Synthesis J. H. Pang et al. Special Topic

Leaving Group Ability in Nucleophilic Aromatic Amination by Sodium Hydride–Lithium Iodide Composite

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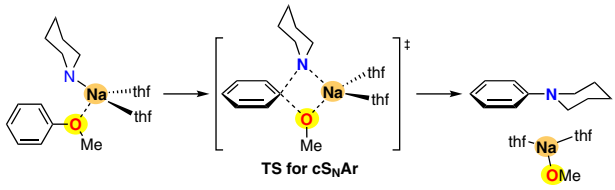
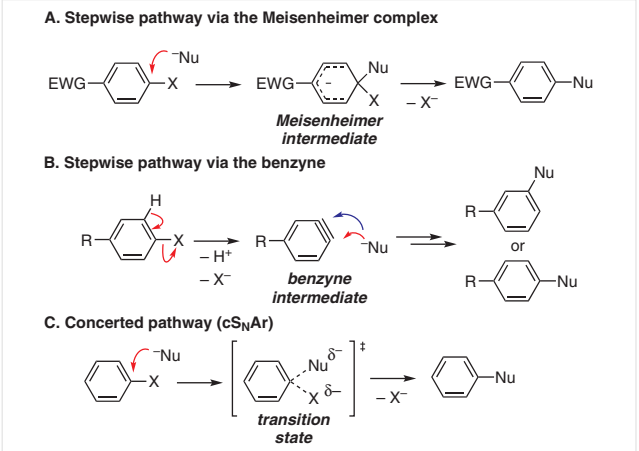
Abstract The methoxy group is generally considered as a poor leaving group for nucleophilic substitution reactions. This work verified the superior ability of the methoxy group in nucleophilic amination of arenes mediated by the sodium hydride and lithium iodide through experimental and computational approaches.

Key words nucleophilic amination, concerted aromatic substitution, methoxy group, sodium hydride, DFT calculations

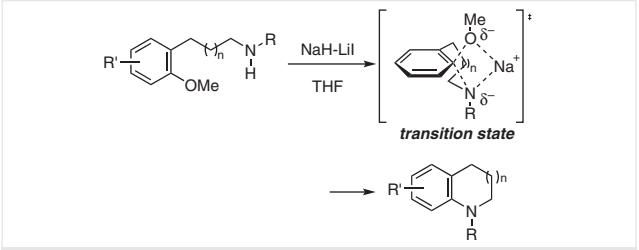
The nucleophilic substitution reaction is a central subject in chemical synthesis, enabling construction of carbon–carbon and carbon–heteroatom bonds from various sets of nucleophiles and electrophiles.[1] The choice of leaving group on the electrophile is one of the important factors to ensure the nucleophilic substitution reaction occurs in a highly efficient and selective manner at the same time preventing undesired side reactions, such as elimination reactions.

In nucleophilic aromatic substitution (S_NAr) reactions,[2] where an sp^2 hybridized aromatic carbon with leaving group (X) is substituted by a nucleophile (Nu), several mechanistic scenarios can be conceived: two-step pathways through a Meisenheimer complex (Scheme 1A) or a benzyne (Scheme 1B) as the reaction intermediate are commonly accepted reaction mechanisms, whereas a concerted process (cS_NAr) has been considered as a rare case (Scheme 1C).[3–6] Recently, Jacobsen and co-workers revealed through experimental and computational studies that the ability of the leaving group greatly affects the reaction course of nucleophilic aromatic substitution reactions, implying that there might be more cases of cS_NAr than expected.[7,8] Our group has also recently developed the intra- and intermolecular nucleophilic amination of methoxy(hetero)arenes by NaH in the presence of LiI in THF (Scheme 2), where a methoxy group, which is generally considered as a poor leaving group, is substituted with sodium (lithium) amide nucleophile presumably under the cS_NAr mechanism.[9–11] This work verified the superior ability of the methoxy group to other conventional leaving groups in intermolecular nucleophilic aromatic amination through experimental and computational approaches. The leaving group ability of the aryloxy groups was also investigated.





Scheme 1 Nucleophilic aromatic substitution reactions



Scheme 2 Nucleophilic amination of methoxyarenes by NaH–LiI

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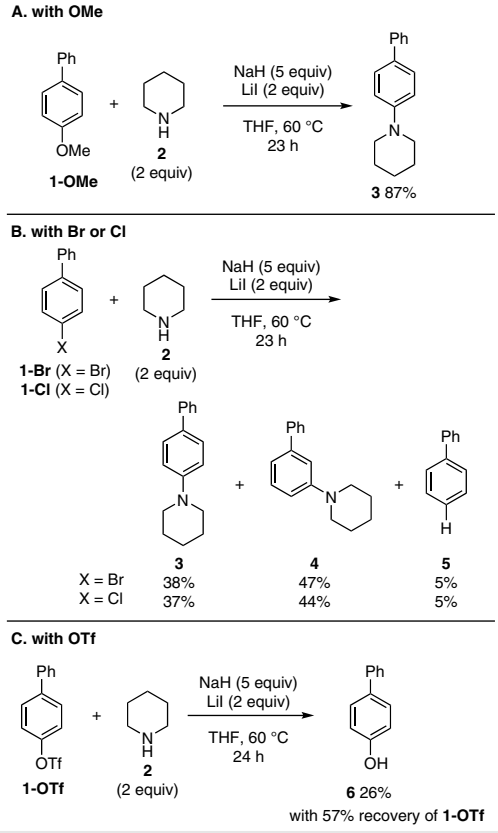
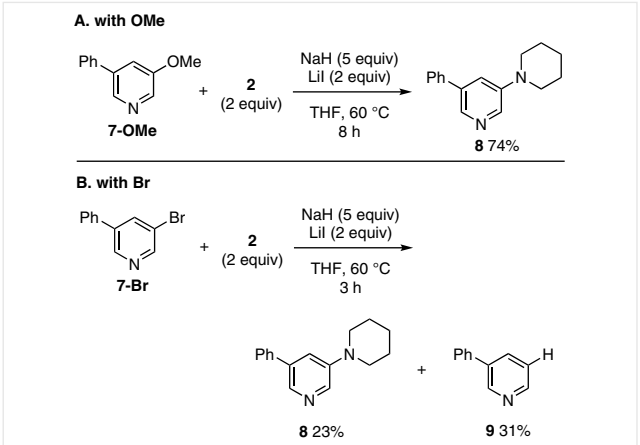
We commenced our investigation with reactivity comparison between methoxy- and (pseudo)haloarenes (Scheme 3). For this purpose, we utilized substrates **1** based on a biphenyl motif. The reaction of 4-methoxybiphenyl (**1-OMe**) with 2 equiv of piperidine (**2**) in the presence of NaH (5 equiv) and LiI (2 equiv) in THF at 60 °C gave aminated product **3** in 87% yield as the sole product (Scheme 3A). On the other hand, a mixture of *para*-aminated **3** and *meta*-aminated **4** was formed from bromide **1-Br** and chloride **1-Cl** through a transient benzyne intermediate (Scheme 3B).[12] We also isolated a small amount of biphenyl (**5**) that should be formed via hydrodehalogenation by the NaH–LiI system.[13] The reaction of triflate **1-OTf** gave only phenol **6** through acyl substitution (Scheme 3C).



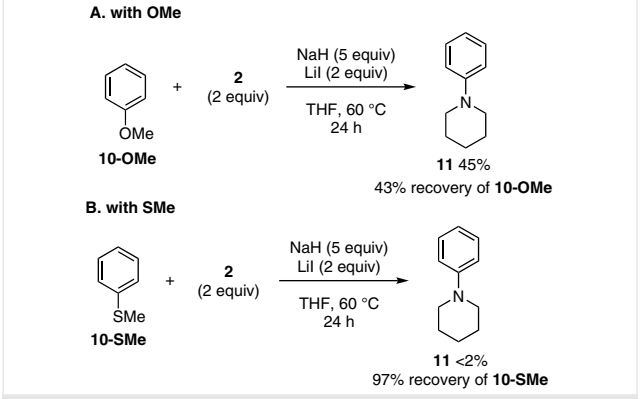
Scheme 3 Methoxyarenes vs (pseudo)haloarenes

The ability of the leaving group in the installation of the amine functionality onto the pyridine scaffold was also tested using substrates **7**. Methoxypyridine **7-OMe** was aminated to afford **8** as the sole product in 74% yield (Scheme 4A). On the other hand, the reaction of 3-bromopyridine **7-Br** afforded amine **8** in only 23% yield along with the formation of hydrodebrominated product **9** in 31% yield (Scheme 4B).



Scheme 4 Methoxypyridine vs bromopyridine

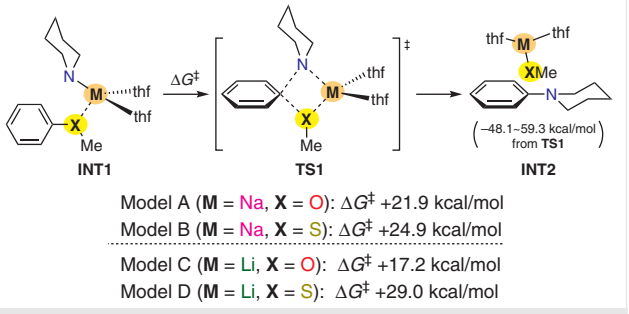
Tobisu and co-workers recently reported a method for construction of dibenzothiophenes via concerted intramolecular nucleophilic aromatic substitution of thioanisoles by a benzothiolate anion.[14] This stimulated us to investigate reactivity difference between anisole (**10-OMe**) and thioanisole (**10-SMe**) toward the intermolecular nucleophilic amination (Scheme 5). We found an obvious reactivity difference: almost no aminated product **11** was formed from the reaction with thioanisole (**10-SMe**) under the present reaction conditions (Scheme 5B).



Scheme 5 Anisole vs thioanisole

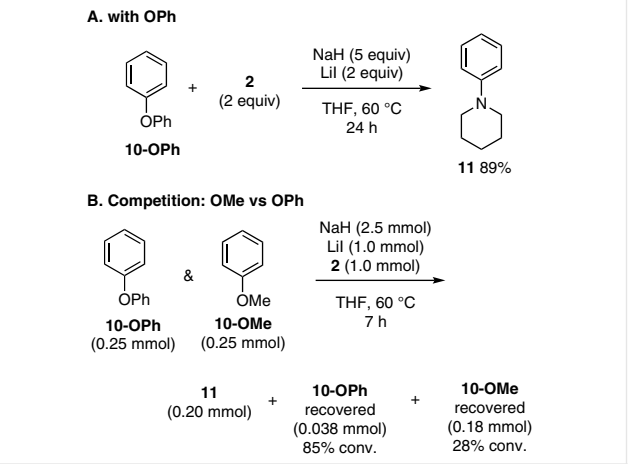
DFT calculations were performed at the B3LYP/6-31+G* (scrf = pcm, THF) level of theory to gain insight into the observed reactivity difference between anisole (**10-OMe**) and thioanisole (**10-SMe**) (Scheme 6).[15] When Na piperidide, which should be generated under the present reaction conditions, promoted the reaction, structurally similar transition state structures were obtained with both **10-OMe** and **10-SMe** (model A and B). However, the activation barrier ($\Delta G^{\ddagger}$) in model A was reasonably lower than that in model B (+21.9 vs +24.9 kcal/mol), which is consistent with the experimental results in Scheme 5. In addition, the reactions promoted by Li piperidide species were also investigated; a

low activation energy (+17.2 kcal/mol) was obtained with **10-OMe** in model C, while very high energy was necessary for the reaction with **10-SMe**. In both of the cases, the countercation (sodium or lithium) and the sulfur atom in TS1 seems to have a weak interaction (cf. Na–O length: 2.34 Å in model A and Na–S length: 2.95 Å in model B; Li–O length: 1.95 Å in model C and Li–S length: 3.01 Å in model D; see the Supporting Information), probably making it difficult to build up the organized 4-membered transition state. Although it is not certain as to which countercation (either Na or Li) plays a dominant role in the present process, the reaction with **10-OMe** should proceed much faster in both cases. It should be also noted that all model reactions were found to proceed in a concerted fashion.



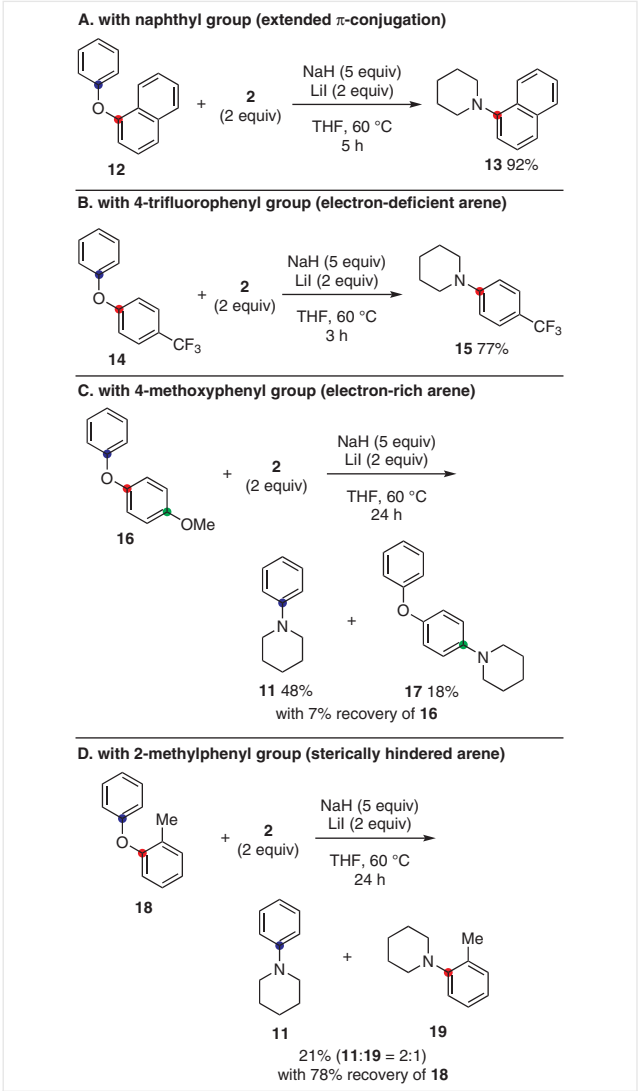
Scheme 6 DFT calculations for the model reactions of **10-OMe** or **10-SMe** with Na or Li piperidide at the B3LYP/6-31+G* (scrf = pcm, THF) level of theory

The reaction of diphenyl ether (**10-OPh**) proceeded smoothly to give **11** in 89% yield (Scheme 7A). The higher leaving group ability of the phenoxy group could be ascertained by a competitive reaction between **10-OPh** and **10-OMe** (Scheme 7B).



Scheme 7 Nucleophilic aromatic substitution of diphenyl ether (**10-OPh**) and anisole (**10-OMe**)

These findings intrigued us to investigate electronic and steric factors for the nucleophilic amination of unsymmetrical biaryl ethers (Scheme 8). The reaction of 1-phenoxynaphthalene (**12**) gave 1-(1-naphthyl)piperidine (**13**) in 92% yield as a single product, suggesting that the naphthyl carbon (marked in red), which has lower LUMO due to longer π-conjugation, is preferred for nucleophilic attack (Scheme 8A). Similarly, in the case of 1-phenoxy-4-(trifluoromethyl)benzene (**14**), the more electron-deficient red carbon was aminated to form solely 1-[4-(trifluoromethyl)phenyl]piperidine (**15**) (Scheme 8B). On the other hand, 1-methoxy-4-phenoxybenzene (**16**) possesses three different C(sp^2)–O bonds (Scheme 8C). From the reaction of **16**, formation of amines **11** and **17** was observed, suggesting that the process evades the seemingly most electron-rich sp^2 carbon marked in red for nucleophilic substitution. The



Scheme 8 Nucleophilic aromatic substitution of diaryl ethers

nucleophilic amination of biaryl ethers was found to be very sensitive to steric factors (Scheme 8D): installation of an *ortho*-methyl group (in substrate **18**) made the reaction progress sluggish, resulting in incomplete conversion to afford a mixture of **11** and **19** in 2:1 ratio in only 21% total yield even after stirring for 24 h.

To summarize, this work validated that the methoxy group, which is commonly considered as a poor leaving group, is most superior for nucleophilic aromatic substitution reactions under the NaH–LiI system from the point of view of reaction efficiency and atom economy. Although the aryoxy group generally possesses a better leaving group ability than methoxy, the regioselectivity of the amination of unsymmetrical biaryl ethers is heavily affected by electronic and steric factors.

All experiments were carried out under a N_2 atmosphere with anhydrous solvents. THF was taken from a solvent purification system (PS-400-5, innovative technology Inc.). NaH (60% dispersion in mineral oil), LiI were purchased from Sigma-Aldrich, Inc. LiI was dried over P_2O_5 under reduced pressure at 120 °C. Due to the moisture sensitivity of NaH, it was consistently handled under an argon atmosphere in a glovebox or with Schlenk techniques under a N_2 atmosphere. The arene substrates **1-Br**,[16] **1-Cl**,[17] **1-OTf**,[18] **7-Br**,[19] **12**,[20] **14**,[21] **16**,[22] and **18**[23] were prepared using the reported methods. The substrates **1-OMe**, **7-OMe**, **10-OMe**, **10-SMe**, and **10-OPh** were commercially available and used as received. TLC analyses were performed on silica gel glass plates (Merck silica gel 60), and the spots were visualized with UV light (254 and 365 nm). Flash chromatography was performed using Merck silica gel 60 with distilled solvents. Shimadzu GC-2010 was used for the GC analyses. ^{1}H NMR spectra (400 MHz) were recorded on a Bruker Avance 400 spectrometer in $CDCl_3$ [using TMS (for ^{1}H, δ = 0.00) as internal standard]. ^{13}C NMR spectra (100 MHz) were recorded on a Bruker Avance 400 spectrometer in $CDCl_3$ [using $CDCl_3$ (for ^{13}C, δ = 77.00) as internal standard].

Piperidin-1-ylarenes; General Procedure

To a mixture of NaH (60% dispersion, 100 mg, 2.50 mmol) and LiI (134 mg, 1.00 mmol) in a 25-mL sealed tube was added a solution of arene substrate (0.50 mmol) in THF (0.5 mL) and piperidine (85.2 mg, 99 µL, 1.00 mmol). The reaction was stirred at 60 °C (the reaction time is indicated in the respective scheme) and was quenched with water at 0 °C. The organic materials were extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were washed brine and dried ($MgSO_4$). The volatile materials were removed in vacuo and the resulting crude residue was purified by flash column chromatography (the eluent system is indicated for each substrate) to give the product.

1-(Biphenyl-4-yl)piperidine (3)[9a]

Scheme 3A: reaction time: 23 h; eluent system: 2% EtOAc/hexane; white solid; yield: 103 mg (0.434 mmol, 87%); mp 124–126 °C. The spectroscopic data for **3** are identical to those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56 (d, *J* = 8.2 Hz, 2 H), 7.50 (d, *J* = 8.8 Hz, 2 H), 7.39 (dd, *J* = 8.2, 8.2 Hz, 2 H), 7.26 (t, *J* = 8.2 Hz, 1 H), 6.99 (d, *J* = 8.8 Hz, 2 H), 3.21 (t, *J* = 5.5 Hz, 4 H), 1.75–1.69 (m, 4 H), 1.62–1.55 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.5, 141.1, 131.6, 128.7, 127.7, 126.5, 126.3, 116.4, 50.4, 25.8, 24.4.

1-(Biphenyl-4-yl)piperidine (3)[9a] and 1-(Biphenyl-3-yl)piperidine (4)[24]

Scheme 3B with **1-Br**: reaction time: 23 h; eluent system: 2% EtOAc/hexane; **3** and **4** were obtained as an inseparable mixture as a light brown solid; yield: 99.9 mg (0.421 mmol, 85%; **3**: 38%, **4**: 47%). The spectroscopic data for **3** and **4** are identical to those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59–7.54 (d, *J* = 8.2 Hz, 2 × 0.45 H + 2 × 0.55 H), 7.49 (d, *J* = 8.8 Hz, 2 × 0.45 H), 7.43–7.37 (dd, *J* = 8.2, 8.1 Hz, 2 × 0.45 H + m, 2 × 0.55 H), 7.34–7.24 (t, *J* = 8.2 Hz, 1 × 0.45 H + m, 2 × 0.55 H), 7.14 (t, *J* = 2.0 Hz, 1 × 0.55 H), 7.07 (d, *J* = 7.6 Hz, 1 × 0.55 H), 6.99 (d, *J* = 8.2 Hz, 2 × 0.45 H), 6.93 (dd, *J* = 8.5 Hz, 2.4 Hz, 1 × 0.55 H), 3.22–3.19 (t, *J* = 5.5 Hz, 4 × 0.45 H + t, *J* = 5.5 Hz, 4 × 0.55 H), 1.75–1.69 (m, 4 × 0.45 H + m, 4 × 0.55 H), 1.62–1.55 (m, 2 × 0.45 H + m, 2 × 0.55 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.7, 151.5, 142.2, 142.0, 141.1, 131.6, 129.4, 128.7, 128.6, 127.7, 127.2, 127.1, 126.5, 126.3, 118.3, 116.4, 115.6, 115.5, 50.8, 50.4, 25.9, 25.8, 24.4 (overlapped).

Biphenyl (**5**)[25] was formed in 5% yield based on ^{1}H NMR of the crude material using 1,2-dibromoethane as the internal standard. The spectroscopic data are identical to those reported in the literature.

1-(Biphenyl-4-yl)piperidine (3)[9a] and 1-(Biphenyl-3-yl)piperidine (4)[24]

Scheme 3B with **1-Cl**: reaction time: 23 h; eluent system: 2% EtOAc/hexane; **3** and **4** were obtained as an inseparable mixture as a light brown solid; yield: 97.0 mg (0.409 mmol, 81%; **3**: 37%, **4**: 44%). The spectroscopic data for **3** and **4** are identical to those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59–7.54 (d, *J* = 8.2 Hz, 2 × 0.45 H + 2 × 0.55 H), 7.49 (d, *J* = 8.8 Hz, 2 × 0.45 H), 7.43–7.37 (dd, *J* = 8.2, 8.1 Hz, 2 × 0.45 H + m, 2 × 0.55 H), 7.34–7.24 (t, *J* = 8.2 Hz, 1 × 0.45 H + m, 2 × 0.55 H), 7.14 (t, *J* = 2.0 Hz, 1 × 0.55 H), 7.07 (d, *J* = 7.6 Hz, 1 × 0.55 H), 6.99 (d, *J* = 8.2 Hz, 2 × 0.45 H), 6.93 (dd, *J* = 8.5 Hz, 2.4 Hz, 1 × 0.55 H), 3.22–3.19 (t, *J* = 5.5 Hz, 4 × 0.45 H + t, *J* = 5.5 Hz, 4 × 0.55 H), 1.75–1.69 (m, 4 × 0.45 H + m, 4 × 0.55 H), 1.62–1.55 (m, 2 × 0.45 H + m, 2 × 0.55 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.7, 151.5, 142.2, 142.0, 141.1, 131.6, 129.4, 128.7, 128.6, 127.7, 127.2, 127.1, 126.5, 126.3, 118.3, 116.4, 115.6, 115.5, 50.8, 50.4, 25.9, 25.8, 24.4 (overlapped).

Biphenyl (**5**)[25] was formed in 5% yield based on ^{1}H NMR of the crude material using 1,2-dibromoethane as the internal standard. The spectroscopic data are identical to those reported in the literature.

Biphenyl-4-ol (6)[26]

Scheme 3C: reaction time: 24 h; eluent system: 10% EtOAc/hexane; white solid; yield: 22.1 mg (0.130 mmol, 26%); mp 164–166 °C. The spectroscopic data for **6** are identical to those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 7.4 Hz, 2 H), 7.48 (d, *J* = 8.7 Hz, 2 H), 7.41 (dd, *J* = 7.4, 7.4 Hz, 2 H), 7.30 (t, *J* = 7.4 Hz, 1 H), 6.90 (d, *J* = 8.7 Hz, 2 H), 4.88 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.0, 140.7, 134.0, 128.7, 128.4, 126.7 (overlapped), 115.6.

3-Phenyl-5-(piperidin-1-yl)pyridine (8)[9b]

Scheme 4A: reaction time: 8 h; eluent system: 5% EtOAc/CH_2Cl_2; orange solid; yield: 88.2 mg (0.370 mmol, 74%); mp 73–75 °C. The spectroscopic data for **8** are identical to those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.29 (d, *J* = 2.6 Hz, 1 H), 8.28 (d, *J* = 2.0 Hz, 1 H), 7.57 (d, *J* = 7.4 Hz, 2 H), 7.46 (dd, *J* = 7.4, 7.4 Hz, 2 H), 7.38 (t, *J* = 7.4 Hz, 1 H), 7.34 (dd, *J* = 2.6, 2.0 Hz, 1 H), 3.26 (t, *J* = 5.4 Hz, 4 H), 1.77–1.70 (m, 4 H), 1.65–1.59 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.7, 138.6, 138.6, 137.6, 136.7, 128.9, 127.9, 127.3, 121.2, 49.9, 25.6, 24.1.

3-Phenyl-5-(piperidin-1-yl)pyridine (8)[9b]

Scheme 4B: reaction time: 3 h; yield: 27.1 mg (0.114 mmol, 23%).

3-Phenylpyridine (9)[27]

Scheme 4B: reaction time: 3 h; eluent system: 20% EtOAc/hexane; light yellow oil; yield: 23.7 mg (0.153 mmol, 31%). The spectroscopic data for **9** are identical to those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.85 (dd, *J* = 2.3, 0.8 Hz, 1 H), 8.59 (dd, *J* = 4.8, 1.7 Hz, 1 H), 7.86 (ddd, *J* = 7.9, 2.3, 1.7 Hz, 1 H), 7.59–7.56 (m, 2 H), 7.50–7.45 (m, 2 H), 7.42–7.38 (m, 1 H), 7.35 (ddd, *J* = 7.9, 4.8, 0.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.5, 148.3, 137.8, 136.6, 134.4, 129.1, 128.1, 127.2, 123.6.

1-Phenylpiperidine (11)[9a]

Scheme 5A: reaction time: 24 h; compound **11** was formed in 45% yield with recovery of **10-OMe** in 43% yield based on ^{1}H NMR of the crude material using 1,1,2,2-tetrachloroethane as the internal standard. The spectroscopic data are identical to those reported in the literature.

1-Phenylpiperidine (11)[9a]

Scheme 5B: reaction time: 24 h; compound **11** was formed in <2% yield with recovery of **10-SMe** in 97% yield based on ^{1}H NMR of the crude material using 1,1,2,2-tetrachloroethane as the internal standard. The spectroscopic data are identical to those reported in the literature.

1-Phenylpiperidine (11)[9a]

Scheme 7A: reaction time: 24 h; eluent system: 2% EtOAc/hexane; colorless oil; yield: 70.1 mg (0.435 mmol, 89%). The spectroscopic data for **11** are identical to those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24 (dd, *J* = 8.3, 7.3 Hz, 2 H), 6.94 (d, *J* = 8.3 Hz, 2 H), 6.82 (t, *J* = 7.3 Hz, 1 H), 3.15 (t, *J* = 5.4, 4 H), 1.74–1.68 (m, 4 H), 1.60–1.54 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.3, 129.0, 119.2, 116.6, 50.7, 25.9, 24.3.

1-Phenylpiperidine (11)[9a]

Scheme 7B: To a mixture of NaH (60% dispersion, 102 mg, 2.54 mmol) and LiI (135 mg, 1.01 mmol) in a 25-mL sealed tube was added a solution diphenyl ether (**10-OPh**; 42.6 mg, 0.250 mmol) and anisole (**10-OMe**; 27.2 mg, 0.252 mmol) in THF (0.5 mL), piperidine (85.2 mg, 98.8 μL, 1.00 mmol), and dodecane (84.8 mg, 0.498 mmol). The reaction was stirred at 60 °C for 7 h. A sample of the reaction mixture was taken to perform gas chromatography analyses to determine recovery of **10-OMe** (72% yield). The reaction was quenched with water at 0 °C. The organic materials were extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were washed with brine and dried ($MgSO_4$). The volatile materials were removed in vacuo and the resulting crude residue was purified by flash column chromatography (2% EtOAc/hexane) to give **11** (32.6 mg, 0.202 mmol) as a clear oil and **10-OPh** (6.2 mg, 0.037 mmol, 15%) as a clear oil. The spectroscopic data for **11** and **10-OPh** are identical to those reported in the literature.

1-(Naphthalen-1-yl)piperidine (13)[9a]

Scheme 8A: reaction time: 5 h; eluent system 2% EtOAc/hexane; colorless oil; yield: 94.8 mg (0.449 mmol, 92%). The spectroscopic data for **13** are identical to those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20–8.18 (m, 1 H), 7.80–7.78 (m, 1 H), 7.50 (d, *J* = 8.0 Hz, 1 H), 7.47–7.41 (m, 2 H), 7.37 (dd, *J* = 8.0, 7.6 Hz, 1 H), 7.03 (dd, *J* = 7.6, 0.9 Hz, 1 H), 3.03 (br s, 4 H), 1.83 (quint, *J* = 5.5 Hz, 4 H), 1.64 (br s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.1, 134.8, 129.2, 128.3, 125.9, 125.7, 125.2, 123.9, 123.0, 114.5, 54.7, 26.7, 24.7.

1-[4-(Trifluoromethyl)phenyl]piperidine (15)[28]

Scheme 8B: reaction time: 3 h; eluent system 4% Et_2O/pentane; colorless oil; yield: 88.5 mg (0.386 mmol, 77%). The spectroscopic data for **15** are identical to those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 8.7 Hz, 2 H), 6.91 (d, *J* = 8.7 Hz, 2 H), 3.27–3.25 (m, 4 H), 1.71–1.67 (m, 4 H), 1.63–1.61 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.8, 126.3 (q, *J* = 3.8 Hz), 124.9 (q, *J* = 270.4 Hz), 119.6 (q, *J* = 32.6 Hz), 114.6, 49.3, 25.4, 24.3.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –61.2.

1-Phenylpiperidine (11)[9a]

Scheme 8C: reaction time: 24 h; eluent system 2% EtOAc/hexane; colorless oil; yield: 38.4 mg (0.238 mmol, 48%). The spectroscopic data for **11** are identical to those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24 (dd, *J* = 8.3, 7.3 Hz, 2 H), 6.94 (d, *J* = 8.3 Hz, 2 H), 6.82 (t, *J* = 7.3 Hz, 1 H), 3.15 (t, *J* = 5.4, 4 H), 1.74–1.68 (m, 4 H), 1.60–1.54 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.3, 129.0, 119.2, 116.6, 50.7, 25.9, 24.3.

1-(4-Phenoxyphenyl)piperidine (17)[29]

Scheme 8C: reaction time: 24 h; eluent system 2% EtOAc/hexane; colorless oil; yield: 23.0 mg (0.091 mmol, 18%). The spectroscopic data for **17** are identical to those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (dd, *J* = 7.7 Hz, 2 H), 7.02 (t, *J* = 7.7 Hz, 1 H), 6.95–6.91 (m, 6 H), 3.10 (t, *J* = 5.4 Hz, 4 H), 1.75–1.70 (m, 4 H), 1.59–1.54 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.6, 149.4, 149.0, 129.5, 122.2, 120.4, 118.1, 117.5, 51.5, 26.0, 24.2.

1-Phenylpiperidine (11)[9a] **and 1-(*o*-Tolyl)piperidine (19)**[30]

Scheme 8D: reaction time 24 h; eluent system: 4% Et_2O/pentane; **11** and **19** were obtained as an inseparable mixture as a pale yellow oil; yield: 16.1 mg (0.106 mmol, 21%; **11**: 14% + **19**: 7%). The spectroscopic data for **11** and **19** are identical to those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24 (dd, *J* = 8.3, 7.3 Hz, 2 × 1 H), 7.17–7.12 (m, 2 × 0.5 H), 6.99 (d, *J* = 7.1 Hz, 1 × 0.5 H), 6.94 (d, *J* = 8.3 Hz, 2 × 1 H + dd, *J* = 7.1, 7.1 Hz, 1 × 0.5 H), 6.82 (t, *J* = 7.3 Hz, 1 × 1 H), 3.16–3.14 (m, 4 × 1 H), 2.84–2.82 (m, 4 × 0.5 H), 2.30 (s, 3 × 0.5 H), 1.73–1.68 (m, 4 × 1 H + m, 4 × 0.5 H), 1.60–1.55 (m, 2 × 1 H + m, 2 × 0.5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.9, 152.3, 132.6, 130.9, 129.0, 126.4, 122.5, 119.2, 118.9, 116.6, 53.3, 50.7, 26.6, 25.9, 24.4, 24.3, 17.8.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0039-1690010.

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