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Copper-Mediated Dehydrogenative Biaryl Coupling of Naphthylamines and 1,3-Azoles

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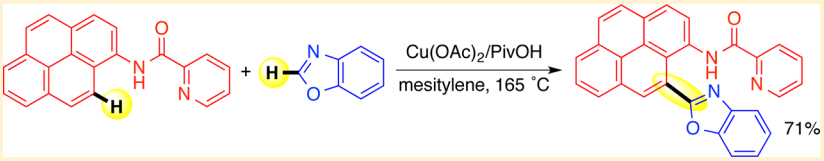
Supporting Information



ABSTRACT: A copper-mediated dehydrogenative biaryl cross-coupling of naphthylamines and 1,3-azoles has been developed. The key to its success is the introduction of N,N-bidentate coordination system based on the picolinamide directing group. The reaction proceeds smoothly without precious transition metal catalysts and provides highly π-extended heterobiaryls directly.

1. INTRODUCTION

In past two decades, transition-metal-promoted C−C bond forming reactions involving C−H cleavage have grown rapidly because of their higher synthetic efficiency compared to the conventional cross-coupling technologies with organic halides and organometallic reagents.[1] Among them, metal-mediated dehydrogenative biaryl coupling of two arenes is now one of the hottest research fields in C−H activation chemistry, because it can obviate preactivation steps of both starting arenes via the 2-fold C−H cleavage. In general, such transformations require palladium,[2] rhodium,[3] and ruthenium[4] catalysts. On the other hand, our group[5] and others[6] have focused on copper salts and complexes as common, abundant, and less expensive alternatives to the above precious metals and developed copper-mediated direct biaryl couplings of some heteroarenes. However, further development of new reaction systems and expansion of substrate scopes are still strongly desired.

Recently, Daugulis reported the copper-mediated direct sulfenylation, amination, and fluorination of arenes with the aid of his original N,N-bidentate coordinating functions including aminoquinoline and picolinamide systems.[7] Around the same time, we also succeeded in the application of aminoquinoline-based coordination strategy to the copper-promoted direct biaryl coupling of benzoic acid derivatives and 1,3-azoles.[5d] In the course of our further study, we have explored other effective bidentate directors to expand the utility of copper-mediated biaryl coupling. As a result, we have found that dehydrogenative direct biaryl coupling of naphthylamines and 1,3-azoles efficiently proceeds by employing a picolinamide-based directing group.[8−11] The present reaction enables the direct heteroarylation at the peri position of the 1-substituted naphthalene, which is in marked contrast and complementary to the aminoquinoline system, giving products coupled at the 2- as well as ortho-positions[5d] and hence provides a rapid and concise approach to 1-amino-8-heteroarylnaphthalenes of important scaffolds in functional materials as well as ligands for metal centers.[12]

2. RESULTS AND DISCUSSION

We began our optimization studies with 1-naphthylamine derivative **1a** and benzoxazole (**2a**) as model substrates (Table 1). Different from the 8-aminoquinoline bidentate system,[5d] $Cu(OAc)_2$ (2.0 equiv) alone did not promote the dehydrogenative coupling at 150 °C in *o*-xylene (entry 1), but the addition of AcOH (1.0 equiv) and higher reaction temperature (160 °C in mesitylene) resulted in formation of desired **3aa** in 20% NMR yield (entry 2). An increase in the amount of $Cu(OAc)_2$ to 3.0 equiv further improved the reaction efficiency (entry 3). Even at 160 °C, AcOH was essential for the good conversion (entry 4), while an excess amount of AcOH was detrimental (entries 5 and 6). Next, some representative carboxylic acids were screened (entries 7−10). As far as we tested, any acid additives were effective for the reaction, with PivOH proving to be optimal (entry 8). Other acetate-type copper salts such as $Cu(OCOi\text{-}Pr)_2$ and Cu(2-ethylhexanoate)$_2$ diminished the yield (entries 11 and 12). Molecular oxygen also gave negative impact on the reaction (entries 13 and 14). Although additional investigation into the solvent system also did not improve the yield (entries 15 and 16), we finally obtained **3aa** in 73% yield by a slight increase of reaction temperature (entry 17). In this case, the homocoupling product of **2a** was also formed but in only 13% yield (0.032 mmol, based on 0.25 mmol). Even under equimolar conditions (entry 18), we could get a comparable yield of **3aa** without formation of the homocouplng product, judged by GC and TLC analysis. Thus, the cross-coupling reaction occurred predominantly over the homocoupling reaction of **2a**. Notably, regardless of conditions, the C−C bond formation occurred site-selectively at the peri position of

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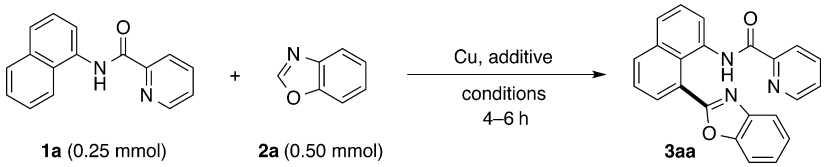
Table 1. Optimization Studies for Copper-Mediated Dehydrogenative Biaryl Coupling of 1-Naphthylamine 1a with Benzoxazole (2a)[a]

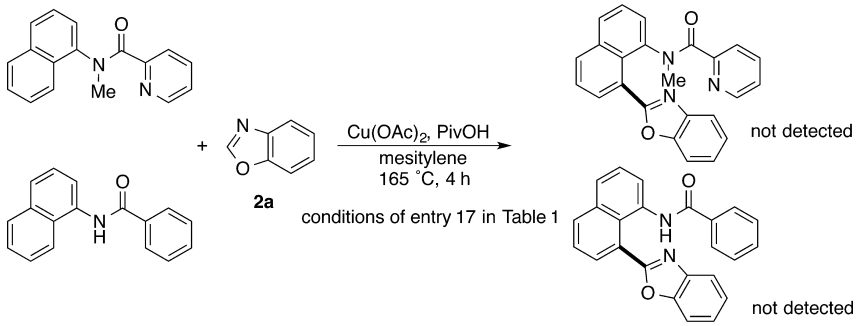


1a (0.25 mmol) **2a** (0.50 mmol) **3aa**

entry	Cu (mmol)	additive (mmol)	conditions	yield (%)[b]
1	$Cu(OAc)_2$ (0.50)	none	*o*-xylene, 150 °C, N_2	trace
2	$Cu(OAc)_2$ (0.50)	AcOH (0.25)	mesitylene, 160 °C, N_2	20
3	$Cu(OAc)_2$ (0.75)	AcOH (0.25)	mesitylene, 160 °C, N_2	61 (57)
4	$Cu(OAc)_2$ (0.75)	none	mesitylene, 160 °C, N_2	trace
5	$Cu(OAc)_2$ (0.75)	AcOH (0.50)	mesitylene, 160 °C, N_2	48
6	$Cu(OAc)_2$ (0.75)	AcOH (0.75)	mesitylene, 160 °C, N_2	5
7	$Cu(OAc)_2$ (0.75)	$EtCO_2H$ (0.25)	mesitylene, 160 °C, N_2	43
8	$Cu(OAc)_2$ (0.75)	PivOH (0.25)	mesitylene, 160 °C, N_2	66 (65)
9	$Cu(OAc)_2$ (0.75)	1-$AdCO_2H$ (0.25)	mesitylene, 160 °C, N_2	65
10	$Cu(OAc)_2$ (0.75)	2,6-$Me_2C_6H_3CO_2H$ (0.25)	mesitylene, 160 °C, N_2	57
11	$Cu(OCOi\text{-}Pr)_2$ (0.75)	PivOH (0.25)	mesitylene, 160 °C, N_2	20
12	Cu(2-ethylhexanoate)$_2$ (0.75)	PivOH (0.25)	mesitylene, 160 °C, N_2	14
13	$Cu(OAc)_2$ (0.75)	PivOH (0.25)	mesitylene, 160 °C, air	23
14	$Cu(OAc)_2$ (0.75)	PivOH (0.25)	mesitylene, 160 °C, O_2	4
15	$Cu(OAc)_2$ (0.75)	PivOH (0.25)	DMF, 165 °C, N_2	59
16	$Cu(OAc)_2$ (0.75)	PivOH (0.25)	DMSO, 180 °C, N_2	24
17	$Cu(OAc)_2$ (0.75)	PivOH (0.25)	mesitylene, 165 °C, N_2	77 (73)
18[c]	$Cu(OAc)_2$ (0.75)	PivOH (0.25)	mesitylene, 165 °C, N_2	75

[a]Reaction conditions: Cu, additive, **1a** (0.25 mmol), **2a** (0.50 mmol), solvent (1.5 mL). [b]^{1}H NMR yield. Yield after purification is given in parentheses. [c]With 0.25 mmol of **2a**.

Scheme 1. Control Experiments



naphthalene ring but not at the position ortho to the amide group, probably resulting from a preferable formation of a five-membered metalacycle (vide infra).[13] Moreover, neither *N*-methyl nor benzoyl analogue of **1a** coupled with **2a** (Scheme 1), and thus anionic and neutral N,N-bidentate chelation nature of the picolinamide in **1a** was critical in this transformation.

With the promising conditions in hand, we then investigated the substrate scope of 1,3-azoles. The representative examples are shown in Table 2. In most cases, the use of 2.0 equiv of 1,3-azoles was found to be essential for the completion of the reaction. In addition to the simple benzoxazole **2a**, methyl- and chloro-substituted benzoxazoles participated in the reaction (**3ab** and **3ac**). The monocyclic 5-phenyloxazole also could be employed to construct the naphthalene−oxazole−benzene π-conjugate system readily (**3ad**). Moreover, electronically diverse methyl, methoxy, and trifluoromethyl groups (**3ae**, **3af**, **3ag**, and **3ah**) were equally tolerated under identical reaction conditions. Additionally notable is high compatibility with cyano, methoxycarbonyl, and nitro functions (**3ai**, **3aj**, and **3ak**). The oxazole that bears the naphthyl substituent also underwent the coupling with **1a** without any difficulties (**3al**). Among other azoles we tested, thiazoles showed acceptable reaction efficiency; parent thiazole and 4,5-dimethylthiazole reacted with **1a** to afford the corresponding π-extended thiazole cores (**4aa** and **4ab**). However, attempts to apply benzothiazoles, imidazoles, triazoles, and 1,3,4-oxadiazoles remained unsuccessful, and products were detected only in less than 20% yield (data not shown).

Subsequently, substitution effects in the 1-naphthylamine were briefly evaluated (Figure 1). The introduction of electron-withdrawing cyano and nitro groups at the C4 position gave only a minor impact on reaction efficiency (**3ca**, **3 cd**, **3da**, and **3dd**), whereas the electron-donating methoxy substituent largely dropped the yield (**3ba**), likely because of the decrease of acidity of NH, which hampers effective cyclometalation (vide infra). It is noteworthy that the reaction of 1-aminopyrene also

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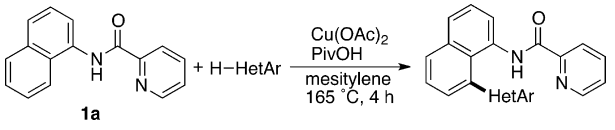
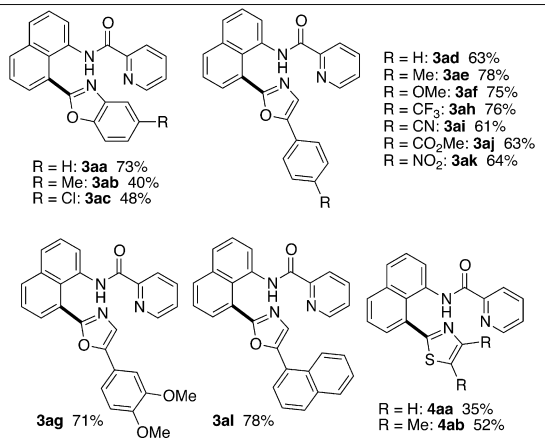
Table 2. Copper-Mediated Dehydrogenative Biaryl Coupling of 1-Naphthylamine Derivative 1a with Various 1,3-Azoles[a]



product, yield



[a]Reaction conditions: $Cu(OAc)_2$ (0.75 mmol), PivOH (0.25 mmol), **1a** (0.25 mmol), H-HetAr (0.50 mmol), mesitylene (1.5 mL), 165 °C, 4 h, N_2.

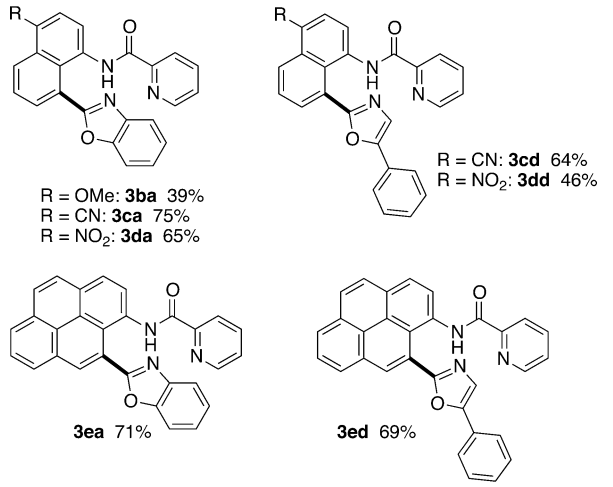
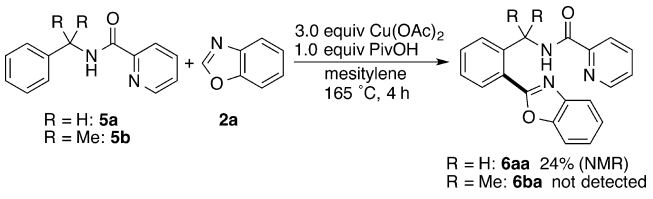


Figure 1. Products of copper-mediated dehydrogenative biaryl coupling of some 1-naphthylamine derivatives.

proceeded very smoothly to furnish the heteroarylated pyrenes **3ea** and **3ed**, demonstrating applicability of this protocol to higher polycondensed aromatic systems.

We also tested structurally related benzylamine derivatives **5** (Scheme 2). However, they were not promising substrates

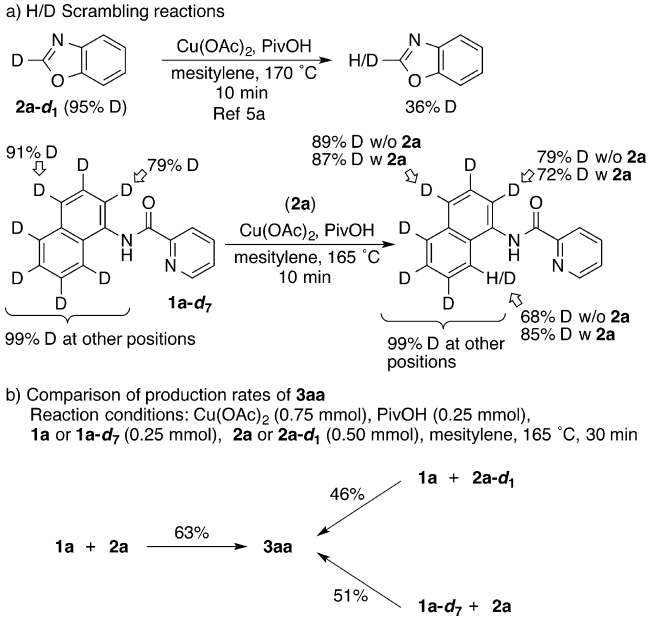
Scheme 2. Preliminary Results with Benzylamine Derivatives 5



under present conditions, while comparable reactivity to the aminoquinoline system was observed in some precedented work.[7,9,10] The exact reason is not clear, but higher planarity associated with the naphthalene may play an important role in the C−H cleavage step.

The following deuterium-labeling experiments provided some mechanistic insight. At an early stage of the reaction (10 min), both **1a**-d_7 and **2a**-d_1 underwent the H/D scrambling, but the larger deuterium content of **2a**-d_1 was lost (Scheme 3a). These results are suggestive of the more

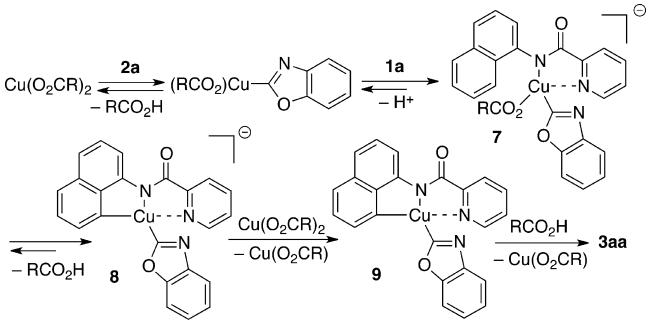
Scheme 3. Deuterium-Labeling Experiments



rapid C−H metalation of benzoxazole (**2a**) than that of naphthylamine **1a**. Although correct values of the kinetic isotope effect could not be calculated by the partial but considerable H/D exchange of both substrates, comparison of production rates of **3aa** indicated no rate-determining C−H cleavage of **1a** and **2a** (Scheme 3b): the introduction of deuterium into either **1a** or **2a** gave only minor impact on the yield of **3aa**. This is in marked contrast with the aminoquinoline-based system where C−H cleavage appeared to be irreversible rate-determining step.[5d]

On the basis of the above results and literature information, although the present mechanistic consideration is premature, we are tempted to assume the reaction mechanism of **1a** with **2a** as shown in Scheme 4. An initial C−H cupration of

Scheme 4. Plausible Mechanism (R = Me or *t*-Bu)



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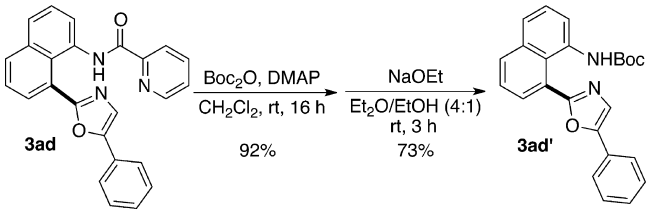
relatively acidic **2a** is followed by N,N-bidentate coordination with **1a** to generate the organocopper intermediate **7**.[14] Subsequent C−H cleavage of the **1a** followed by oxidation (disproportionation) with additional Cu(II) forms the Cu(III) metalacycle **9**.[15,16] The formation of corresponding heterobiaryl **3aa** then follows from productive reductive elimination.[17] Although the origin of selectivity for the cross-coupling over the homocoupling remains to be elucidated, the electron-withdrawing nature of 1,3-azole ligand is believed to play a key role. The relatively high acidity of NH in **1a** can accelerate the cyclometalation steps (**7** and/or **8**). The site-selectivity can be determined by formation of kinetically favored five-membered metelacycle **8**. The exact role of PivOH remains unclear, but it can accelerate C−H cleavage of **1a** through a concerted-metalation−deprotonation pathway.[18] The rate-limiting step remains to be elucidated, but it can involve the oxidation of Cu(II) into Cu(III) or reductive elimination.

Finally, we attempted the removal of the directing group from the coupling product. To our delight, the protection of the NH moiety in **3ad** with Boc_2O was followed by ethanolysis with NaOEt in Et_2O/EtOH (4:1, v/v) to give **3ad′** in a good overall yield (Scheme 5).

Scheme 5. Removal of the Picolinamide Directing Group



3. CONCLUSION

We have developed a copper-mediated biaryl coupling of 1-naphthylamines and 1,3-azoles via 2-fold C−H cleavage, providing naphthalene−azole π-conjugations directly.[19] The key to its success is the introduction of the N,N-double coordination strategy based on a picolinamide system. Moreover, the directing group is readily removable after the coupling event. Detailed mechanistic studies and further development of relevant copper-mediated C−H functionalization are ongoing in our laboratory.

4. EXPERIMENTAL SECTION

Instrumentation and Chemicals. ^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, for $CDCl_3$ solutions. HRMS data were obtained by EI using a double focusing mass spectrometer. GC analysis was carried out using a silicon OV-17 column (i.d. 2.6 mm × 1.5 m) or a CBP-1 capillary column (i.d. 0.5 mm × 25 m). Gel permeation chromatography (GPC) was performed with a $CHCl_3$ eluent (3.5 mL/min, UV detector). Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Mesitylene was freshly distilled from CaH_2 prior to use. Naphthylamine derivatives **1** were prepared from the parent amines and picolinoyl chloride (see Experimental Section). 5-Substituted benzoxazoles were obtained through the condensation of 2-aminophenol derivatives with triethyl orthoformate.[20] 5-Aryloxazoles were prepared by the van Leusen reaction with TosMIC and the corresponding aldehydes.[21] Deuterium-labeling **2a**-d_1 was synthesized according to the literature.[22] Unless otherwise noted, all reactions were carried out under N_2 conditions.

Preparation of Naphthylamine Derivatives 1. Synthesis of **1a** is representative. To a mixture of 1-naphthylamine (1.4 g, 10 mmol), picolinoyl chloride hydrochloride (2.0 g, 11 mmol), and 4-(*N*,*N*-dimethylamino)pyridine (DMAP, 367 mg, 3.0 mmol) in CH_2Cl_2 (30 mL) was added Et_3N (3.0 mL, 22 mmol), and the resulting mixture was stirred at rt for 4 h. The mixture was quenched with water and extracted with CH_2Cl_2. The combined organic layer was washed with brine and dried over sodium sulfate. After concentration in vacuo, the residual solids were triturated with hexane under sonication and then collected to give *N*-(naphthalen-1-yl)picolinamide (**1a**, 2.3 g, 9.2 mmol) in 92% yield in an analytically pure form (>95% purity judged by ^{1}H NMR). The spectrum data were in agreement with the literature.[11] The obtained material can be used for the coupling reaction without further purification.

Preparation of 1a-d_7. $NaNO_3$ (570 mg, 6.7 mmol) was dissolved in TFA (28 mL), and naphthalene-d_8 (99% D, 1.0 g, 7.35 mmol) was added in several portions at room temperature under air. The mixture was stirred for 5 h at the same temperature, cooled to 0 °C with an ice water bath, and then neutralized with 6 M aq NaOH. The organic phase was extracted with diethyl ether and evaporated under reduced pressure. The crude 1-nitronaphthalene-d_7 obtained was used for the next step without further purification.

To a mixture of the above 1-nitronaphthalene-d_7 and concentrated aq HCl (ca. 11 M, 7.0 mL) in EtOH (15 mL), Sn powder (3.5 g, 29 mmol) was added in several portions, and the resulting mixture was stirred at room temperature under air. After 6 h, volatile materials were evaporated in vacuo, and residue was dissolved in water and diethyl ether. The mixture was neutralized with saturated aq K_2CO_3 and then filtered through a pad of Celite. The filtrate was extracted with ethyl acetate, concentrated under reduced pressure, and purified by column chromatography on silica gel with hexane/ethyl acetate (3/1, v/v) to afford 1-naphthylamine-d_7 (720 mg, 4.7 mmol) in a 65% two-step yield. The deuterium content at each position in the naphthalene ring was determined by ^{1}H and ^{2}H NMR analysis, as follows: 79% D at C2; 91% D at C4; 99% D at other positions.

The attachment of the picolinoyl moiety to 1-naphthylamine-d_7 was performed under the same conditions as those for **1a**, and purification by recrystallization from toluene furnished *N*-(naphthalen-1-yl)-picolinamide-d_7 (**1a**-d_7, 930 mg, 3.7 mmol) in 77% yield.

Typical Procedure for Copper-Mediated Dehydrogenative Biaryl Coupling. Synthesis of **3aa** is representative (Table 1, entry 17). $Cu(OAc)_2$ (136 mg, 0.75 mmol), *N*-(naphthalen-1-yl)-picolinamide (**1a**, 62 mg, 0.25 mmol), and benzoxazole (**2a**, 60 mg, 0.50 mmol) were placed in a 20 mL two-necked reaction flask, which was filled with nitrogen by using the standard Schlenk technique. A solution of PivOH (26 mg, 0.25 mmol) in mesitylene (2.5 mL) was then added to the flask, and the suspension was stirred for 4 h at 165 °C. The resulting mixture was allowed to cool to rt and was then quenched with water. A small amount of ethylenediamine was then added to dissolve the residual copper salts into the aqueous phase. Extraction with ethyl acetate, concentration under reduced pressure, and silica gel column purification with hexane/ethyl acetate (2/1, v/v) afforded *N*-(8-(benzo[*d*]oxazol-2-yl)naphthalen-1-yl)picolinamide (**3aa**, 66 mg, 0.18 mmol) in 73% yield.

*N-{8-(Benzo[d]oxazol-2-yl)naphthalen-1-yl}picolinamide (**3aa**).* Purified by column chromatography on silica gel with hexane/ethyl acetate (2:1, v/v) as an eluent; 66 mg (73%), mp 177−178 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (ddd, J = 1.2 Hz, 4.8 Hz, 7.6 Hz, 1H), 7.20 (td, J = 1.2 Hz, 8.0 Hz, 1H), 7.27 (td, J = 1.2 Hz, 7.6 Hz, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.57−7.69 (m, 4H), 7.74 (d, J = 7.6 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.97 (dd, J = 1.2 Hz, 7.2 Hz, 1H), 8.03 (dt, J = 1.2 Hz, 7.6 Hz, 1H), 8.07 (d, J = 7.2 Hz, 1H), 8.10 (dd, J = 1.2 Hz, 8.4 Hz, 1H), 10.41 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 110.5, 120.0, 122.0, 122.9, 124.2, 124.7, 125.8, 126.2, 126.4, 126.6, 127.3, 131.9, 132.2, 132.7, 135.3, 136.8, 142.1, 147.1, 147.4, 149.1, 151.2, 162.9, 164.6; HRMS (EI) m/z (M^+) calcd for $C_{23}H_{15}N_3O_2$: 365.1164, found: 365.1163.

*N-{8-(5-Methylbenzo[d]oxazol-2-yl)naphthalen-1-yl}-picolinamide (**3ab**).* Purified by column chromatography on silica gel with hexane/ethyl acetate (2:1, v/v) as an eluent; 38 mg (40%), mp 181−182 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.10 (s, 3H), 6.98 (ddd, J = 0.4 Hz, 1.6 Hz, 8.4 Hz, 1H),

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7.10 (ddd, J = 1.2 Hz, 4.8 Hz, 7.6 Hz, 1H), 7.21 (d, J = 8.4 Hz, 1H), 7.48 (t, J = 0.8 Hz, 1H), 7.57 (dd, J = 7.2 Hz, 8.4 Hz, 1H), 7.62−7.68 (m, 3H), 7.88 (dd, J = 1.2 Hz, 8.0 Hz, 1H), 7.94 (dd, J = 1.6 Hz, 6.8 Hz, 1H), 8.00−8.05 (m, 2H), 8.08 (dd, J = 1.2 Hz, 8.4 Hz, 1H), 10.38 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 21.4, 109.8, 119.9, 122.0, 123.1, 124.7, 125.5, 126.0, 126.2, 126.48, 126.54, 127.3, 131.9, 132.0, 132.5, 133.8, 135.2, 136.7, 142.3, 147.4, 149.2, 149.4, 162.9, 164.6; HRMS (EI) m/z (M^+) calcd for $C_{24}H_{17}N_3O_2$: 379.1321, found: 379.1320.

*N-{8-(5-Chlorobenzo[d]oxazol-2-yl)naphthalen-1-yl}-picolinamide (**3ac**).* Purified by column chromatography on silica gel with hexane/ethyl acetate (2:1, v/v) as an eluent; 48 mg (48%), mp 188−190 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (dd, J = 2.0 Hz, 8.4 Hz, 1H), 7.19−7.24 (m, 2H), 7.59 (dd, J = 7.2 Hz, 8.0 Hz, 1H), 7.64−7.70 (m, 3H), 7.81 (ddd, J = 0.8 Hz, 1.6 Hz, 4.8 Hz, 1H), 7.91 (d, J = 7.2 Hz, 1H), 7.92 (dd, J = 1.6 Hz, 6.8 Hz, 1H), 7.99 (d, J = 7.6 Hz, 1H), 8.03 (dt, J = 1.2 Hz, 8.0 Hz, 1H), 8.12 (dd, J = 0.8 Hz, 8.0 Hz, 1H), 10.13 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 111.2, 119.9, 122.2, 122.5, 124.7, 125.1, 125.9, 126.75, 126.81 (two signals were overlapped), 127.5, 129.6, 131.8, 132.0, 132.9, 135.2, 137.0, 143.2, 147.5, 149.1, 149.7, 162.9, 166.1; HRMS (EI) m/z (M^+) calcd for $C_{23}H_{14}ClN_3O_2$: 399.0775, found: 399.0773.

*N-{8-(5-Phenyloxazol-2-yl)naphthalen-1-yl}picolinamide (**3ad**).* Purified by column chromatography on silica gel with hexane/ethyl acetate (2:1, v/v) as an eluent; 62 mg (63%), mp 141−143 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20−7.30 (m, 4H), 7.23 (s, 1H), 7.41 (dd, J = 1.6 Hz, 8.4 Hz, 2H), 7.49−7.56 (m, 2H), 7.63 (t, J = 8.0 Hz, 1H), 7.83−7.88 (m, 3H), 7.98 (d, J = 7.2 Hz, 1H), 8.03 (d, J = 8.4 Hz, 1H), 8.18 (dd, J = 0.8 Hz, 4.4 Hz, 1H), 10.19 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 122.2, 122.7, 123.1, 123.8, 124.7, 125.9, 126.35, 126.40, 126.9, 127.3, 127.4, 128.1, 128.5, 131.6, 131.9, 132.0, 135.2, 136.6, 147.4, 149.4, 151.7, 162.2, 162.8; HRMS (EI) m/z (M^+) calcd for $C_{25}H_{17}N_3O_2$: 391.1321, found: 391.1324.

*N-[8-{5-(4-Methylphenyl)oxazol-2-yl}naphthalen-1-yl]-picolinamide (**3ae**).* Purified by column chromatography on silica gel with hexane/ethyl acetate (2:1, v/v) as an eluent; 79 mg (78%), mp 65−66 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 3H), 7.11 (d, J = 8.0 Hz, 2H), 7.18 (s, 1H), 7.22 (ddd, J = 1.2 Hz, 4.8 Hz, 7.6 Hz, 1H), 7.32 (d, J = 8.4 Hz, 2H), 7.54 (td, J = 1.6 Hz, 7.6 Hz, 2H), 7.63 (t, J = 7.6 Hz, 1H), 7.84−7.91 (m, 3H), 7.99 (d, J = 7.2 Hz, 1H), 8.03 (dd, J = 1.2 Hz, 8.0 Hz, 1H), 8.20 (ddd, J = 0.8 Hz, 1.6 Hz, 4.8 Hz, 1H), 10.25 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 21.3, 122.1, 122.3, 123.2, 123.9, 124.77, 124.81, 126.0, 126.3, 126.4, 126.8, 127.3, 129.2, 131.6, 131.9, 132.1, 135.3, 136.7, 138.2, 147.4, 149.5, 152.1, 161.9, 162.8; HRMS (EI) m/z (M^+) calcd for $C_{26}H_{19}N_3O_2$: 405.1477, found: 405.1474.

*N-[8-{5-(4-Methoxyphenyl)oxazol-2-yl}naphthalen-1-yl]-picolinamide (**3af**).* Purified by column chromatography on silica gel with hexane/ethyl acetate (2:1, v/v) as an eluent; 79 mg (75%), mp 136−137 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80 (s, 3H), 6.83 (dd, J = 2.0 Hz, 6.8 Hz, 2H), 7.10 (s, 1H), 7.23 (ddd, J = 1.2 Hz, 4.8 Hz, 7.6 Hz, 1H), 7.34 (dd, J = 2.0 Hz, 6.8 Hz, 2H), 7.50−7.52 (m, 2H), 7.63 (t, J = 8.0 Hz, 1H), 7.83−7.90 (m, 3H), 7.98 (d, J = 7.2 Hz, 1H), 8.02 (dd, J = 1.2 Hz, 8.0 Hz, 1H), 8.21 (ddd, J = 1.2 Hz, 1.6 Hz, 4.8 Hz, 1H), 10.22 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 55.2, 114.0, 120.4, 122.21, 122.19, 123.2, 124.7, 125.4, 125.9, 126.26, 126.32, 126.8, 127.3, 131.6, 131.8, 132.0, 135.2, 136.7, 147.4, 149.4, 151.8, 159.6, 161.6, 162.8; HRMS (EI) m/z (M^+) calcd for $C_{26}H_{19}N_3O_3$: 421.1426, found: 421.1423.

*N-[8-{5-(3,4-Dimethoxyphenyl)oxazol-2-yl}naphthalen-1-yl]-picolinamide (**3ag**).* Purified by column chromatography on silica gel with hexane/ethyl acetate (2:1, v/v) as an eluent; 80 mg (71%), mp 200−202 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.88 (s, 3H), 3.89 (s, 3H), 6.76 (d, J = 8.4 Hz, 1H), 6.91 (d, J = 2.0 Hz, 1H), 6.94 (dd, J = 2.0 Hz, 8.4 Hz, 1H), 7.11 (s, 1H), 7.22 (ddd, J = 1.2 Hz, 4.8 Hz, 7.6 Hz, 1H), 7.52−7.57 (m, 2H), 7.63 (t, J = 7.6 Hz, 1H), 7.83−7.89 (m, 3H), 7.97 (d, J = 7.2 Hz, 1H), 8.04 (d, J = 8.0 Hz, 1H), 8.24 (dd, J = 0.8 Hz, 4.0 Hz, 1H), 10.11 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 55.9, 55.9, 107.2, 111.1, 116.7, 120.6, 121.5, 122.1, 123.2, 124.8, 125.9, 126.3, 126.9, 127.3, 131.6, 131.8, 132.0, 135.2, 136.6, 147.4, 148.9, 149.1, 149.4, 151.8, 161.6, 162.7 (One signal was overlapped by other ones); HRMS (EI) m/z (M^+) calcd for $C_{27}H_{21}N_3O_4$: 451.1532, found: 451.1531.

*N-[8-{5-(4-(Trifluoromethyl)phenyl)oxazol-2-yl}naphthalen-1-yl]-picolinamide (**3ah**).* Purified by column chromatography on silica gel with hexane/ethyl acetate (2:1, v/v) as an eluent; 87 mg (76%), mp 128−129 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (ddd, J = 1.2 Hz, 4.8 Hz, 7.6 Hz, 1H), 7.32 (s, 1H), 7.47−7.59 (m, 6H), 7.66 (t, J = 8.0 Hz, 1H), 7.84 (ddd, J = 1.2 Hz, 2.8 Hz, 7.2 Hz, 2H), 7.91 (d, J = 8.4 Hz, 1H), 7.94 (d, J = 7.2 Hz, 1H), 8.08 (dd, J = 1.2 Hz, 8.4 Hz, 1H), 8.22 (ddd, J = 0.8 Hz, 1.6 Hz, 4.8 Hz, 1H), 9.99 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 122.3, 122.8, 123.88 (q, J = 270 Hz), 123.93, 124.5, 124.8, 125.6 (q, J = 3.8 Hz), 126.1, 126.6, 126.9, 127.2, 127.6, 129.9 (q, J = 32 Hz), 130.7 (q, J = 1.0 Hz), 131.8, 131.8, 132.2, 135.3, 136.7, 147.4, 149.3, 150.4, 162.7, 163.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.65 (s); HRMS (EI) m/z (M^+) calcd for $C_{26}H_{16}F_3N_3O_2$: 459.1195, found: 459.1196.

*N-[8-{5-(4-Cyanophenyl)oxazol-2-yl}naphthalen-1-yl]-picolinamide (**3ai**).* Purified by column chromatography on silica gel with hexane/ethyl acetate (2:1, v/v) as an eluent; 63 mg (61%), mp 201−202 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15−7.18 (m, 1H), 7.26 (s, 1H), 7.38 (d, J = 8.4 Hz, 2H), 7.51−7.44 (m, 4H), 7.58 (t, J = 8.0 Hz, 1H), 7.75−7.77 (m, 2H), 7.81−7.86 (m, 2H), 7.99 (d, J = 8.4 Hz, 1H), 8.14 (d, J = 4.0 Hz, 1H), 9.86 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 111.2, 118.5, 122.2, 122.6, 124.1, 124.8, 125.5, 126.1, 126.6, 126.9, 127.2, 127.6, 131.3, 131.7, 131.8, 132.3, 132.4, 135.19, 136.8, 147.4, 149.2, 149.9, 162.6, 163.7; HRMS (EI) m/z (M^+) calcd for $C_{26}H_{16}N_4O_2$: 416.1273, found: 416.1274

*Methyl 4-[2-{8-(Picolinamido)naphthalen-1-yl}oxazol-5-yl]-benzoate (**3aj**).* Purified by column chromatography on silica gel with hexane/ethyl acetate (1:1, v/v) as an eluent; 71 mg (63%), mp 59−61 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.92 (s, 3H), 7.21 (ddd, J = 1.2 Hz, 4.8 Hz, 7.6 Hz, 1H), 7.33 (s, 1H), 7.45 (dt, J = 1.6 Hz, 8.4 Hz, 2H), 7.50 (dt, J = 1.6 Hz, 7.6 Hz, 1H), 7.55 (dd, J = 7.2 Hz, 8.0 Hz, 1H), 7.64 (t, J = 8.0 Hz, 1H), 7.82−7.89 (m, 3H), 7.93−7.97 (m, 3H), 8.04−8.06 (m, 1H), 8.18 (ddd, J = 0.8 Hz, 1.6 Hz, 4.8 Hz, 1H), 10.03 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 52.1, 122.2, 122.7, 123.5, 124.6, 124.7, 126.0, 126.4, 126.7, 127.1, 127.5, 129.3, 129.8, 131.4, 131.7, 131.8, 132.1, 135.1, 136.7, 147.4, 149.2, 150.7, 162.7, 163.2, 166.4; HRMS (EI) m/z (M^+) calcd for $C_{27}H_{19}N_3O_4$: 449.1376, found: 449.1375.

*N-[8-{5-(4-Nitrophenyl)oxazol-2-yl}naphthalen-1-yl]picolinamide (**3ak**).* Purified by column chromatography on silica gel with hexane/ethyl acetate (2:1, v/v) as an eluent; 70 mg (64%), mp 216−218 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (ddd, J = 1.2 Hz, 4.8 Hz, 7.6 Hz, 1H), 7.40 (s, 1H), 7.51−7.60 (m, 4H), 7.67 (t, J = 8.0 Hz, 1H), 7.84−7.87 (m, 2H), 7.93 (t, J = 8.4 Hz, 2H), 8.09 (dd, J = 1.2 Hz, 8.0 Hz, 1H), 8.15 (dt, J = 2.0 Hz, 9.2 Hz, 2H), 8.24 (ddd, J = 0.8 Hz, 1.6 Hz, 4.8 Hz, 1H), 9.95 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 122.2, 122.5, 124.1, 124.2, 124.9, 126.1, 126.2, 126.6, 127.0, 127.2, 127.6, 131.7, 131.8, 132.4, 133.2, 135.2, 136.9, 146.9, 147.4, 149.3, 149.7, 162.6, 164.1; HRMS (EI) m/z (M^+) calcd for $C_{25}H_{16}N_4O_4$: 436.1172, found: 436.1174.

*N-[8-{5-(Naphthalen-1-yl)oxazol-2-yl}naphthalen-1-yl]-picolinamide (**3al**).* Purified by column chromatography on silica gel with hexane/ethyl acetate (2:1, v/v) as an eluent; 86 mg (78%), mp 153−154 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (ddd, J = 1.2 Hz, 4.8 Hz, 7.6 Hz, 1H), 7.43−7.52 (m, 5H), 7.45 (s, 1H), 7.57−7.62 (m, 2H), 7.66 (t, J = 8.0 Hz, 1H), 7.81−7.95 (m, 4H), 8.03 (t, J = 7.2 Hz, 2H), 8.07 (dd, J = 1.2 Hz, 8.4 Hz, 1H), 8.25 (ddd, J = 1.2 Hz, 1.6 Hz, 4.8 Hz, 1H), 10.47 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 122.4, 123.2, 124.6, 124.8, 125.2, 126.0 (two signals were overlapped), 126.1, 126.3, 126.5, 126.7, 126.9, 127.3, 128.7, 129.3, 129.6, 131.7, 132.1, 132.2, 133.7, 135.4, 136.8, 147.6, 149.7, 150.7, 162.5, 162.9 (two signals were overlapped by other ones); HRMS (EI) m/z (M^+) calcd for $C_{29}H_{19}N_3O_2$: 441.1477, found: 441.1476.

*N-{8-(Benzo[d]oxazol-2-yl)-4-methoxynaphthalen-1-yl}-picolinamide (**3ba**).* Purified by column chromatography on silica gel

with hexane/ethyl acetate (2:1, v/v) as an eluent; 39 mg (39%), mp 158−160 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.08 (s, 3H), 7.01 (d, J = 8.4 Hz, 1H), 7.07 (ddd, J = 1.2 Hz, 4.8 Hz, 7.6 Hz, 1H), 7.17 (td, J = 1.2 Hz, 7.6 Hz, 1H), 7.22 (td, J = 1.2 Hz, 7.6 Hz, 1H), 7.33 (ddd, J = 0.8 Hz, 1.2 Hz, 8.2 Hz, 1H), 7.55−7.69 (m, 4H), 7.81 (dd, J = 0.4 Hz, 8.4 Hz, 1H), 7.92 (dd, J = 1.6 Hz, 7.2 Hz, 1H), 7.99 (dt, J = 0.8 Hz, 8.0 Hz, 1H), 8.59 (dd, J = 1.2 Hz, 8.4 Hz, 1H), 10.05 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 55.9, 104.6, 110.4, 119.9, 121.9, 122.7, 124.1, 124.2, 124.8, 125.7, 126.36, 127.0, 127.5, 128.1, 132.5, 136.7, 142.1, 147.4, 149.2, 151.2, 154.4, 163.2, 164.8 (one signal was overlapped by othe ones); HRMS (EI) m/z (M^+) calcd for $C_{24}H_{17}N_3O_3$: 395.1270, found: 395.1272.

*N-{8-(Benzo[d]oxazol-2-yl)-4-cyanonaphthalen-1-yl}-picolinamide (**3ca**).* Purified by column chromatography on silica gel with hexane/ethyl acetate (2:1, v/v) as an eluent; 73 mg (75%), mp 195−197 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (ddd, J = 1.2 Hz, 4.8 Hz, 7.6 Hz, 1H), 7.25−7.35 (m, 2H), 7.40 (dd, J = 0.4 Hz, 8.0 Hz, 1H), 7.49 (ddd, J = 0.8 Hz, 1.6 Hz, 4.8 Hz, 1H), 7.67 (td, J = 1.6 Hz, 8.0 Hz, 1H), 7.78−7.82 (m, 2H), 8.05 (dt, J = 0.8 Hz, 8.0 Hz, 1H), 8.10 (d, J = 8.0 Hz, 1H), 8.14 (dd, J = 1.2 Hz, 7.2 Hz, 1H), 8.31 (d, J = 8.0 Hz, 1H), 8.53 (dd, J = 1.2 Hz, 8.4 Hz, 1H), 10.80 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 107.8, 110.6, 117.7, 120.3, 122.2, 123.0, 123.8, 124.5, 125.0, 125.5, 126.3, 127.3, 129.7, 133.5, 133.6, 134.5, 137.1, 137.3, 142.0, 147.4, 148.4, 151.3, 162.6, 163.2; HRMS (EI) m/z (M^+) calcd for $C_{24}H_{14}N_4O_2$: 390.1117, found: 390.1119.

*N-{8-(Benzo[d]oxazol-2-yl)-4-nitronaphthalen-1-yl}picolinamide (**3da**).* Purified by GPC; 67 mg (65%), mp 191−192 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (ddd, J = 1.2 Hz, 4.8 Hz, 7.6 Hz, 1H), 7.24 (td, J = 1.2 Hz, 7.6 Hz, 1H), 7.29 (td, J = 1.2 Hz, 7.6 Hz, 1H), 7.36−7.39 (m, 1H), 7.55 (ddd, J = 1.2 Hz, 1.6 Hz, 4.8 Hz, 1H), 7.67 (td, J = 1.6 Hz, 7.6 Hz, 1H), 7.75 (ddd, J = 0.8 Hz, 1.6 Hz, 8.0 Hz, 1H), 7.83 (dd, J = 7.2 Hz, 8.8 Hz, 1H), 8.04 (dt, J = 1.2 Hz, 8.0 Hz, 1H), 8.13 (dd, J = 1.2 Hz, 7.2 Hz, 1H), 8.39 (bs, 2H), 8.83 (dd, J = 1.2 Hz, 8.8 Hz, 1H), 10.61 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 110.6, 120.3, 122.2, 122.3, 123.7, 124.6, 125.1, 125.5, 125.8, 126.3, 127.2, 127.4, 127.9, 133.4, 137.1, 137.9, 142.2, 144.4, 147.5, 148.3, 151.4, 162.6, 163.4; HRMS (EI) m/z (M^+) calcd for $C_{23}H_{14}N_4O_4$: 410.1015, found: 410.1016.

*N-{10-(Benzo[d]oxazol-2-yl)pyren-1-yl}picolinamide (**3ea**).* Purified by column chromatography on silica gel with hexane/ethyl acetate (1:1, v/v) as an eluent; 78 mg (71%), mp 170−172 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (ddd, J = 1.2 Hz, 4.8 Hz, 7.6 Hz, 1H), 7.19 (td, J = 1.2 Hz, 8.0 Hz, 1H), 7.26 (td, J = 1.2 Hz, 7.6 Hz, 1H), 7.36 (d, J = 7.6 Hz, 1H), 7.64 (td, J = 1.6 Hz, 7.6 Hz, 1H), 7.71 (td, J = 0.8 Hz, 1.6 Hz, 4.8 Hz, 1H), 7.76 (dd, J = 0.4 Hz, 7.2 Hz, 1H), 7.99−8.11 (m, 4H), 8.20 (d, J = 7.2 Hz, 1H), 8.25 (d, J = 7.2 Hz, 1H), 8.32 (d, J = 8.4 Hz, 1H), 8.51 (d, J = 8.4 Hz, 1H), 8.59 (s, 1H), 10.59 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 110.5, 120.0, 122.0, 122.1, 122.4, 124.2, 125.0, 125.3, 125.8, 126.2, 126.3, 126.5, 126.6, 126.7, 127.4, 127.8, 129.2, 129.7, 130.7, 131.2, 134.9, 126.8, 142.1, 147.5, 149.1, 151.2, 163.0, 164.8 (one signal was overlapped by othe ones); HRMS (EI) m/z (M^+) calcd for $C_{29}H_{17}N_3O_2$: 439.1321, found: 439.1324.

*N-{4-Cyano-8-(5-phenyloxazol-2-yl)naphthalen-1-yl}-picolinamide (**3 cd**).* Purified by column chromatography on silica gel with hexane/ethyl acetate (2:1, v/v) as an eluent; 67 mg (64%), mp 185−187 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27−7.35 (m, 4H), 7.34 (s, 1H), 7.44−7.46 (m. 2H), 7.62 (td, J = 1.6 Hz, 7.6 Hz, 1H), 7.79 (dd, J = 7.2 Hz, 8.4 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 8.04 (dd, J = 1.2 Hz, 7.2 Hz, 1H), 8.08 (d, J = 8.0 Hz, 1H), 8.23 (dd, J = 0.8 Hz, 4.0 Hz, 1H), 8.30 (d, J = 8.0 Hz, 1H), 8.49 (dd, J = 1.2 Hz, 8.4 Hz, 1H), 10.63 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 107.9, 117.7, 122.5, 123.1, 123.4, 123.96, 124.02, 125.4, 126.5, 127.2, 127.4, 128.6, 128.7, 129.0, 133.0, 133.4, 134.5, 137.0, 137.4, 147.6, 148.8, 152.5, 160.9, 162.6; HRMS (EI) m/z (M^+) calcd for $C_{26}H_{16}N_4O_2$: 416.1273, found: 416.1275.

*N-{4-Nitro-8-(5-phenyloxazol-2-yl)naphthalen-1-yl}picolinamide (**3dd**).* Purified by recrystallization from toluene; 50 mg (46%), mp 216−217 °C (from toluene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (s, 1H), 7.28−7.35 (m, 4H), 7.41 (dd, J = 1.6 Hz, 8.0 Hz, 2H), 7.61 (td, J = 1.6 Hz, 7.6 Hz, 1H), 7.82 (dd, J = 7.2 Hz, 8.8 Hz, 1H), 7.91 (dt, J = 0.8 Hz, 7.6 Hz, 1H), 8.04 (dd, J = 1.2 Hz, 7.2 Hz, 1H), 8.24 (ddd, J = 0.8 Hz, 1.6 Hz, 4.8 Hz, 1H), 8.30 (d, J = 8.4 Hz, 1H), 8.37 (d, J = 8.4 Hz, 1H), 8.78 (dd, J = 1.2 Hz, 8.8 Hz, 1H), 10.43 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 122.5, 123.1, 123.9, 124.0, 124.9, 126.2, 126.5, 126.6, 127.2, 127.4, 128.0, 128.6, 128.75, 132.9, 137.1, 138.0, 142.1, 144.5, 147.6, 148.7, 152.6, 161.0, 162.5; HRMS (EI) m/z (M^+) calcd for $C_{25}H_{16}N_4O_4$: 436.1172, found: 436.1177.

*N-{10-(5-Phenyloxazol-2-yl)pyren-1-yl}picolinamide (**3ed**).* Purified by column chromatography on silica gel with hexane/ethyl acetate (2:1, v/v) as an eluent; 80 mg (69%), mp 208−210 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21−7.31 (m, 4H), 7.27 (s, 1H), 7.41−7.43 (m, 2H), 7.52 (dd, J = 1.6 Hz, 7.6 Hz, 1H), 7.88 (dt, J = 0.8 Hz, 8.0 Hz, 1H), 7.97−8.08 (m, 3H), 8.17 (d, J = 7.6 Hz, 1H), 8.21 (dd, J = 0.8 Hz, 7.6 Hz, 1H), 8.24 (ddd, J = 0.8 Hz, 1.6 Hz, 4.8 Hz, 1H), 8.29 (d, J = 8.4 Hz, 1H), 8.42−8.45 (m, 2H), 10.35 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 122.2, 122.5, 122.7, 122.9, 123.9, 125.0, 125.9, 126.0, 126.07, 126.14, 126.4, 126.7, 126.9, 127.4, 127.6, 128.2, 128.5 (two signals were overlapped), 129.2, 129.7, 130.6, 131.0, 134.0, 136.6, 147.4, 149.4, 151.8, 162.5, 162.9; HRMS (EI) m/z (M^+) calcd for $C_{31}H_{19}N_3O_2$: 465.1477, found: 465.1483.

*N-{8-(Thiazol-2-yl)naphthalen-1-yl}picolinamide (**4aa**).* Purified by column chromatography on silica gel with hexane/ethyl acetate (2:1, v/v) as an eluent; 29 mg (35%), mp 100−101 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, J = 3.2 Hz, 1H), 7.38 (ddd, J = 1.2 Hz, 4.8 Hz, 7.2 Hz, 1H), 7.49 (t, J = 7.6 Hz, 1H), 7.57 (dd, J = 1.2 Hz, 6.8 Hz, 1H), 7.62 (t, J = 7.6 Hz, 1H), 7.78 (td, J = 1.6 Hz, 7.6 H, 1H), 7.84−7.86 (m, 2H), 8.00 (dd, J = 1.2 Hz, 8.0 Hz, 1H), 8.04 (d, J = 7.2 Hz, 1H), 8.10 (d, J = 8.0 Hz, 1H), 8.45 (dd, J = 0.8 Hz, 4.0 Hz, 1H), 10.07 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 119.5, 122.2, 124.5, 125.6, 126.0, 126.30, 126.32, 127.1, 129.1, 131.4, 132.1, 132.4, 135.5, 137.1, 143.2, 147.4, 149.8, 162.7, 169.7; HRMS (EI) m/z (M^+) calcd for $C_{19}H_{13}N_3OS$: 331.0779, found: 331.0782.

*N-{8-(4,5-Dimethylthiazol-2-yl)naphthalen-1-yl}picolinamide (**4ab**).* Purified by column chromatography on silica gel with hexane/ethyl acetate (2:1, v/v) as an eluent; 47 mg (52%), mp 128−130 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.09 (s, 3H), 2.33 (s, 3H), 7.39 (ddd, J = 1.2 Hz, 4.8 Hz, 7.6 Hz, 1H), 7.46 (t, J = 7.6 Hz, 1H), 7.53 (dd, J = 1.2 Hz, 6.8 Hz, 1H), 7.59 (t, J = 8.0 Hz, 1H), 7.79 (dd, J = 1.6 Hz, 7.6 Hz, 1H), 7.82−7.83 (m, 1H), 7.93−7.97 (m, 2H), 8.16 (d, J = 7.6 Hz, 1H), 8.44 (d, J = 4.4 Hz, 1H), 9.98 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 10.9, 14.7, 122.3, 124.4, 125.9, 126.1, 126.2, 126.7, 127.2, 127.3, 129.6, 130.9, 131.5, 132.3, 135.5, 137.1, 147.2, 148.8, 150.2, 162.7, 165.0; HRMS (EI) m/z (M^+) calcd for $C_{21}H_{17}N_3OS$: 359.1092, found: 359.1088.

Typical Procedure for Removal of the Directing Group (Scheme 5). A mixture of *N*-{8-(5-phenyloxazol-2-yl)naphthalen-1-yl}picolinamide (**3ad**, 66 mg, 0.17 mmol), Boc_2O (197 mg, 0.90 mmol), and 4-(*N*,*N*-dimethylamino)pyridine (DMAP, 44 mg, 0.36 mmol) was stirred in CH_2Cl_2 (2.0 mL) at room temperature for 16 h. After the completion of the reaction was confirmed by TLC analysis, the volatile materials were then evacuated under reduced pressure. The residue was purified by chromatography on silica gel with hexane/ethyl acetate (2:1, v/v) to provide *tert*-butyl {8-(5-phenyloxazol-2-yl)-naphthalen-1-yl}(picolinoyl)carbamate (77 mg, 0.16 mmol) in 92% yield.

The above product (54 mg, 0.11 mmol) was dissolved in Et_2O/EtOH (4.8 mL/1.2 mL), and EtONa (23 mg, 0.33 mmol) was then added in one portion. After being stirred at room temperature for 3 h, the mixture was quenched with water. Extraction with ethyl acetate, evaporation in vacuo, and purification by silica gel column chromatography (hexane/ethyl acetate, 3:1, v/v) afforded *tert*-butyl {8-(5-phenyloxazol-2-yl)naphthalen-1-yl}carbamate (**3ad′**, 31 mg, 0.081 mmol) in 73% yield.

*tert-Butyl {8-(5-Phenyloxazol-2-yl)naphthalen-1-yl}carbamate (**3ad′**).* Purified by column chromatography on silica gel with hexane/ethyl acetate (3:1, v/v) as an eluent; 31 mg (73%), mp 143−144 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz,

$CDCl_3$) δ 1.28 (s, 9H), 7.32−7.37 (m,1H), 7.41−7.46 (m, 2H), 7.49−7.57 (m, 2H), 7.55 (s, 1H), 7.70−7.75 (m, 3H), 7.85−7.89 (m, 2H), 8.00 (dd, J = 1.2 Hz, 8.4 Hz, 1H), 8.24 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 28.1, 79.6, 122.2, 122.9, 124.3, 124.4, 125.5, 126.1, 126.4, 127.7, 128.7, 129.0, 131.4, 132.4, 133.3, 135.3, 152.1, 153.9, 162.7 (one signal was overlapped by other ones); HRMS (EI) m/z (M^+) calcd for $C_{24}H_{22}N_2O_3$: 386.1630, found: 386.1632.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra for products. 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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