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Palladium-Catalyzed *peri*-Selective Chalcogenation of Naphthylamines with Diaryl Disulfides and Diselenides via C−H Bond Cleavage

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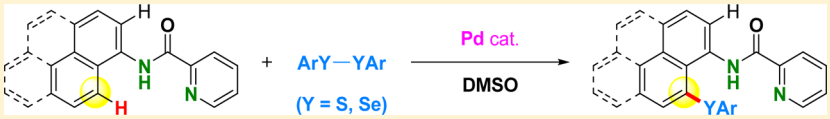
Supporting Information



ABSTRACT: A palladium-catalyzed and picolinamide-directed C−H thiolation of naphthylamine derivatives with diaryl disulfides has been developed to provide a convenient route to 8-sulfenyl-1-naphthylamines. The reaction proceeds via a 5-membered palladacycle intermediates to afford the *peri*-thiolated products exclusively, in contrast to the conventional *ortho*-functionalization. Moreover, the related direct selenation was also achieved with diaryl diselenides, giving the corresponding selenated products with perfect site-selectivity.

INTRODUCTION

8-Sulfenyl-1-naphthylamine scaffolds are an important structural motif in a wide variety of functional molecules[1] and pharmaceuticals[2] (Figure 1). Despite their structural utility, an efficient synthesis for such interesting compounds has not been available, and the construction of 8-sulfenyl-1-naphthylamine skeletons is usually difficult. For instance, electrophilic nitration of 1-naphthalenesulfonic acids, which is a representative synthetic reaction, affords a mixture of 1,5- and 1,8-difunctionalized naphthalenes, but its site-selectivity is totally uncontrollable.[3] Therefore, thiolation of 1-naphthylamine derivatives is regarded as the better way to prepare 1,8-difunctionalized naphthalenes because of the ready availability of starting materials. Although conventional cross-couplings of aryl halides with thiols represents the most reliable C−S bond-forming reaction, there still remains the difficulty of preparing the starting naphthyl halides.

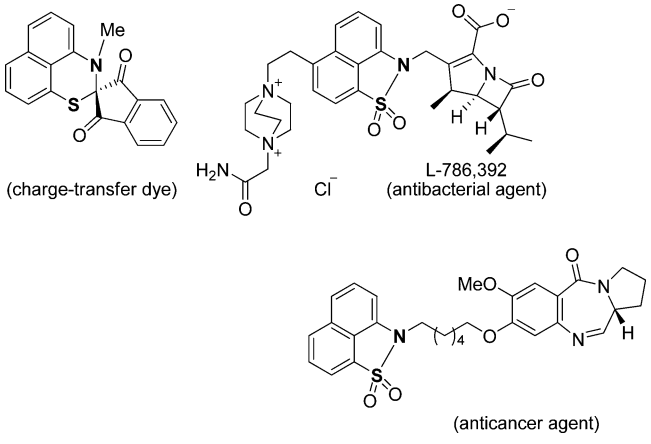
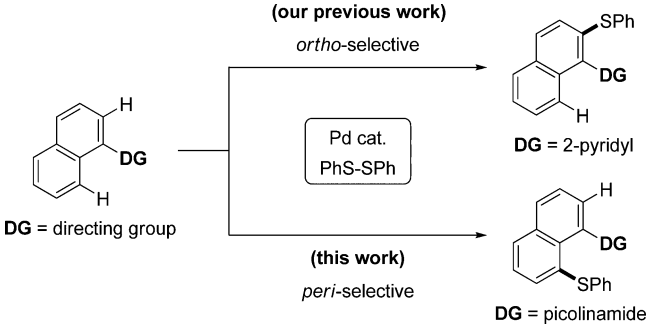


Figure 1. 8-Sulfur-containing 1-naphthylamine derivatives.

Of the several C−S bond-forming reactions, the direct introduction of sulfenyl moieties into arenes through C−H bond cleavage is the preferred synthetic method.[4] In the past two decades, chelate-assisted direct functionalization has been well studied.[5] However, there have been few reports on the direct thiolation of aryl C−H bonds until recently.[6,7] Our group has also reported that C−H thiolation of 2-(1-naphthyl)-pyridine occurs exclusively at the *ortho* position (Scheme 1, top).[6]

Scheme 1. Site-Selective Direct Thiolation



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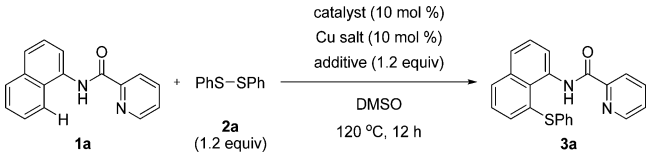
More recently, several groups have reported the *peri*-functionalization of naphthalene rings with an *N*,*N*-bidentate coordination system.[8,9] Because of the synthetic utility of the products, arylation,[8a,b] heteroarylation,[8c] etherification,[8d] amination,[8e] and alkylation[8f] of naphthylamine derivatives have been achieved using palladium or copper catalysts. During the course of our investigation of directing groups, we found that C−H thiolation of the naphthalene rings proceeded at the *peri*-position with perfect site-selectivity when a picolinamide group[5f] was used as an auxiliary instead of a 2-pyridyl group. Herein, we report the auxiliary-controlled and palladium-catalyzed direct thiolation of naphthylamine derivatives with diaryl disulfides and the related selenation with diaryl diselenides in a site-selective fashion (Scheme 1, bottom).

RESULTS AND DISCUSSION

Direct Thiolation. Our effort was initially focused on the direct thiolation of *N*-(1-naphthyl)picolinamide (**1a**) with diphenyl disulfide (**2a**) as a model reaction. The results are summarized in Table 1. Treatment of **1a** with **2a** (1.2 equiv) in the presence of $PdCl_2(NCPh)_2$ (10 mol %) in DMSO at 120 °C yielded *peri*-thiolated product **3a** in 57% NMR yield (entry 1). The reaction proceeded with perfect site-selectivity, with no *ortho*-thiolated product observed. The precise structure of **3a** was unambiguously determined by X-ray crystallography (Figure S2, Supporting Information).[10] Essentially no reaction occurred in the absence of a catalyst (entry 2), and neither $[Cp^*RhCl_2]_2$[7d] nor $Cu(OAc)_2$[7a,c] was found to be efficient in the present reaction (entries 3 and 4). Other palladium(II) catalysts such as $Pd(OAc)_2$, $PdCl_2$, or $PdCl_2(PPh_3)_2$ did not produce high yields (entries 5−7). Unlike the reaction of 2-arylpyridines,[6] the addition of phosphine ligands was not necessary, yielding no positive impact on the present reaction. Palladium(0) precursors, such as $Pd(dba)_2$ and $Pd(PPh_3)_4$, were also ineffective (entries 8 and 9). Moreover, we found that a catalytic amount of added $CuCl_2$ promoted the reaction to some extent (entry 10), while $Cu(OAc)_2$, CuCl, or Cu metal did not improve the yields (entries 11−13). Next, some representative acid additives were investigated, which were known to promote C−H functionalization (entries 14−19).[11] PivOH was the best of those we tested: PivOH, AcOH, $AdCO_2H$, *p*-TsOH, CF_3CO_2H, and CF_3SO_3H. Additional investigation of the solvent system revealed that DMSO was essential for the reaction, while toluene (0%), DMF (5%), and 1,4-dioxane (0%) were inferior. Under the conditions in entry 14, unreacted starting material **1a** was recovered in 7% yield and no identifiable byproduct was detected. Further modifications, such as catalyst loading, the quantity of **2a**, temperatures, and reaction times, did not yield significant improvement of the conversion of **1a** or the yield of **3a**. Note that the yield decreased under otherwise optimal conditions without $CuCl_2$ (entry 20). A palladium catalyst was shown to be essential for the present reaction to proceed. In the absence of palladium, no reaction occurred and unreacted substrate **1a** was recovered (entry 21).

With the new set of reaction conditions in hand, we explored the substrate scope of disulfide, as shown in Table 2. Along with **2a** (entry 1), diaryl disulfides **2b**−**d** bearing electron-donating (OMe) and -withdrawing functional groups (CF_3 and CO_2Et) participated equally in the reaction of **1a**, affording the corresponding products **3b**−**d** in moderate to good yields (entries 2−4). The reaction was remarkably functional-group tolerant, with the chloro and bromo moieties compatible with

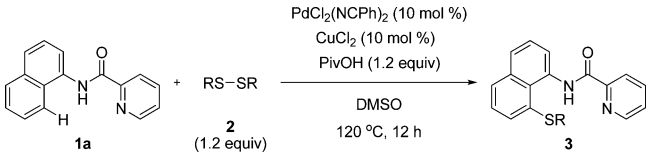
Table 1. Site-Selective Direct Thiolation of *N*-(1-Naphthyl)picolinamide (1a) with Diphenyl Disulfide (2a)[a]



entry	catalyst	Cu salt	additive	yield[b] (%)
1	$PdCl_2(NCPh)_2$	none	none	57
2	none	none	none	0
3	$[Cp^*RhCl_2]_2$	none	none	0
4	$Cu(OAc)_2$	none	none	3
5	$Pd(OAc)_2$	none	none	11
6	$PdCl_2$	none	none	41
7	$PdCl_2(PPh_3)_2$	none	none	38
8	$Pd(dba)_2$	none	none	0
9	$Pd(PPh_3)_4$	none	none	0
10	$PdCl_2(NCPh)_2$	$CuCl_2$	none	73
11	$PdCl_2(NCPh)_2$	$Cu(OAc)_2$	none	24
12	$PdCl_2(NCPh)_2$	CuCl	none	53
13	$PdCl_2(NCPh)_2$	Cu	none	54
14	$PdCl_2(NCPh)_2$	$CuCl_2$	PivOH	82 (80)
15	$PdCl_2(NCPh)_2$	$CuCl_2$	$AdCO_2H$	69
16	$PdCl_2(NCPh)_2$	$CuCl_2$	AcOH	66
17	$PdCl_2(NCPh)_2$	$CuCl_2$	CF_3CO_2H	52
18	$PdCl_2(NCPh)_2$	$CuCl_2$	CF_3SO_3H	36
19	$PdCl_2(NCPh)_2$	$CuCl_2$	*p*-TsOH	33
20	$PdCl_2(NCPh)_2$	none	PivOH	55
21	none	$CuCl_2$	PivOH	0

[a]The reactions were conducted with **1a** (0.25 mmol), **2a** (0.30 mmol), catalyst (0.025 mmol), Cu salt (0.025 mmol), and additive (0.30 mmol) in DMSO (0.50 mL) at 120 °C for 12 h. [b]Yields were determined by the ^1H NMR analysis of a crude mixture using dibromomethane as an internal standard. The yield based on **1a** after silica gel column chromatography is shown in parenthesis.

Table 2. Palladium-Catalyzed Site-Selective Direct Thiolation of *N*-(1-Naphthyl)picolinamide (1a) with Various Disulfides 2[a]



entry	Ar	2	product	yield[b] (%)
1	Ph	**2a**	**3a**	80
2	$4\text{-}MeOC_6H_4$	**2b**	**3b**	68
3[c]	$4\text{-}CF_3C_6H_4$	**2c**	**3c**	64
4[c]	$4\text{-}EtO_2CC_6H_4$	**2d**	**3d**	55
5[c]	$4\text{-}ClC_6H_4$	**2e**	**3e**	65
6	$4\text{-}BrC_6H_4$	**2f**	**3f**	62
7[c]	$2\text{-}MeC_6H_4$	**2g**	**3g**	71
8[c]	2-thienyl	**2h**	**3h**	51
9	Me	**2i**	**3i**	0

[a]All the reactions were conducted with **1a** (0.25 mmol), **2** (0.30 mmol), $PdCl_2(NCPh)_2$ (0.025 mmol), $CuCl_2$ (0.025 mmol), and PivOH (0.30 mmol) in DMSO (0.50 mL) at 120 °C for 12 h. [b]Yields based on **1a** after silica gel column chromatography. [c]At 100 °C.

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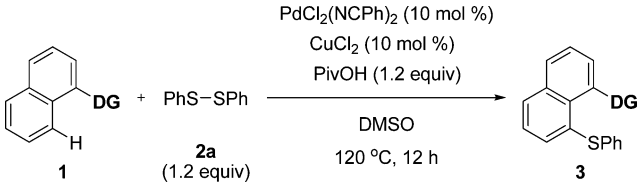
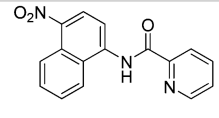
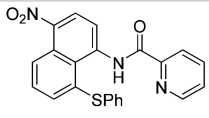
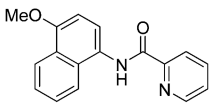
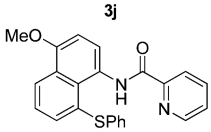
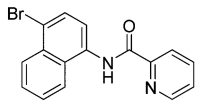
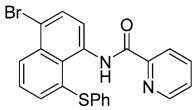
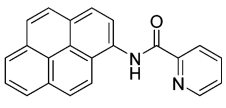
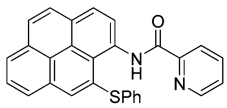
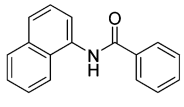
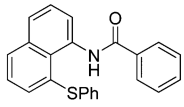
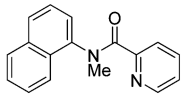
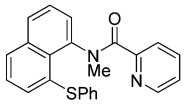
the reaction conditions (entries 5 and 6). The substitution pattern of diaryl disulfides did not negatively affect the reaction efficiency. Indeed, *ortho*-substituted diaryl disulfide **2g** reacted to yield **3g** in 71% yield (entry 7). Moreover, di(2-thienyl) disulfide (**2h**) could also be employed (entry 8), although most **1a** remained unreacted in the reaction with dimethyl disulfide (**2i**) (entry 9).

The conditions we developed for *peri*-selective direct thiolation of **1a** could be applied to a variety of naphthylamine derivatives **1** (Table 3). When nitro- and methoxy-substituted

Table 3. Palladium-Catalyzed Site-Selective Direct Thiolation of Naphthylamines 1 with Diphenyl Disulfide (2a)[a]



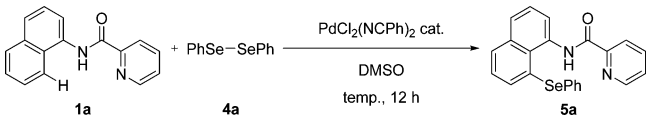
entry	substrate, **1**	product, **3**	yield[b] (%)
1	 **1b**	 **3j**	74
2	 **1c**	 **3k**	54
3[c]	 **1d**	 **3l**	83
4[c]	 **1e**	 **3m**	62
5	 **1f**	 **3n**	0
6	 **1g**	 **3o**	0

[a]All of the reactions were conducted with **1** (0.25 mmol), **2a** (0.30 mmol), $PdCl_2(NCPh)_2$ (0.025 mmol), $CuCl_2$ (0.025 mmol), and PivOH (0.30 mmol) in DMSO (0.50 mL) at 120 °C for 12 h. [b]Yields based on **1** after silica gel column chromatography. [c]At 100 °C.

naphthylamines **1b** and **1c** were reacted with **2a**, the desired products **3j** and **3k** were obtained in 74% and 54% yields, respectively (entries 1 and 2). Notably, a bromo group was tolerated, offering an opportunity for further functionalization (entry 3). Although cross-coupling reactions of aryl bromides with disulfides are well-known,[12] C−S bond formation occurred only through C−H bond cleavage. Furthermore, pyrenylamine derivative **1e** was found to undergo direct thiolation smoothly to give **3m** in 62% yield (entry 4). We next examined the effect of directing groups. No direct thiolation occurred when *N*-(1-naphthyl)benzamide (**1f**) and *N*-methylamide **1g** were used as the substrate in place of **1a** (entries 5 and 6). The presence of an N−H bond as well as a pyridine nitrogen was crucial for the successful direct functionalization.

Direct Selenation. The successful results of direct thiolation led us to examine the related direct selenation of **1a** with diphenyl diselenide (**4a**) (Table 4).[13] Under conditions

Table 4. Site-Selective Direct Selenation of *N*-(1-Naphthyl)picolinamide (1a) with Diphenyl Diselenide (4a)[a]



				yield[b] (%)	
entry	$PdCl_2(NCPh)_2$ (mol %)	**4a** (equiv)	temp (°C)	**5a**	**1a**
1[c]	10	1.2	120	25	19
2	10	1.2	120	29	0
3	10	0.60	120	58	5
4	5	0.60	120	75	10
5	1	0.60	120	46	53
6	5	0.60	100	87 (80)	8
7	5	0.60	80	32	55
8[d]	5	0.60	100	86	7

[a]The reactions were conducted with **1a** (0.25 mmol), **4a**, and $PdCl_2(NCPh)_2$ in DMSO (0.50 mL) for 12 h. [b]Yields were determined by the ^1H NMR analysis of a crude mixture using dibromomethane as an internal standard. The yield based on **1a** after silica gel column chromatography is shown in parenthesis. [c]$CuCl_2$ (0.025 mmol) and PivOH (0.30 mmol) were added. [d]The reaction was performed for 24 h.

optimized for direct thiolation, the desired product **5a** was obtained in only 25% yield, though most of the starting material **1a** was consumed (entry 1). We assumed that such reaction conditions would be quite harsh for direct selenation, which might cause some undesirable overreactions. Although no byproduct has been identified yet, one of the possible overreactions may be an electrophilic selenation.[14] Additives such as $CuCl_2$ and PivOH did not seem to be necessary for the reaction (entry 2). The mass balance of the reaction was substantially improved by diminishing the amount of **4a**, which could suppress the side reactions. The reaction with 0.6 equiv of **4a** provided **5a** in 58% yield (entry 3). It was noteworthy that the catalyst loading could be reduced to 5 mol % (entry 4), while the reaction with 1 mol % of the catalyst gave low conversion of **1a** (entry 5). The best result was finally obtained when the reaction was carried out at 100 °C (entry 6). Neither a lower reaction temperature nor a longer reaction time further improved the yield of **5a** (entries 7 and 8). Under these conditions, the reaction of **1a** with diphenyl ditelluride was attempted, but no direct telluration product was observed and **1a** was completely recovered.

We were pleased to find that various diselenides **4** could be used for the direct selenation of **1a** (Table 5). The reaction tolerated several functional groups such as bromo and chloro groups on the aromatic rings to furnish **5b** and **5c** in good yields as well as **5a** (entries 1−3). Representative substrates

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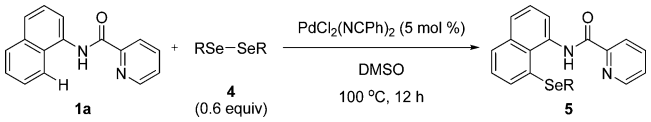
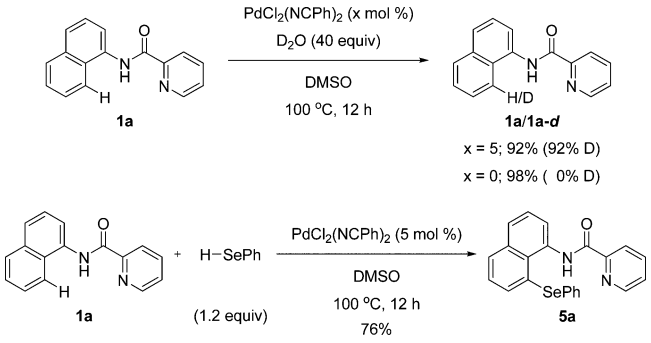
Table 5. Palladium-Catalyzed Site-Selective Direct Selenation of Naphthylamine 1a with Various Diselenides 4[a]



entry	Ar	4	product	yield[b] (%)
1	Ph	**4a**	**5a**	80
2	4-BrC_6H_4	**4b**	**5b**	94
3	4-ClC_6H_4	**4c**	**5c**	88
4	4-$MeOC_6H_4$	**4d**	**5d**	74
5[c]	2-$CF_3C_6H_4$	**4e**	**5e**	59
6	2-MeC_6H_4	**4f**	**5f**	75
7	2-thienyl	**4g**	**5g**	39
8	Me	**4h**	**5h**	0

[a]The reactions were conducted with **1a** (0.25 mmol), **4** (0.15 mmol), and $PdCl_2(NCPh)_2$ (0.0125 mmol) in DMSO (0.50 mL) at 100 °C for 12 h. [b]Yields based on **1a** after silica gel column chromatography. [c]The reaction was performed at 80 °C for 24 h with 10 mol % of $PdCl_2(NCPh)_2$.

Scheme 2. Control Experiments



were selected to investigate electronic effects on **4**. Consequently, both electron-rich and -poor substrates **4d** and **4e** led to the formation of the corresponding products **5d** and **5e** in 74% and 59% yields, respectively (entries 4 and 5). Additionally, the reaction with the sterically congested diselenides **4f** proceeded well without a substantial drop in efficiency (entry 6). The reaction with di(2-thienyl) diselenide (**4g**) also provided the corresponding product **5g**, though the formation of some byproducts was observed (entry 7). The 2-position of thiophenes was highly susceptible to attack by electrophiles, which may explain the low yield of **5g**. By contrast, dimethyl diselenide (**4h**) did not react, and substrate **1a** was recovered quantitatively, probably due to the low reactivity of **4h**.

Plausible Reaction Mechanism. The following preliminary control experiments provided some insights into the mechanism of direct chalcogenation described herein (Scheme 2). H/D exchange was clearly observed in the reaction of **1a** with an excess of D_2O. The deuterated product **1a-*d*** (92% D incorporation) was obtained in 92% yield, while in the absence of the palladium catalyst no **1a-*d*** was detected. As expected, the substitution took place only at the *peri*-position of **1a**. These results led us to conclude that the C−H palladation step was reversible and disulfides were not involved in the C−H bond cleavage. However, our attempts to isolate the putative palladacycle intermediate remain unsuccessful so far. In the case of direct selenation, 0.6 equiv of diselenide **4** was enough to complete the reaction. Indeed, the reaction of **1a** with benzeneselenol (1.2 equiv) provided **5a** in 76% yield under identical conditions, instead of **4a**, suggesting that selenols are readily oxidized to diselenides **4** by DMSO because of the high general reactivity of selenols.

Furthermore, kinetic isotope effects (k_H/k_D) were determined by monitoring the conversion at an early stage. Initial reaction rates for **1a** and **1a-*d*** were obtained by plotting the product yields against the reaction time (Scheme 3 and Figure 2). The introduction of deuterium into **1a** had only a minor

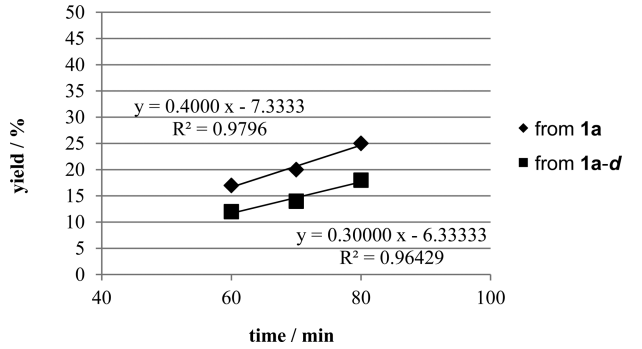
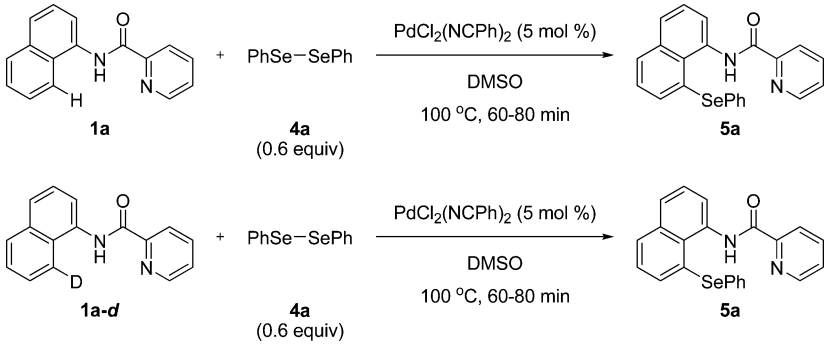


Figure 2. Yields of **5a** from reactions of **1a** or **1a-*d*** with **4a** for 60, 70, and 80 min.

impact on the production rate of **5a** (k_H/k_D = 1.3).[15] Similarly, the intramolecular k_H/k_D was found to be 1.3, based on ^1H NMR spectroscopic analysis of the recovered substrate **1a**/**1a-*d*** (Scheme 4). The observed lack of primary KIE implied that the rate-determining step of the reaction did not involve C−H bond cleavage.[16]

Scheme 3. Parallel Experiments



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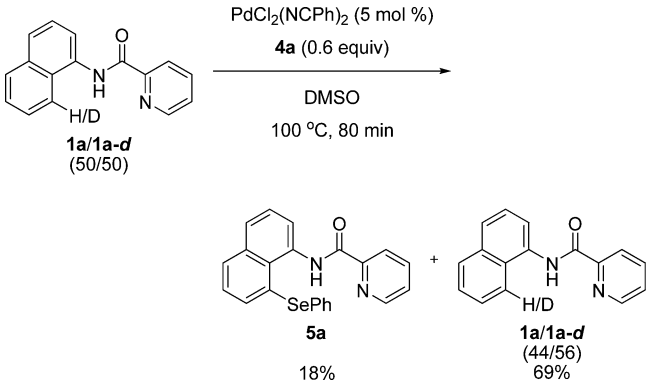
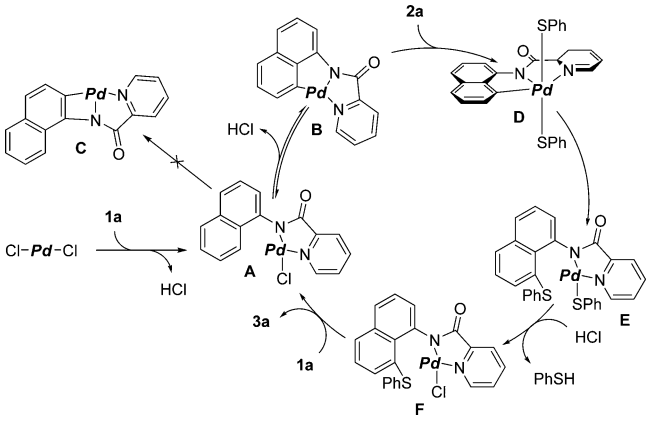
Scheme 4. Intramolecular Competition



On the basis of the above results and previous studies reported by us,[6,13] we propose the reaction mechanism of the direct thiolation to be that shown in Scheme 5. As the initial

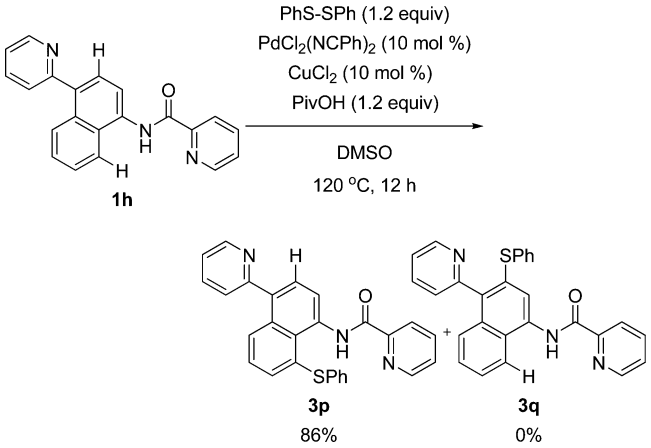
Scheme 5. Plausible Reaction Mechanism



step, palladium complex **A** is ligated with a picolinamide moiety in **1a**, from which the reversible cyclopalladation selectively occurs at the *peri*-position of **1a** to give the thermodynamically favored **B**. The site-selectivity of the reaction could be explained by the instability of the strained four-membered palladacycle intermediate **C**.[17−19] The subsequent oxidative addition of **2a** to **B** forms the high-valent palladium(IV) species **D**,[20] a step supported by the fact that direct selenation with the more reactive diselenide proceeded smoothly at lower temperature. Reductive C−S bond formation from **D** provides the product-ligated palladium complex **E**. The following ligand exchange between SPh and Cl affords the intermediate **F** and benzenethiol.[13] Benzenethiol was not observed in the reaction mixture, as it could rapidly be oxidized with DMSO to give **2a**.[21] This is the reason why benzenethiol did not affect the palladium catalyst. The final product dissociation and simultaneous capture of the liberated palladium by **1a** regenerates the initial palladium complex **A** to complete the catalytic cycle. The exact role of additives remains unclear, but PivOH can accelerate C−H bond cleavage in **1a** through a concerted metalation-deprotonation (CMD) pathway.[11] A catalytic amount of copper salt might play a role as a Lewis acid to promote oxidative addition of **2a** to **B** and/or accelerate C−S bond-forming reductive elimination,[22] though we had no experimental results to support either of these possibilities. The related direct selenation probably proceeded in a similar manner. It should be noted that a possible palladium(II)-based mechanism cannot be ruled out in which a Cu−SPh intermediate generated from the reaction of disulfide and the added copper salt would promote the transmetalation with **B**.[23]

We could demonstrate the chelate-controlled direct thiolation of naphthalenes, in which *N*-(1-naphthyl)picolinamides underwent *peri*-functionalization, while *ortho*-functionalization of naphthalenes was achieved with a 2-pyridyl directing group.[6] Both palladium-catalyzed reactions proceeded under similar conditions. We then investigated the reaction of naphthalene **1h** having two different directing 2-pyridyl and picolinamide groups (Scheme 6). Interestingly, *peri*-thiolation occurred with

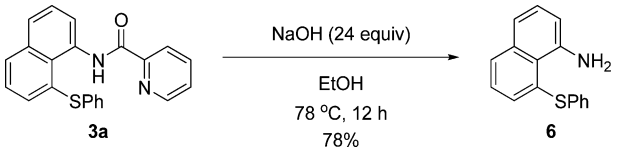
Scheme 6. *peri*-Selectivity versus *ortho*-Selectivity



perfect site-selectivity to afford **3p** in 86% yield, and *ortho*-thiolated product **3q** was not obtained. These results clearly showed that the bidentate picolinamide group coordinates palladium more strongly, which would form the more stable palladacycle intermediate.

Finally, we investigated the removal of the picolinamide directing group from the direct thiolation product, finding that the amide moiety could be simply hydrolyzed (Scheme 7).[8a] The product **3a** was heated with NaOH in ethanol to afford 8-benzenesulfenyl-1-naphthylamine (**6**) in 78% yield.

Scheme 7. Removal of the Directing Group



CONCLUSION

In summary, we have developed the palladium-catalyzed *peri*-selective direct chalcogenation of naphthylamine derivatives with diaryl disulfides and diselenides. The catalytic C−S bond formation event occurred without exception at the *peri*-position in naphthylamines, which is in sharp contrast to the previous *ortho*-functionalization. This selectivity is ascribed to the formation of the thermodynamically stable five-membered palladacycle intermediate. The directing group employed was readily removable after the chalcogenation, thus affording an important molecular component for materials science and medicinal chemistry. Detailed mechanistic studies and further

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development of relevant direct chalcogenations are ongoing in our laboratory.

EXPERIMENTAL SECTION

Chemicals. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Bis-(benzonitrile)palladium dichloride was prepared according to the literature.[24] Compounds **1a**,[8a] **1b,c**,[8c] **1e−g**,[8c] **2b,c**,[25] **2d**,[26] **2e**,[25] **2f**,[27] **2g**,[28] **2h**,[29] **4b−d**,[30] **4e**,[31] **4f,g**,[32] and **1a-*d***[8a] showed the identical spectra reported in the literature. Compounds **2a**, **2i**, and **4a** were available from chemical suppliers.

Preparation of *N*-(4-Bromo-1-naphthyl)picolinamide (1d). The title compound was obtained as a white solid (1.94 g, 6.0 mmol, 60%) according to the literature.[33] Mp: 168−169 °C. IR (KBr): 3466 (m), 3350 (m), 1692 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.52−7.57 (m, 1H), 7.62−7.67 (m, 2H), 7.83−7.86 (m, 1H), 7.93−7.98 (m, 1H), 8.08−8.12 (m, 1H), 8.29−8.37 (m, 3H), 8.70−8.71 (m, 1H), 10.77 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, rt): δ 118.8, 119.2, 121.0, 122.7, 126.9, 127.2, 127.5, 127.7, 128.3, 130.1, 132.4, 132.5, 138.0, 148.3, 149.9, 162.4. Anal. Calcd for $C_{16}H_{11}BrN_2O$: C, 58.74; H, 3.39; N, 8.56. Found: C, 58.68; H, 3.11; N, 8.51.

***N*-[-(2-Pyridyl)-1-naphthyl]picolinamide (1h).** The title compound was obtained as a white solid (1.58 g, 4.9 mmol, 81%) according to the literature.[8c] Mp: 123 °C. IR (KBr): 3364 (m), 3061 (m), 1699 (s) cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$, rt): δ 7.33−7.35 (m, 1H), 7.53−7.56 (m, 2H), 7.60−7.64 (m, 2H), 7.68 (d, J = 7.8 Hz, 1H), 7.84 (t, J = 7.8 Hz, 1H), 7.97 (t, J = 7.8 Hz, 1H), 8.18 (d, J = 8.4 Hz, 1H), 8.21 (d, J = 8.4 Hz, 1H), 8.38 (d, J = 7.8 Hz, 1H), 8.53 (d, J = 7.8 Hz, 1H), 8.73−8.74 (m, 1H), 8.80−8.81 (m, 1H), 10.88 (s, 1H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 117.9, 120.6, 122.0, 122.5, 125.2, 126.3, 126.5, 126.6, 126.67, 126.73, 127.8, 131.8, 133.0, 135.4, 136.6, 137.8, 148.2, 149.5, 150.0, 159.2, 162.3. Anal. Calcd for $C_{21}H_{15}N_3O$: C, 77.52; H, 4.65; N, 12.91. Found: C, 77.69; H, 4.28; N, 12.92.

Typical Procedure for Palladium-Catalyzed Site-Selective Direct Thiolation of Naphthylamine Derivatives 1 with Disulfides 2: Synthesis of *N*-(8-Benzenesulfenyl-1-naphthyl)-picolinamide (3a) (Table 2, Entry 1). Diphenyl disulfide (**2a**, 66 mg, 0.30 mmol), bis(benzonitrile)palladium dichloride (9.6 mg, 0.025 mmol), copper(II) chloride (3.4 mg, 0.025 mmol), pivalic acid (31 mg, 0.30 mmol), and *N*-(1-naphthyl)picolinamide (**1a**, 62 mg, 0.25 mmol) were placed in a 20 mL Schlenk tube under an Ar atmosphere. DMSO (0.50 mL) was then added at room temperature. The mixture was stirred at 120 °C for 12 h. After the mixture was allowed to cool to room temperature, saturated sodium thiosulfate solution (5 mL) was added to quench the reaction. The mixture was extracted with dichloromethane (5 mL) three times. The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate = 3/1) to provide **3a** (71.4 mg, 0.20 mmol, 80%). White solid. Mp: 123−124 °C. IR (KBr): 3308 (s), 3061 (m), 1690 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 6.80−6.82 (m, 2H), 6.95−7.01 (m, 3H), 7.42−7.47 (m, 2H), 7.58 (t, J = 8.0 Hz, 1H), 7.77−7.85 (m, 3H), 7.95 (d, J = 8.0 Hz, 1H), 8.10 (d, J = 8.0 Hz, 1H), 8.35 (d, J = 8.0 Hz, 1H), 8.64 (d, J = 4.0 Hz, 1H), 12.23 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, rt): δ 122.7, 123.7, 125.66, 125.69, 125.9, 126.2, 126.4, 126.86, 126.90, 127.5, 128.8, 131.7, 133.8, 136.5, 137.3, 138.1, 138.3, 148.0, 150.7, 162.8. Anal. Calcd for $C_{22}H_{16}N_2OS$: C, 74.13; H, 4.52; N, 7.86. Found: C, 73.79; H, 4.64; N, 7.81.

*N-[8-(4-Methoxybenzenesulfenyl)-1-naphthyl]picolinamide (**3b**).* The title compound was obtained as a white solid (65.9 mg, 0.17 mmol, 68%). Mp: 107−108 °C. IR (KBr): 3401 (s), 3055 (m), 1682 (s), 1246 (s), 1028 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 3.70 (s, 3H), 6.67 (d, J = 8.4 Hz, 2H), 7.00 (d, J = 8.4 Hz, 2H), 7.35 (t, J = 7.6 Hz, 1H), 7.44−7.57 (m, 3H), 7.75 (d, J = 7.6 Hz, 1H), 7.81−7.87 (m, 2H), 8.21−8.23 (m, 1H), 8.27 (d, J = 7.2 Hz, 1H), 8.66−8.67 (m, 1H), 12.01 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, rt): δ 55.4, 114.8, 122.8, 123.8, 125.6, 126.2, 126.3, 127.06, 127.08, 127.2, 129.7, 130.0, 131.3, 133.3, 134.6, 136.3, 137.4, 148.1, 150.6, 158.8, 163.0. HRMS (FAB+): calcd for $C_{23}H_{19}N_2O_2S$ 387.1167, found 387.1181 $[M + H]^+$.

*N-{8-[4-(Trifluoromethyl)benzenesulfenyl]-1-naphthyl}-picolinamide (**3c**).* The title compound was obtained as a white solid (67.9 mg, 0.16 mmol, 64%). Mp: 120−121 °C. IR (KBr): 3316 (s), 3057 (m), 1682 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 6.76 (d, J = 8.4 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H), 7.43−7.45 (m, 1H), 7.49 (t, J = 7.6 Hz, 1H), 7.62 (t, J = 8.0 Hz, 1H), 7.77−7.88 (m, 3H), 7.98−8.04 (m, 2H), 8.29 (d, J = 7.6 Hz, 1H), 8.59−8.61 (m, 1H), 11.97 (s, 1H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 122.8, 123.2, 124.1 (q, J_{C-F} = 270 Hz), 124.9, 125.3, 125.4 (q, J_{C-F} = 4 Hz), 125.9, 126.4, 126.7, 127.1 (q, J_{C-F} = 33 Hz), 127.4, 128.1, 132.9, 133.3, 136.6, 137.6, 139.7, 144.0, 147.8, 150.2, 162.6. $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$, rt): δ −62.6. Anal. Calcd for $C_{23}H_{15}F_3N_2OS$: C, 65.09; H, 3.56; N, 6.60. Found: C, 65.04; H, 3.33; N, 6.50.

*N-[8-(4-Ethoxycarbonylbenzenesulfenyl)-1-naphthyl]picolinamide (**3d**).* The title compound was obtained as a white solid (58.9 g, 0.14 mmol, 55%). Mp: 116−117 °C. IR (KBr): 3287 (m), 3059 (m), 1713 (s), 1686 (s), 1273 (s) cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$, rt): δ 1.30 (t, J = 7.2 Hz, 3H), 4.26 (q, J = 7.2 Hz, 2H), 6.74 (d, J = 8.4 Hz, 2H), 7.45 (t, J = 7.2 Hz, 1H), 7.49 (t, J = 7.2 Hz, 1H), 7.59−7.62 (m, 3H), 7.81 (t, J = 8.4 Hz, 2H), 7.87−7.88 (m, 1H), 8.03 (d, J = 7.2 Hz, 2H), 8.36 (d, J = 7.8 Hz, 1H), 8.61−8.62 (m, 1H), 12.08 (s, 1H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 14.4, 60.9, 122.6, 123.4, 124.0, 125.0, 125.8, 126.3, 126.6, 127.07, 127.10, 127.6, 129.7, 132.8, 133.5, 136.6, 137.3, 139.7, 145.1, 147.9, 150.4, 162.6, 166.2. HRMS (FAB+): calcd for $C_{25}H_{21}N_2O_3S$ 429.1273, found 429.1280 $[M + H]^+$.

*N-[8-(4-Chlorobenzenesulfenyl)-1-naphthyl]picolinamide (**3e**).* The title compound was obtained as a white solid (63.3 mg, 0.16 mmol, 65%). Mp: 114−115 °C. IR (KBr): 3179 (s), 3038 (m), 1680 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 6.70 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 7.42−7.46 (m, 2H), 7.59 (t, J = 8.0 Hz, 1H), 7.77−7.79 (m, 2H), 7.84 (t, J = 7.6 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 8.11 (d, J = 8.0 Hz, 1H), 8.34 (d, J = 7.6 Hz, 1H), 8.62−8.64 (m, 1H), 12.10 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, rt): δ 122.7, 124.0, 125.0, 125.7, 126.3, 126.5, 127.0, 127.4, 127.7, 128.8, 131.4, 132.1, 133.4, 136.5, 136.8, 137.3, 138.5, 148.0, 150.5, 162.7. Anal. Calcd for $C_{22}H_{15}ClN_2OS$: C, 67.60; H, 3.87; N, 7.17. Found: C, 67.47; H, 3.84; N, 7.12.

*N-[8-(4-Bromobenzenesulfenyl)-1-naphthyl]picolinamide (**3f**).* The title compound was obtained as a white solid (67.6 mg, 0.16 mmol, 62%). Mp: 125−126 °C. IR (KBr): 3177 (s), 3059 (m), 1678 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): 6.64 (d, J = 8.8 Hz, 2H), 7.06 (d, J = 8.8 Hz, 2H), 7.43−7.50 (m, 2H), 7.60 (t, J = 8.0 Hz, 1H), 7.77−7.89 (m, 3H), 7.97 (d, J = 8.0 Hz, 1H), 8.11 (d, J = 8.0 Hz, 1H), 8.30−8.32 (m, 1H), 8.62−8.64 (m, 1H), 12.07 (s, 1H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, rt): δ119.2, 122.8, 124.1, 124.8, 125.7, 126.3, 126.6, 127.1 127.6, 127.9, 131.7, 132.2, 133.5, 136.5, 137.3, 137.6, 138.7, 148.0, 150.5, 162.8. Anal. Calcd for $C_{22}H_{15}BrN_2OS$: C, 60.70; H, 3.47; N, 6.43. Found: C, 60.50; H, 3.30; N, 6.30.

*N-[8-(2-Methylbenzenesulfenyl)-1-naphthyl]picolinamide (**3g**).* The title compound was obtained as a white solid (65.7 mg, 0.18 mmol, 71%). Mp: 125−126 °C. IR (KBr): 3277 (m), 3061 (w), 1682 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 2.24 (s, 3H), 6.65−6.67 (m, 1H), 6.88−6.96 (m, 3H), 7.38−7.42 (m, 2H), 7.57−7.61 (m, 2H), 7.78−7.82 (m, 2H), 7.91 (d, J = 8.0 Hz, 1H), 8.08 (d, J = 8.0 Hz, 1H), 8.18−8.20 (m, 1H), 8.54−8.56 (m, 1H), 11.75 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, rt): δ 20.0, 122.6, 124.7, 125.9, 126.0, 126.1, 126.3, 126.6, 126.9, 127.3, 127.6, 128.4, 129.7, 131.0, 133.4, 135.6, 136.36, 136.44, 137.1, 137.2, 147.8, 150.5, 162.9. Anal. Calcd for $C_{23}H_{18}N_2OS$: C, 74.57; H, 4.90; N, 7.56. Found: C, 74.47; H, 4.64; N, 7.49.

*N-[8-(2-Thiophenesulfenyl)-1-naphthyl]picolinamide (**3h**).* The title compound was obtained as a white solid (46.6 mg, 0.13 mmol, 51%). Mp: 135−136 °C. IR (KBr): 3327 (m), 3049 (w), 1686 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 6.95−6.98 (m, 1H), 7.13 (d, J = 3.6 Hz, 1H), 7.31 (t, J = 7.6 Hz, 1H), 7.36−7.39 (m, 2H), 7.46−7.49 (m, 1H), 7.54 (t, J = 7.6 Hz, 1H), 7.73−7.76 (m, 2H), 7.90 (t, J = 7.6 Hz, 1H), 8.13 (d, J = 7.6 Hz, 1H), 8.35 (d, J = 7.6 Hz, 1H), 8.70

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(brs, 1H), 11.52 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, rt): δ 122.9, 124.8, 125.6, 126.2, 126.5, 126.8, 127.5, 127.9, 128.9, 130.7, 130.8, 133.07, 133.11, 133.2, 134.5, 136.2, 137.5, 148.4, 150.5, 163.3. Anal. Calcd for $C_{20}H_{14}N_2OS_2$: C, 66.27; H, 3.89; N, 7.73. Found: C, 65.96; H, 3.55; N, 7.72.

N-(8-Benzenesulfenyl-4-nitro-1-naphthyl)picolinamide (**3j**). The title compound was obtained as a yellow solid (74.3 mg, 0.19 mmol, 74%). Mp: 186 °C. IR (KBr): 3157 (m), 3059 (m), 1692 (s), 1510 (s), 1327 (s), 847 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 6.85−6.88 (m, 2H), 7.04−7.08 (m, 3H), 7.50−7.53 (m, 1H), 7.63−7.67 (m, 1H), 7.88−7.93 (m, 2H), 8.18 (d, *J* = 8.0 H, 1H), 8.23 (d, *J* = 8.8 Hz, 1H), 8.60−8.69 (m, 3H), 12.90 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, rt): δ 119.4, 123.1, 124.9, 125.6, 126.5, 126.6, 126.8, 127.5, 127.9, 128.5, 128.6, 129.2, 136.7, 137.7, 139.1, 139.7, 144.2, 148.2, 149.9, 163.1. Anal. Calcd for $C_{22}H_{15}N_3O_3S$: C, 65.82; H, 3.77; N, 10.47. Found: C, 65.71; H, 3.63; N, 10.46.

N-(8-Benzenesulfenyl-4-methoxy-1-naphthyl)picolinamide (**3k**). The title compound was obtained as a yellow solid (51.9 mg, 0.13 mmol, 54%). Mp: 152−153 °C. IR (KBr): 3335 (m), 3049 (w), 1680 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 4.05 (s, 3H), 6.78−6.80 (m, 2H), 6.94−6.99 (m, 4H), 7.41−7.44 (m, 2H), 7.75−7.82 (m, 2H), 8.06−8.08 (m, 2H), 8.48 (d, *J* = 8.4 Hz, 1H), 8.61−8.63 (m, 1H), 11.68 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, rt): δ 56.0, 104.6, 122.6, 124.9, 125.1, 125.3, 125.6, 126.01, 126.03, 127.1, 128.0, 128.76, 128.78, 129.2, 137.2, 138.2, 138.3, 148.0, 150.7, 153.8, 162.8. HRMS (FAB+): calcd for $C_{23}H_{19}N_2O_2S$ 387.1167, found 387.1170 $[M + H]^+$.

N-(8-Benzenesulfenyl-4-bromo-1-naphthyl)picolinamide (**3l**). The title compound was obtained as a white solid (90.6 mg, 0.21 mmol, 83%). Mp: 165−166 °C. IR (KBr): 3435 (s), 3156 (s), 1676 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 6.81−6.84 (m, 2H), 6.99−7.03 (m, 3H), 7.45−7.48 (m, 1H), 7.52−7.56 (m, 1H), 7.80−7.86 (m, 2H), 7.89 (d, *J* = 8.4, 1H), 8.11 (d, *J* = 7.6, Hz, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 8.46 (d, *J* = 8.4 Hz, 1H), 8.63−8.65 (m, 1H), 12.22 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, rt): δ 120.2, 122.8, 123.8, 126.1, 126.4, 126.9, 127.3, 127.4, 128.7, 129.0 (2C), 130.6, 130.8, 133.8, 134.3, 137.4, 138.4, 148.0, 150.3, 162.7. Anal. Calcd for $C_{22}H_{15}BrN_2OS$: C, 60.70; H, 3.47; N, 6.43. Found: C, 61.02; H, 3.17; N, 6.44.

N-(10-Benzenesulfenyl-1-pyrenyl)picolinamide (**3m**). The title compound was obtained as a yellow solid (66.5 mg, 0.15 mmol, 62%). Mp: 178−179 °C. IR (KBr): 3246 (w), 3048 (w), 1680 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 6.85−6.87 (m, 2H), 6.93−6.97 (m, 3H), 7.51−7.54 (m, 1H), 7.89 (td, *J* = 7.6, 1.6 Hz, 1H), 7.99−8.16 (m, 5H), 8.24 (dd, *J* = 7.6, 1.2 Hz, 1H), 8.28 (d, *J* = 8.4 Hz, 1H), 8.44 (s, 1H), 8.72−8.76 (m, 2H), 12.44 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, rt): δ 122.5, 122.7, 124.3, 124.8, 125.0, 125.2, 125.7, 126.3, 126.4, 126.5, 126.61, 126.63, 126.8, 127.3, 128.2, 128.8, 129.4, 130.5, 131.6, 132.6, 137.3, 137.7, 140.2, 148.1, 150.6, 162.6. Anal. Calcd for $C_{28}H_{18}N_2OS$: C, 78.11; H, 4.21; N, 6.51. Found: C, 77.75; H, 3.95; N, 6.48.

N-[8-Benzenesulfenyl-4-(2-pyridyl)-1-naphthyl]picolinamide (**3p**). The title compound was obtained as a yellow solid (93.4 mg, 0.22 mmol, 86%). Mp: 158−159 °C. IR (KBr): 3179 (m), 3005 (m), 1680 (s) cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$, rt): δ 6.81 (d, *J* = 7.2 Hz, 2H), 6.95−7.00 (m, 3H), 7.34−7.36 (m, 1H), 7.40−7.45 (m, 2H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.80−7.86 (m, 3H), 8.11 (d, *J* = 7.2 Hz, 1H), 8.20 (d, *J* = 7.8 Hz, 1H), 8.47 (d, *J* = 7.8 Hz, 1H), 8.64−8.66 (m, 1H), 8.79−8.80 (m, 1H), 12.41 (s, 1H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 122.3, 122.67, 122.73, 125.4, 125.6, 125.8, 126.0, 126.2, 126.6, 127.7, 128.2, 128.8, 129.4, 134.2, 134.3, 136.85, 136.87, 137.2, 138.1, 138.6, 148.0, 149.5, 150.6, 159.5, 162.8. HRMS (FAB+): calcd for $C_{27}H_{20}N_3OS$ 434.1327, found 434.1343 $[M + H]^+$.

Typical Procedure for Palladium-Catalyzed Site-Selective Direct Selenation of Naphthylamine Derivatives 1 with Diselenides 4: Synthesis of *N*-(8-Phenylselanyl-1-naphthyl)-picolinamide (5a) (Table 5, Entry 1). *N*-(1-Naphthyl)picolinamide (**1a**, 62 mg, 0.25 mmol), diphenyl diselenide (**4a**, 47 mg, 0.15 mmol), and bis(benzonitrile)palladium dichloride (4.8 mg, 0.0125 mmol) were placed in a 20 mL Schlenk tube under an Ar atmosphere. DMSO (0.50 mL) was then added at room temperature. The mixture was stirred at 100 °C for 12 h. After the mixture was allowed to cool to room temperature, saturated sodium thiosulfate solution (5 mL) was added to quench the reaction. The mixture was extracted with dichloromethane (5 mL) three times. The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate = 5/1) to provide **5a** (80.3 mg, 0.20 mmol, 80%). White solid. Mp: 164−165 °C. IR (KBr): 3354 (m), 3073 (w), 1694 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.17−7.22 (m, 3H), 7.30−7.34 (m, 2H), 7.53−7.65 (m, 3H), 7.92−7.98 (m, 2H), 8.13 (d, *J* = 8.4 Hz, 1H), 8.36−8.40 (m, 2H), 8.46 (d, *J* = 8.0 Hz, 1H), 8.71−8.73 (m, 1H), 10.87 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, rt): δ 118.6, 121.0, 122.7, 125.1, 126.7, 126.8, 126.9, 127.1, 127.2, 129.2, 129.4, 131.1, 132.4, 133.8, 135.0, 135.3, 138.0, 148.3, 150.0, 162.4. Anal. Calcd for $C_{22}H_{16}N_2OSe$: C, 65.51; H, 4.00; N, 6.95. Found: C, 65.37; H, 3.69; N, 6.88.

N-[8-(4-Bromophenylselanyl)-1-naphthyl]picolinamide (**5b**). The title compound was obtained as a yellow solid (113.3 mg, 0.23 mmol, 94%). Mp: 181−182 °C. IR (KBr): 3329 (m), 3057 (w), 1697 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.12−7.15 (m, 2H), 7.26−7.30 (m, 2H), 7.54−7.66 (m, 3H), 7.95−7.99 (m, 2H), 8.14 (d, *J* = 8.4 Hz, 1H), 8.36−8.43 (m, 3H), 8.73 (d, *J* = 4.8 Hz, 1H), 10.90 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, rt): δ 118.4, 120.6, 121.1, 122.7, 124.2, 126.9, 127.0, 127.1, 127.4, 129.1, 131.7, 132.2, 132.4, 134.3, 134.9, 135.9, 138.0, 148.3, 149.9, 162.4. Anal. Calcd for $C_{22}H_{15}BrN_2OSe$: C, 54.79; H, 3.14; N, 5.81. Found: C, 54.62; H, 2.97; N, 5.70.

N-[8-(4-Chlorophenylselanyl)-1-naphthyl]picolinamide (**5c**). The title compound was obtained as a yellow solid (96.5 mg, 0.22 mmol, 88%). Mp: 170−171 °C. IR (KBr): 3329 (m), 3057 (w), 1697 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.13−7.16 (m, 2H), 7.20−7.23 (m, 2H), 7.55−7.66 (m, 3H), 7.94−8.00 (m, 2H), 8.14 (d, *J* = 8.0 Hz, 1H), 8.37−8.42 (m, 3H), 8.72−8.74 (m, 1H), 10.91 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, rt): δ 118.4, 121.1, 122.7, 124.4, 126.87, 126.94, 127.1, 127.4, 129.1, 129.5, 130.9, 132.1, 132.7, 134.2, 134.9, 135.7, 138.0, 148.3, 149.9, 162.4. HRMS (FAB+): calcd for $C_{22}H_{15}{}^{35}ClN_2O^{80}Se$ 438.0038, found 438.0019 $[M]^+$.

N-[8-(4-Methoxyphenylselanyl)-1-naphthyl]picolinamide (**5d**). The title compound was obtained as a yellow solid (80.0 mg, 0.18 mmol, 74%). Mp: 117−118 °C. IR (KBr): 3354 (m), 3069 (w), 1690 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 3.78 (s, 3H), 6.81 (d, *J* = 8.8 Hz, 2H), 7.42 (d, *J* = 8.8 Hz, 2H), 7.52−7.64 (m, 3H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.95 (t, *J* = 8.0 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 8.28 (d, *J* = 8.0 Hz, 1H), 8.35 (d, *J* = 7.6 Hz, 1H), 8.41 (d, *J* = 7.6 Hz, 1H), 8.71 (d, *J* = 4.0 Hz, 1H), 10.78 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, rt): δ 55.4, 115.3, 118.8, 121.0, 121.1, 122.6, 126.72, 126.74, 126.9, 127.1, 127.5, 128.4, 132.5, 132.8, 134.1, 134.9, 137.9, 148.3, 150.0, 159.5, 162.3. Anal. Calcd for $C_{23}H_{18}N_2O_2Se$: C, 63.74; H, 4.19; N, 6.46. Found: C, 63.66; H, 3.85; N, 6.49.

N-{8-[2-(Trifluoromethyl)phenylselanyl]-1-naphthyl}picolinamide (**5e**). The title compound was obtained as a white solid (69.7 mg, 0.15 mmol, 59%). Mp: 144 °C. IR (KBr): 3356 (m), 3057 (w), 1697 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 6.87 (d, *J* = 8.0 Hz, 1H), 7.07 (t, *J* = 8.0 Hz, 1H), 7.18 (t, *J* = 8.0 Hz, 1H), 7.54−7.66 (m, 4H), 8.00 (t, *J* = 8.0 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 8.17 (d, *J* = 8.4 Hz, 1H), 8.39−8.42 (m, 2H), 8.48 (d, *J* = 8.0 Hz, 1H), 8.73−8.76 (m, 1H), 10.99 (s, 1H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 118.4, 121.0, 122.8, 122.9 (q, J_{C-F} = 2.9 Hz), 124.4 (q, J_{C-F} = 272 Hz), 125.8, 126.9 (q, J_{C-F} = 5.6 Hz), 127.0, 127.1, 127.2, 127.7, 128.9 (q, J_{C-F} = 31 Hz), 129.4, 131.5, 132.2, 133.0, 135.0, 135.5, 137.9, 138.1, 148.3, 149.8, 162.4; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$, rt): δ −61.7. Anal. Calcd for $C_{23}H_{15}F_3N_2OSe$: C, 58.61; H, 3.21; N, 5.94. Found: C, 58.43; H, 3.11; N, 5.84.

N-[8-(o-Tolylselanyl)-1-naphthyl]picolinamide (**5f**). The title compound was obtained as a yellow solid (78.5 mg, 0.19 mmol, 75%). Mp: 138−139 °C. IR (KBr): 3335 (m), 3053 (w), 1692 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 2.48 (s, 3H), 6.90−6.96 (m, 2H), 7.09−7.14 (m, 1H), 7.20−7.22 (m, 1H), 7.54−7.66 (m, 3H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.97 (t, *J* = 8.0 Hz, 1H), 8.14 (d, *J* = 8.0 Hz, 1H), 8.36−8.41 (m, 3H), 8.72−8.73 (m, 1H), 10.88 (s, 1H). $^{13}C\{^1H\}$

NMR (100 MHz, $CDCl_3$, rt): δ 22.1, 118.7, 121.0, 122.7, 124.7, 126.8, 126.85 (3C), 127.1, 127.2, 129.0, 130.3, 131.3, 132.9, 133.7, 134.8, 135.0, 138.0, 138.2, 148.3, 150.0, 162.4. Anal. Calcd for $C_{23}H_{18}N_2OSe$: C, 66.19; H, 4.35; N, 6.71. Found: C, 66.06; H, 4.22; N, 6.63.

*N-[8-(2-Thienylselanyl)-1-naphthyl]picolinamide (**5g**).* The title compound was obtained as a yellow solid (40.2 mg, 0.098 mmol, 39%). Mp: 151−152 °C. IR (KBr): 3354 (m), 3076 (w), 1694 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.01−7.03 (m, 1H), 7.34 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.42 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.52−7.55 (m, 1H), 7.61−7.68 (m, 3H), 7.95 (t, *J* = 7.6 Hz, 1H), 8.08−8.13 (m, 1H), 8.28 (d, *J* = 7.6 Hz, 1H), 8.35 (d, *J* = 7.6 Hz, 1H), 8.43−8.47 (m, 1H), 8.70−8.72 (m, 1H), 10.77 (s, 1H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 118.8, 121.1, 122.6, 124.0, 126.74, 126.75, 126.90, 126.95, 127.8, 128.1, 128.3, 131.3, 131.6, 132.8, 133.5, 136.2, 137.9, 148.2, 149.9, 162.3. HRMS (FAB+): calcd for $C_{20}H_{15}N_2OS^{80}Se$ 411.0070, found 411.0092 $[M + H]^+$.

Preparation of 1a-*d* (Scheme 2).[8a] *N*-(1-Naphthyl)picolinamide (**1a**, 248 mg, 1.0 mmol) and bis(benzonitrile)palladium dichloride (19 mg, 0.050 mmol) were placed in a 20 mL Schlenk tube under an Ar atmosphere. D_2O (800 mg, 40 mmol) and DMSO (2.4 mL) were then added at room temperature. The resulting mixture was stirred at 100 °C for 12 h. After being cooled to room temperature, the reaction mixture was diluted with ethyl acetate (5 mL) and filtered through a pad of Celite. The filtrate was washed with water (5 mL) three times, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate = 3/1), providing **1a-*d*** (228 mg, 0.92 mmol, 92% yield, 92% D incorporation).

Procedure for Hydrolysis of 3a: Synthesis of 8-Benzenesulfenyl-1-naphthylamine (6) (Scheme 7).[8a] Picolinamide **3a** (36 mg, 0.10 mmol) and sodium hydroxide (96 mg, 2.4 mmol) were placed in a 20 mL Schlenk tube and dissolved in ethanol (1.2 mL) under an Ar atmosphere. The resulting mixture was stirred at reflux for 12 h. The reaction mixture was allowed to cool to room temperature, diluted with ethyl acetate (5 mL), filtered through Celite, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate = 5/1) to provide **6** (19.7 mg, 0.078 mmol, 78%) as a yellow liquid. Bp: 230 °C/2.0 Torr. IR (neat): 3458 (m), 3350 (m), 1611 (s), 1337 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 5.28 (brs, 2H), 6.73−6.76 (m, 1H), 7.06−7.14 (m, 3H), 7.19−7.23 (m, 2H), 7.26−7.30 (m, 2H), 7.34 (t, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 7.2 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, rt): δ 112.3, 118.8, 123.2, 125.3, 125.7, 126.6, 126.8, 126.9, 129.0, 131.6, 136.9, 137.3, 138.7, 144.6. HRMS (FAB+): calcd for $C_{16}H_{13}NS$ 251.0769, found 251.0776 $[M]^+$.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures; characterization data for all the compounds; X-ray data for **3a**, including CIF. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(10) Crystallographic data for the structure of **3a** have been deposited with the Cambridge Crystallographic Data Centre as the deposition number CCDC 1027098. This data can be obtained free of charge from on application to CCDC, 12 Union Road, Cambridge

CB2 1EZ, UK [fax: +44 (0)1223 336033 or www.ccdc.cam.ac.uk/data_request/cif].
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