1) as eluent (47.9 mg, yield 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23-8.20 (m, 1H), 7.47-7.41 (m, 1H), 7.36-7.29 (m, 2H), 7.21-7.10 (m, 5H), 7.07-6.99 (m, 2H), 6.81-6.75 (m, 1H), 6.71 (d, *J* = 8.4 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.72. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.8 (d, *J* = 245.3 Hz), 158.9, 148.2, 145.9, 142.0 (d, *J* = 3.1 Hz), 137.4, 129.5, 128.2 (d, *J* = 8.3 Hz), 126.1, 124.7, 116.3, 116.1 (d, *J* = 7.6 Hz), 113.2. HRMS (ESI-TOF) *m/z* calculated for $C_{17}H_{13}FN_2$ $[M+H]^+$: 265.1136, found: 265.1137.

***N*-phenyl-*N*-(4-(trifluoromethyl)phenyl)pyridin-2-amine (6e).** Prepared by general procedure B at 100°C, isolated as yellow syrup liquid using petroleum ether/dichloromethane (3:1) as eluent (24.0 mg, yield 39%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33-8.24 (m, 1H), 7.55-7.47 (m, 3H), 7.41-7.35 (m, 2H), 7.25-7.16 (m, 5H), 6.91-6.86 (m, 1H), 6.80 (d, *J* = 8.4 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.00. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.5, 149.2, 148.4, 145.4, 137.7, 129.9, 127.1, 126.2 (q, *J* = 3.8 Hz), 125.7, 124.9 (q, *J* = 32.7 Hz), 124.3 (q, *J* = 272.4 Hz), 124.1, 117.5, 115.2. HRMS (ESI-TOF) *m/z* calculated for $C_{18}H_{13}F_3N_2$ $[M+H]^+$: 315.1104, found: 315.1106.

***N*-(*p*-tolyl)-*N*-(4-(trifluoromethyl)phenyl)pyridin-2-amine (6f).** Prepared by general procedure B at 80°C, isolated as yellow oil using petroleum ether/dichloromethane (3:1) as eluent (25.4 mg, yield 39%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30-8.22 (m, 1H), 7.54-7.44 (m, 3H), 7.24-7.15 (m, 4H), 7.11-7.05 (m, 2H), 6.90-6.83 (m, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 2.37 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -61.95. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.5, 149.2, 148.2, 142.7, 137.7, 135.8, 130.6, 127.3, 126.1 (q, *J* = 3.8 Hz), 124.7 (q, *J* = 32.6 Hz), 124.3 (q, *J* = 272.5 Hz), 123.8, 117.2, 114.9, 21.0. HRMS (ESI-TOF) *m/z* calculated for $C_{19}H_{15}F_3N_2$ $[M+H]^+$: 329.1260, found: 329.1260.

3-methyl-*N*,*N*-diphenylpyridin-2-amine (6g). Isolated as a pale-yellow oil using petroleum ether/diethyl ether (10:1) as eluent (25.0 mg, yield 48%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25-8.20 (m, 1H), 7.46-7.40 (m, 1H), 7.21-7.10 (m, 4H), 6.97 (dd, *J* = 7.2, 4.8 Hz, 1H), 6.95-6.83 (m, 6H), 1.89 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.8, 147.3, 146.9, 140.6, 129.7, 129.3, 123.0, 122.7, 120.8, 18.6. HRMS (ESI-TOF) *m/z* calculated for $C_{18}H_{16}N_2$ $[M+H]^+$: 261.1386, found: 261.1387.

4-methyl-*N*,*N*-diphenylpyridin-2-amine (6h). Isolated as white solid using petroleum ether/ethyl acetate (30:1) as eluent (19.6 mg, yield 38%, mp 85–87 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 4.8 Hz, 1H), 7.36-7.28 (m, 4H), 7.20-7.08 (m, 6H), 6.63 (d, *J* = 4.8 Hz, 1H), 6.59 (s, 1H), 2.20 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.2, 148.5, 147.9, 146.3, 129.3, 126.3, 124.4, 117.8, 114.5, 21.1. HRMS (ESI-TOF) *m/z* calculated for $C_{18}H_{16}N_2$ $[M+H]^+$: 261.1386, found: 261.1389.

5-methyl-*N*,*N*-diphenylpyridin-2-amine (6i). Isolated as pale-yellow solid using petroleum ether/ethyl acetate (10:1) as eluent (35.4 mg, yield 68%, mp 71–73 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11-8.06 (m, 1H), 7.34-7.27 (m, 5H), 7.18-7.12 (m, 4H), 7.12-7.07 (m, 2H), 6.73 (d, *J* = 8.4 Hz, 1H), 2.25 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.1, 148.2, 146.4, 138.3, 129.3, 125.8, 125.7, 124.0, 114.6, 17.6. HRMS (ESI-TOF) *m/z* calculated for $C_{18}H_{16}N_2$ $[M+H]^+$: 261.1386, found: 261.1386.

6-methyl-*N*,*N*-diphenylpyridin-2-amine (6j). Isolated as white syrup liquid using petroleum ether/ethyl acetate (50:1) as eluent (48.3 mg, yield 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 1.6 Hz, 1H), 7.32-7.26 (m, 4H), 7.21-7.14 (m, 4H), 7.13-7.06 (m, 2H), 6.67 (d, *J* = 7.6 Hz, 1H), 6.51 (d, *J* = 8.4 Hz, 1H), 2.39 (s, 3H).^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.5, 157.2, 146.3, 137.6, 129.1, 126.0, 124.0, 115.9, 111.5, 24.4. HRMS (ESI-TOF) *m/z* calculated for $C_{18}H_{16}N_2$ $[M+H]^+$: 261.1386, found: 261.1390.

Gram Scale of the Desulfitative Cross-Coupling Reaction

Gram-scale synthesis of compound 2a: In the glovebox, 4-(pyridin-2-ylsulfonyl)morpholine (4.5 mmol, 1.03 g), $Ni(COD)_2$ (10 mol%, 123.8 mg), IPr • HCl (20 mol%, 382.5 mg), BPh_3 (20 mol%, 217.9 mg), and NaO*t*Bu (2.0 equiv, 865.0 mg) were added into an oven-dried 75 mL screw cap Teflon-sealed tube with a magnetic stirring bar, followed by addition of xylenes (22.5 mL). The tube was closed and removed out of the glovebox and heated to 60 °C in heating block. After 16 h, the tube was cooled to room temperature. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography to give the desired product **2a**. Isolated as yellow oil using petroleum ether/ ethyl acetate (15:1) as eluent (528 mg, yield 72%).

Gram-scale synthesis of compound 4a: In the glovebox, *N*-methyl-*N*-phenylpyridine-2-sulfonamide (4.5 mmol, 1.12 g), $Ni(COD)_2$ (10 mol%, 123.8 mg), dcypt (12 mol%, 257.2 mg), BPh_3 (20 mol%, 217.9 mg), and NaO*t*Bu (1.5 equiv, 648.7 mg) were added into an oven-dried 75 mL screw cap Teflon-sealed tube with a magnetic stirring bar, followed by addition of xylenes (22.5 mL). The tube was closed and removed out of the glovebox and heated to 60 °C in heating block. After 16 h, the tube was cooled to room temperature. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography to give the desired product **4a**. Isolated as yellow oil using petroleum ether/ dichloromethane (1:5) as eluent (730 mg, yield 88%).

Gram-scale synthesis of compound 6a: In the glovebox, *N*,*N*-diphenylpyridine-2-sulfonamide (3.5 mmol, 1.09 g), $Ni(COD)_2$ (10 mol%, 96.3 mg), dcypt (12 mol%, 200.2 mg), BPh_3 (20 mol%, 169.5 mg), and NaO*t*Bu (1.5 equiv, 504.5 mg) were added into an oven-dried 75 mL screw cap Teflon-sealed tube with a magnetic stirring bar, followed by addition of xylenes (17.5 mL). The tube was closed and removed out of the glovebox and heated to 60 °C in heating block. After 16 h, the tube was cooled to room temperature. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography to give the desired product **6a**. Isolated as pale yellow solid using petroleum ether/ ethyl acetate (30:1) as eluent (776 mg, yield 90%).

Synthesis of compound 8: In the glovebox, *N*-benzyl-*N*-(2-(dimethylamino)ethyl)pyridine-2-sulfonamide (0.2 mmol), $Ni(COD)_2$ (10 mol%, 5.5 mg), IPr·HCl (20 mol%, 17.0 mg), BPh_3

(20 mol %, 9.7 mg), and NaO*t*Bu (2.0 equiv, 38.5 mg) were added into an oven-dried 4 mL vial with a magnetic stirring bar, followed by addition of xylenes (1.0 mL). The vial was sealed and removed out of the glovebox and heated to 60 °C in heating block. After 16 h, the vial was cooled to room temperature. The mixture was concentrated *in vacuo* and the residue was purified by flash column chromatography to give the desired product N^1-benzyl-N^2,N^2-dimethyl-N^1-(pyridin-2-yl)ethane-1,2-diamine **8**. Isolated as yellow oil using methanol/dichloromethane/triethylamine (20:1:0.1) as eluent (25.0 mg, yield 49%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20-8.10 (m, 1H), 7.40-7.36 (m, 1H), 7.33-7.27 (m, 2H), 7.25-7.19 (m, 3H), 6.56-6.51 (m, 1H), 6.45 (d, J = 8.8 Hz, 1H), 4.77 (s, 2H), 3.67 (t, J = 7.6 Hz, 2H), 2.52 (t, J = 7.6 Hz, 2H), 2.27 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.1, 148.1, 138.8, 137.2, 128.5, 127.0, 126.9, 111.9, 105.8, 56.7, 52.0, 46.6, 45.7. HRMS (ESI-TOF) *m/z* calculated for $C_{16}H_{21}N_3$ [M+H]$^+$: 256.1808, found: 256.1807.

Procedure of Cross-over Experiment between 3f and 3o.

In the glovebox, compound **3f** (0.1 mmol), **3o** (0.1 mmol), $Ni(COD)_2$ (10 mol%, 5.5 mg), dcypt (12 mol%, 11.5 mg), BPh_3 (20 mol %, 9.7 mg), and NaO*t*Bu (1.5 equiv, 28.8 mg) were added into an oven-dried 4 ml vial with a magnetic stirring bar, followed by addition of xylenes (1.0 mL). The vial was sealed and removed out of the glovebox and heated to 60 °C in heating block for 16 h. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad with EtOAc. The compounds and the yields were detected by GC-MS and GC.

ASSOCIATED CONTENT

Supporting Information

^{1}H, ^{13}C, ^{19}F NMR spectra of compounds found in the Supporting Information. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

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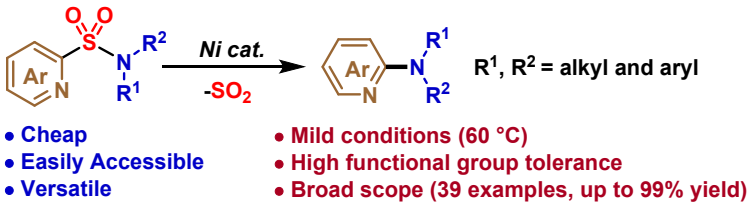
Ni cat.
-SO2
Ar
N
R1, R2 = alkyl and aryl
• Cheap
• Easily Accessible
• Versatile
• Mild conditions (60 °C)
• High functional group tolerance
• Broad scope (39 examples, up to 99% yield)