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Palladium-Catalyzed C8 Alkylation of 1-Naphthylamides with Alkyl Halides via Bidentate-Chelation Assistance

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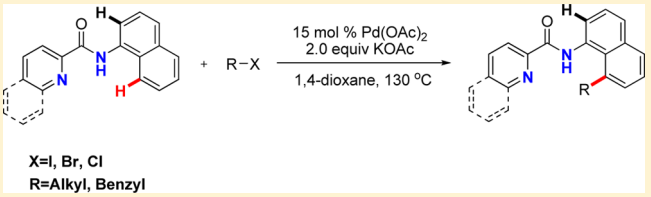
Supporting Information

ABSTRACT: A Pd-catalyzed regioselective alkylation of C8−H bonds in 1-naphthylamides containing a quinolinamide or picolinamide moiety as a bidentate directing group with alkyl halides is reported. The amide directing group can be easily hydrolyzed under basic conditions. Various alkyl halides including alkyl iodides and benzyl bromide or chloride can be employed as coupling partners, exclusively providing 8-alkyl-1-naphthylamide derivatives.



Direct and selective functionalization of C−H bonds has emerged as one of the most promising and powerful synthetic tools for the creation of C−C bonds.[1] The usual approach is to use monodentate directing groups to achieve *o*-C−H functionalization.[2] Despite the broad utility of this approach, the exploration of novel types of directing groups is still very important to meet a synthetic task. Bidentate directing groups have recently attracted considerable attention of researchers because of their unique potential for the activation of inert C−H bonds. Considerable progress has been accomplished by various research groups, who have mainly focused on the use of 8-aminoquinoline or picolinamide analogues as the auxiliary groups.[3] Among these impressive efforts, direct alkylations of *β*-C−H bonds in carboxylic acids[4] and *γ*-C−H bonds in amines[5] with alkyl halides have been accomplished. As an example of the alkylation of *β*-C−H bonds in carboxylic acids, in 2010 the Daugulis group reported the palladium-catalyzed alkylation of *β*-C−H bonds in propionic or benzoic acid derivatives with primary alkyl iodides or benzyl bromides by employing an 8-aminoquinoline auxiliary.[4a] This methodology has been used by Shi et al. in *β*-C−H alkylation of *α*-amino acid derivatives.[4b] Also, the groups of Chatani, Ackermann, and Ge have recently described the nickel-catalyzed direct alkylation of *β*-C−H bonds in aromatic and aliphatic carboxylic acids with alkyl iodides or bromides by employing 8-aminoquinoline as a bidentate directing group.[4c−e] As an example of the alkylation of *γ*-C−H bonds in amines, in 2011 Chen and co-workers reported the palladium-catalyzed *ortho* alkylation of picolinamide-protected benzylamine substrates with alkyl halides.[5a] Subsequently, they extended the method to the alkylation of *γ*-C−H bonds in aliphatic amine substrates with primary alkyl iodides.[5b] In these transformations, the direct alkylation of C−H bonds in aromatic amines with alkyl halides is limited to an example reported very recently by the Daugulis group[5c] in which *N*-(naphthalen-1-yl)picolinamide was alkylated using *n*-octyl iodide in 49% yield at 140 °C.

Our group has a strong interest in the functionalization of 1-naphthylamine scaffolds, which widely exist in dyes[6] and electroluminescent materials[7] as an important structural unit. In 2013, we reported the quinolinamide-directed regioselective C8 arylation of 1-naphthylamides with aryl iodides under the catalysis of $Pd(OAc)_2$ (Scheme 1, eq 1).[8] Compared with the realized C−H bond arylation, C−H bond alkylation is more challenging because the oxidative addition of alkyl halides is unfavorable and the resulting alkylmetal intermediates tend to undergo *β*-hydride elimination reactions. Encouraged by these results on C8 arylation of 1-naphthylamides, we proceeded to investigate whether the bidentate directing group could also facilitate the C8 alkylation of 1-naphthylamides with alkyl halides (Scheme 1, eq 2).

We initiated our studies by exploring reaction conditions for the envisioned direct C8 alkylation of *N*-(naphthalen-1-yl)picolinamide (**1a**) with 1-iodobutane (**2c**) (Table 1). To our delight, the desired alkylated product **3c** was generated in 67% yield under the original C8 arylation conditions[8] (entry 1). Screening of solvents indicated that 1,4-dioxane gave a higher yield (entries 2−6). A control experiment without the use of an additive resulted in a drastically decreased yield (entry 7), which showed that an inorganic base additive is necessary for the transformation. Variation of the type of additive was also investigated (entries 8−15). The use of AgOAc as a halide scavenger was inefficient (entry 8). The examined inorganic base and organic acid additives displayed lower efficiencies (entries 9−15); even K_2CO_3 and Cs_2CO_3 completely suppressed the formation of product **3c** (entries 10 and 12). It was mentioned that the C2-alkylated product was not detected in

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Scheme 1. Pd(II)-Catalyzed Regioselective C8 Functionalization of 1-Naphthylamides

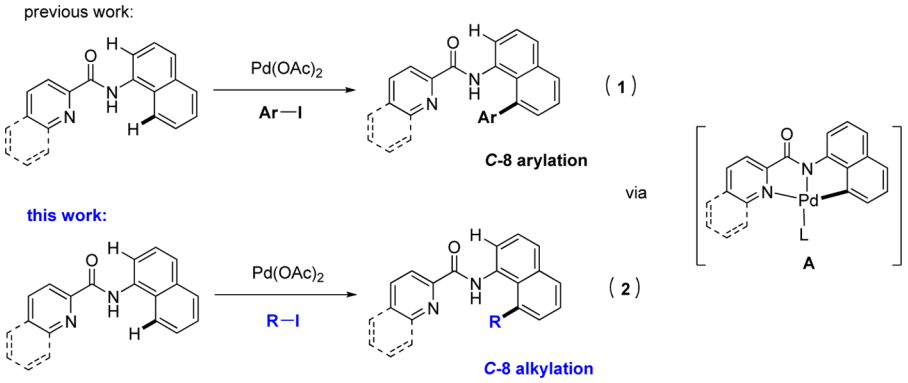
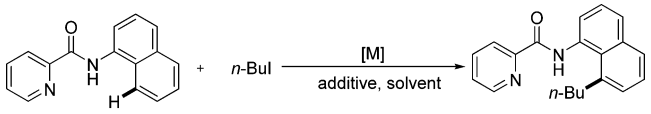


Table 1. Optimization of the Reaction Conditions[a]



1a 2c 3c

entry	catalyst (mol %)	additive	solvent	yield (%)[b]
1	$Pd(OAc)_2$	KOAc	xylene	67
2	$Pd(OAc)_2$	KOAc	toluene	20
3	$Pd(OAc)_2$	KOAc	DMSO	26
4	$Pd(OAc)_2$	KOAc	$ClCH_2CH_2Cl$	8
5	$Pd(OAc)_2$	KOAc	*t*-BuOH	5
6	**$Pd(OAc)_2$**	**KOAc**	**1,4-dioxane**	**72**
7	$Pd(OAc)_2$	–	1,4-dioxane	5
8	$Pd(OAc)_2$	AgOAc	1,4-dioxane	32
9	$Pd(OAc)_2$	NaOAc	1,4-dioxane	25
10	$Pd(OAc)_2$	K_2CO_3	1,4-dioxane	N.D. (80)[c]
11	$Pd(OAc)_2$	Na_2CO_3	1,4-dioxane	42
12	$Pd(OAc)_2$	Cs_2CO_3	1,4-dioxane	N.D. (21)[c]
13	$Pd(OAc)_2$	HOAc	1,4-dioxane	20
14	$Pd(OAc)_2$	CF_3COOH	1,4-dioxane	8
15	$Pd(OAc)_2$	$(BnO)_2PO_2H$	1,4-dioxane	10
16	$PdCl_2$	KOAc	1,4-dioxane	52
17	$Pd(PPh_3)_2Cl_2$	KOAc	1,4-dioxane	trace (92)[c]
18	$Pd_2(dba)_3$	KOAc	1,4-dioxane	N.D. (94)[c]

[a]Reaction conditions: **1a** (0.25 mmol), Pd catalyst (0.0375 mmol), **2c** (1.0 mmol), additive (0.5 mmol), solvent (5 mL), 130 °C, 24 h. [b]Isolated yields. [c]The isolated yield of recycled substrate **1a** is shown in parentheses.

these reactions. Other palladium catalysts such as $PdCl_2$, $Pd(PPh_3)_2Cl_2$, and $Pd_2(dba)_3$ were investigated. Product **3c** was obtained in 52% yield when $PdCl_2$ was used as the catalyst (entry 16). However, $Pd(PPh_3)_2Cl_2$ and $Pd_2(dba)_3$ were almost inactive, presumably because the ligands hindered the coordination of catalyst with the substrate (entries 17 and 18). Therefore, the optimal reaction was achieved with 2 equiv of KOAc as the additive in 1,4-dioxane at 130 °C for 24 h (Table 1, entry 6).

With the optimized reaction conditions in hand, we explored the substrate scope of the alkyl halides. As shown in Table 2, various straight-chain primary alkyl iodides presented great compatibility with the reaction conditions (entries 1–5). It is worth mentioning that MeI (**2a**) was identified as the superior methylation reagent to afford the corresponding product in high yield (entry 1).[9] Moreover, alkyl diiodide **2e** also participated well in the reaction to afford predominantly the monoalkylation product **3e** with a trace amount of dialkylation (entry 5); the reserved iodo functional group added flexibility to further elaborate the alkylated product. The dialkylation product **3ea** was obtained in 29% yield when **3e** was used as the alkylation reagent in place of **2e** under the standard conditions (entry 6), indicating that the picolinamide moiety in **3e** probably retarded the reaction. Unexpectedly, secondary alkyl iodides **2f–h** were found to be reactive, albeit in lower yields, showing that steric hindrance clearly reduced the reactivity (entries 7–9). In addition, benzyl bromide (**2i**) and benzyl chloride (**2j**) could also be employed effectively in the reaction to give the desired products (entries 10 and 11). However, when butyl iodide was replaced with butyl bromide, no product was obtained.

We next examined the effect of the directing group (Scheme 2). When the analogue naphthylquinoline-2-carboxamide **1b** was used in place of **1a** as the substrate, the 1-naphthylamide **1b** could be alkylated by straight-chain primary alkyl iodides such as methyl iodide **2a**, *n*-propyl iodide **2b**, *n*-butyl iodide **2c**, and 10-iododecyl iodide **2e** in moderate to good yields under the standard reaction conditions (Scheme 2, **3j–m**). No coupling, including C2 alkylation reactions, occurred when the corresponding amide *N*-(naphthalen-1-yl)benzamide (**1c**) or *tert*-butyl *N*-naphthalen-1-ylcarbamate (**1d**) was used as the substrate in place of **1a** (see the ^{1}H NMR spectra of the crude products **1c** and **1d** in the Supporting Information), indicating that the coordination in a bidentate *N,N* fashion is a vital step for the reaction to proceed.

On the basis of previous studies,[4a,d,8,10] the C–H alkylation reaction likely proceeds through a sequential C–H activation (palladation)/oxidative addition pathway, and a Pd(II)/(IV) manifold might be operative. Although previous theoretical calculations on the analogous C–H arylation reaction[8] proved that a sequential oxidative addition/C–H activation pathway was unfavorable, the pathway could not be excluded.[11]

Futhermore, the amide directing group could be simply hydrolyzed (Scheme 3). The alkylated substrate **3c** was heated with NaOH in ethanol at 130 °C to afford 8-butylnaphthalen-1-amine (**3q**) in 65% yield.

In conclusion, we have developed a methodology for the Pd-catalyzed, bidentate-auxiliary-directed regioselective alkylation of 1-naphthylamides with alkyl halides. A broad range of primary alkyl iodides as well as benzyl bromide and chloride are competent reagents in this transformation. In particular, the use of MeI provides an efficient and straightforward method for preparing high-value methylation products from readily available precursors. The picolinamide directing group is simply

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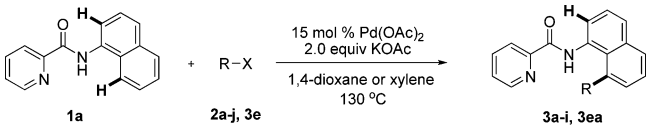
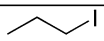
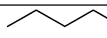
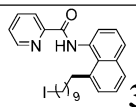
Table 2. Scope of Alkyl Iodides[a]



entry	R-X	product	yield (%)[b]
1	CH_3I **2a**	**3a**	82
2	 **2b**	**3b**	76
3	 **2c**	**3c**	72(66[c])
4	 **2d**	**3d**	80
5	 **2e**	**3e**	73
6[d]	 **3e**	**3ea**	29
7	 **2f**	**3f**	36
8	 **2g**	**3g**	38
9	 **2h**	**3h**	15
10[e]	 **2i**	**3i**	54
11[f]	 **2j**		62

[a]Reaction conditions: **1a** (0.25 mmol, 62 mg), $Pd(OAc)_2$ (0.0375 mmol, 9 mg), RI (1.0 mmol), KOAc (0.5 mmol, 49 mg), 1,4-dioxane (5 mL), 130 °C, 24 h. [b]Isolated yields. [c]Isolated yield on a 4.04 mmol scale for 24 h. [d]Substrate **1a** on a 0.18 mmol scale. [e]Reaction in xylene (5 mL) for 4 h. [f]Reaction in xylene (5 mL) for 48 h.

detached under basic conditions, providing a synthetic method for 8-alkyl-1-naphthylamines.

EXPERIMENTAL SECTION

General Methods. The reactions were carried out in oven-dried flasks under air, unless otherwise stated. ^1H NMR spectra were recorded using a 400 MHz spectrometer, and the chemical shifts are reported in δ units, parts per million relative to the internal standard TMS (0 ppm) for $CDCl_3$ (7.26 ppm). The peak patterns are indicated as follows: s, singlet; d, doublet; dd, doublet of doublets; t, triplet; q, quartet; m, multiplet. Coupling constants (J) are reported in hertz. ^{13}C NMR spectra were measured using a 100 MHz spectrometer relative to the internal solvent signal (center peak is 77.00 ppm in $CDCl_3$). Electrospray ionization (ESI) high-resolution mass spectrometry (HRMS) was performed on an FT-ICR spectrometer. Amide derivatives **1a** and **1b** were synthesized according to the literature procedures.[8,12] *N*-(Naphthalen-1-yl)benzamide (**1c**)[13] and *tert*-butyl *N*-naphthalen-1-ylcarbamate (**1d**)[14] were prepared by known methods. Other materials were purchased from common commercial sources and used without additional purification.

Preparation of Amide Compounds 1a and 1b.[8,12] Picolinic acid or quinoline-2-carboxylic acid (20 mmol), naphthalen-1-amine (20 mmol, 2.86 g), and Et_3N (40 mmol, 5.6 mL) were dissolved in CH_2Cl_2 (40 mL), and $POCl_3$ (3.76 mL) was added dropwise at 0 °C. The reaction mixture was stirred at 0 °C for 0.5 h. Subsequently, the reaction was performed at room temperature for about 2 h until naphthalen-1-amine was consumed completely. At the conclusion of the reaction, the reaction mixture was allowed to cool to 0 °C, and ice−water was added slowly to quench the reaction. The organic layer was collected, and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phases were washed with saturated $NaHCO_3$ (2 × 40 mL) and dried over $MgSO_4$. The solvent was evaporated under reduced pressure, and the residue was crystallized from CH_2Cl_2/petroleum ether to give the desired product.

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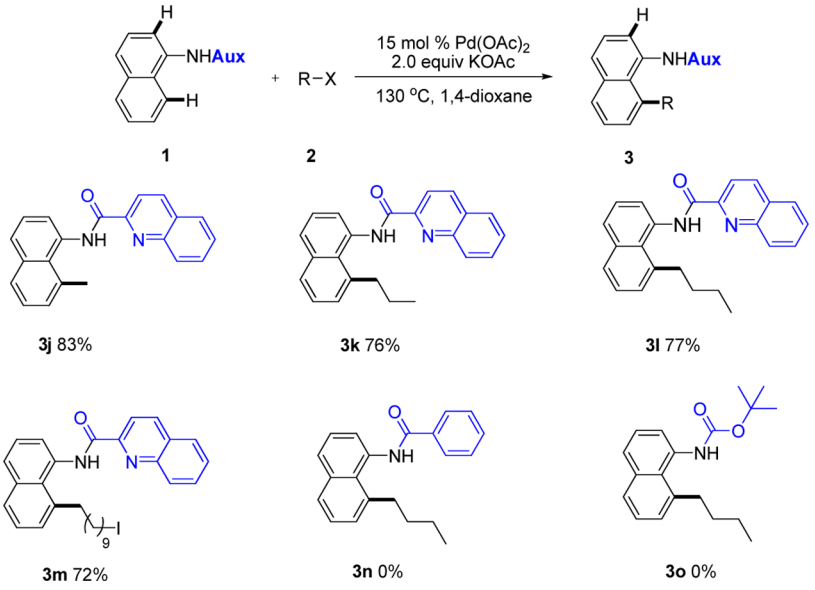
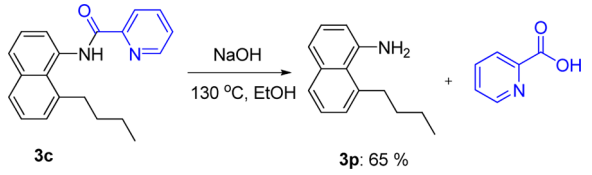
Scheme 2. Screening of 1-Naphthylamide Auxiliaries



Scheme 3. Hydrolysis of Amide 3c



*N-(Naphthalen-1-yl)picolinamide (**1a**, CAS no. 75358-95-1).*[10] 2.98 g, 60% yield; pink solid; mp 128−129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.75 (s, 1H), 8.70 (d, J = 5.2 Hz, 1H), 8.41 (d, J = 7.2 Hz, 1H), 8.36 (d, J = 7.6 Hz, 1H), 8.09 (d, J = 8.4 Hz, 1H), 7.91 (m, 2H), 7.70 (d, J = 8.4 Hz, 1H), 7.55 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 150.1, 148.2, 137.8, 134.1, 132.4, 128.8, 126.5, 126.4, 126.3, 126.0, 125.9, 125.0,122.5, 120.5, 118.6; HRMS (ESI) calcd for $C_{16}H_{12}N_2O$ $[M + H]^+$ 249.1022, found 249.1020.

*N-(Naphthalen-1-yl)quinoline-2-carboxamide (**1b**, CAS no. 298193-67-6).* 4.29 g, 72% yield; pink solid; mp 146−147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.95 (s, 1H), 8.43 (d, J = 8.4 Hz, 2H), 8.36 (d, J = 8.0 Hz, 1H), 8.25 (d, J = 8.4 Hz, 1H), 8.16 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 8.0 Hz, 2H), 7.81 (t, J = 7.2 Hz, 1H), 7.71 (d, J = 8.4 Hz, 1H), 7.59 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 149.9, 146.3, 138.0, 134.2, 132.5, 130.4, 129.9, 129.5, 128.9, 128.2, 127.9, 126.5, 126.3, 126.1, 126.0, 125.1, 120.5, 118.8, 118.7; HRMS (ESI) calcd for $C_{20}H_{14}N_2O$ $[M + H]^+$ 299.1179, found 299.1182.

Typical Procedure for Alkylation Products 3a−o and 3ea. A mixture of naphthylamide (0.25 mmol, 1.0 equiv), $Pd(OAc)_2$ (0.0375 mmol, 15 mol %), alkyl iodide (1.0 mmol, 4.0 equiv), anhydrous KOAc (0.5 mmol, 2.0 equiv), and 1,4-dioxane (5 mL) was placed in a 35 mL Schlenk tube with a rubber plug under air. The tube was heated at 130 °C for 24 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate (5 mL), filtered through Celite, and concentrated in vacuo. The residue was purified by silica gel column chromatography with ethyl acetate/petroleum ether to afford the desired product.

*N-(8-Methylnaphthalen-1-yl)picolinamide (**3a**).* 54 mg, 82% yield; light-yellow solid after purification by column chromatography (eluent, ethyl acetate/petroleum ether = 1/10 v/v); mp 184−185 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.59 (s, 1H), 8.63 (d, J = 4.4 Hz, 1H), 8.34 (d, J = 7.6 Hz, 1H), 8.05 (d, J = 7.2 Hz, 1H), 7.89 (t, J = 7.6 Hz, 1H), 7.71 (t, J = 7.2 Hz, 2H), 7.47 (m, 2H), 7.32 (t, J = 7.6 Hz, 1H), 7.25 (d, J = 7.2 Hz, 1H), 2.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 150.1, 148.2, 137.7, 135.8, 133.2, 132.6, 130.1, 128.1, 127.7, 127.4, 126.4, 125.5, 125.3, 123.5, 122.7, 25.1; HRMS (ESI) calcd for $C_{17}H_{14}N_2O$ $[M + H]^+$ 263.1179, found 263.1175.

*N-(8-Propylnaphthalen-1-yl)picolinamide (**3b**).* 55 mg, 76% yield; light-yellow solid after purification by column chromatography (eluent, ethyl acetate/petroleum ether = 1/10 v/v); mp 115−116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.50 (s, 1H), 8.62 (d, J = 4.8 Hz, 1H), 8.35 (d, J = 7.6 Hz, 1H), 8.00 (d, J = 7.2 Hz, 1H), 7.88 (t, J = 8.0 Hz, 1H), 7.73 (t, J = 8.6 Hz, 2H), 7.46 (m, 2H), 7.34 (t, J = 7.6 Hz, 1H), 7.29 (d, J = 6.8 Hz, 1H), 3.25 (t, J = 8.0 Hz, 2H), 1.67 (m, 2H), 0.80 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 150.1, 148.1, 137.7, 137.6, 136.2, 132.6, 129.8, 128.0, 127.9, 127.4, 126.5, 125.4, 125.1, 124.5, 122.7, 39.5, 25.8, 14.0; HRMS (ESI) calcd for $C_{19}H_{18}N_2O$ $[M + H]^+$ 291.1492, found 291.1489.

*N-(8-Butylnaphthalen-1-yl)picolinamide (**3c**).* 55 mg, 72% yield; light-yellow solid after purification by column chromatography (eluent, ethyl acetate/petroleum ether = 1/10 v/v); mp 115−116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.49 (s, 1H), 8.62 (d, J = 4.8 Hz, 1H), 8.35 (d, J = 7.6 Hz, 1H), 8.00 (d, J = 7.2 Hz, 1H), 7.88 (t, J = 7.8 Hz, 1H), 7.73 (t, J = 9.6 Hz, 2H), 7.47 (m, 2H), 7.34 (t, J = 7.2 Hz, 1H), 7.29 (d, J = 7.2 Hz, 1H), 3.27 (t, J = 8.0 Hz, 2H), 1.63 (m, 2H), 1.22 (m, 2H), 0.78 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 150.2, 148.1, 137.8, 137.7, 136.2, 132.6, 129.5, 127.9, 127.8, 127.4, 126.5, 125.5, 125.1, 124.5, 122.7, 37.3, 34.8, 22.7, 14.0; HRMS (ESI) calcd for $C_{20}H_{20}N_2O$ $[M + H]^+$ 305.1648, found 305.1643.

*N-(8-Decylnaphthalen-1-yl)picolinamide (**3d**).* 78 mg, 80% yield; light-yellow viscous liquid after purification by column chromatography (eluent, ethyl acetate/petroleum ether = 1/10 v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.49 (s, 1H), 8.62 (d, J = 4.0 Hz, 1H), 8.36 (d, J = 8.0 Hz, 1H), 7.98 (d, J = 7.2 Hz, 1H), 7.90 (t, J = 8.0 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.47 (m, 2H), 7.35 (t, J = 7.6 Hz, 1H), 7.29 (d, J = 6.0 Hz, 1H), 3.26 (t, J = 8.0 Hz, 2H), 1.63 (m, 2H), 1.19 (m, 14H), 0.87 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 150.2, 148.1, 137.9, 137.7, 136.2, 132.5, 129.5, 127.9, 127.4, 126.5, 125.5, 125.1, 124.6, 122.7, 37.7, 32.9, 31.9, 29.8, 29.7, 29.6, 29.5, 29.4, 22.8, 14.2; HRMS (ESI) calcd for $C_{26}H_{32}N_2O$ $[M + H]^+$ 389.2587, found 389.2583.

*N-(8-(10-Iododecyl)naphthalen-1-yl)picolinamide (**3e**).* 94 mg, 73% yield; light-yellow solid after purification by column chromatography (eluent, ethyl acetate/petroleum ether = 1/10 v/v); mp 162−163 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.48 (s, 1H), 8.63 (d, J = 4.8 Hz, 1H), 8.36 (d, J = 7.6 Hz, 1H), 7.98 (d, J = 7.6 Hz, 1H), 7.92 (t, J = 8.0 Hz, 1H), 7.74 (t, J = 9.4 Hz, 2H), 7.48 (m, 2H), 7.35 (t, J = 7.2 Hz, 1H), 7.29 (d, J = 6.8 Hz, 1H), 3.26 (t, J = 8.0 Hz, 2H), 3.15 (t, J = 6.8 Hz, 2H), 1.77 (m, 2H), 1.62 (m, 2H), 1.22 (t, J = 7.2 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 150.2, 148.0, 137.8, 137.7, 136.2,

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132.5, 129.5, 127.9, 127.4, 126.5, 125.5, 125.1, 124.6, 122.7, 37.6, 33.5, 32.7, 30.5, 29.6, 29.5, 29.4, 29.3, 28.5, 7.5; HRMS (ESI) calcd for $C_{26}H_{31}IN_2O$ $[M + H]^+$ 515.1554, found 515.1547.

*N,N′-(8,8′-(Decane-1,10-diyl)bis(naphthalene-8,1-diyl))-dipicolinamide (**3ea**).* 33 mg, 29% yield; light-yellow solid after purification by column chromatography (eluent, ethyl acetate/petroleum ether = 1/3 v/v); mp 103−104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.49 (s, 2H), 8.61 (d, J = 4.8 Hz, 2H), 8.36 (d, J = 7.6 Hz, 2H), 8.00 (d, J = 7.2 Hz, 2H), 7.89 (t, J = 8.0 Hz, 2H), 7.76 (m, 4H), 7.51 (t, J = 8.0 Hz, 2H), 7.45 (dd, J = 4.8, 7.6 Hz, 2H), 7.38 (t, J = 7.2 Hz, 2H), 7.31 (d, J = 7.2 Hz, 2H), 3.28 (t, J = 8.0 Hz, 4H), 1.62 (m, 4H), 1.10 (m, 8H), 0.98 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 150.2, 148.0, 137.8, 137.7, 136.2, 132.5, 129.5, 127.9, 127.4, 126.5, 125.5, 125.1, 124.6, 122.7, 37.6, 32.7, 29.6, 29.5, 29.4; HRMS (ESI) calcd for $C_{42}H_{42}N_4O_2$ $[M + H]^+$ 635.3381, found 635.3375.

*N-(8-Isopropylnaphthalen-1-yl)picolinamide (**3f**).* 26 mg, 36% yield; light-yellow viscous liquid after purification by column chromatography (eluent, ethyl acetate/petroleum ether = 1/10 v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.46 (s, 1H), 8.66 (d, J = 4.4 Hz, 1H), 8.39 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 6.8 Hz, 1H), 7.95 (t, J = 7.6 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.49 (m, 4H), 4.24 (m, 1H), 1.39 (d, J = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 150.2, 148.1, 144.4, 137.7, 136.1, 132.2, 128.1, 127.6, 127.1, 126.5, 125.5, 125.1, 125.0, 124.4, 122.7, 30.1, 25.3; HRMS (ESI) calcd for $C_{19}H_{18}N_2O$ $[M + H]^+$ 291.1492, found 291.1487.

*N-(8-Cyclopentylnaphthalen-1-yl)picolinamide (**3g**).* 30 mg, 38% yield; light-yellow viscous liquid after purification by column chromatography (eluent, ethyl acetate/petroleum ether = 1/10 v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.52 (s, 1H), 8.65 (d, J = 4.8 Hz, 1H), 8.39 (d, J = 7.2 Hz, 1H), 8.08 (d, J = 7.6 Hz, 1H), 7.94 (t, J = 7.6 Hz, 1H), 7.76 (d, J = 7.6 Hz, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.52 (m, 3H), 7.42 (t, J = 8.0 Hz, 1H), 4.21 (m, 1H), 2.23 (m, 2H), 1.76 (m, 4H), 1.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1, 150.2, 148.0, 141.4, 137.7, 136.0, 132.4, 127.8, 127.6, 127.5, 126.5, 125.4, 125.1, 125.0, 124.4, 122.8, 43.2, 35.8, 25.0; HRMS (ESI) calcd for $C_{21}H_{20}N_2O$ $[M + H]^+$ 317.1648, found 317.1652.

*N-(8-Cyclohexylnaphthalen-1-yl)picolinamide (**3h**).* 13 mg, 15% yield; light-yellow viscous liquid after purification by column chromatography (eluent, ethyl acetate/petroleum ether = 1/10 v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.32 (s, 1H), 8.67 (d, J = 4.4 Hz, 1H), 8.40 (d, J = 7.6 Hz, 1H), 7.96 (m, 2H), 7.77 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.48 (m, 4H), 3.81 (t, J = 11.6 Hz, 1H), 2.04 (d, J = 12.0 Hz, 2H), 1.71 (d, J = 12.8 Hz, 2H), 1.51 (m, 3H), 1.13 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 150.1, 148.1, 143.5, 137.7, 136.1, 132.3, 128.2, 127.4, 127.3, 126.6, 125.5, 125.3, 125.2, 124.9, 122.8, 40.8, 35.7, 26.9, 26.3; HRMS (ESI) calcd for $C_{22}H_{22}N_2O$ $[M + H]^+$ 331.1805, found 331.1801.

*N-(8-Benzylnaphthalen-1-yl)picolinamide (**3i**).* 46 mg, 54% yield; light-yellow solid after purification by column chromatography (eluent, ethyl acetate/petroleum ether = 1/10 v/v); mp 172−173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.01 (s, 1H), 8.37 (d, J = 4.4 Hz, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.79 (m, 4H), 7.49 (t, J = 7.6 Hz, 1H), 7.38 (m, 2H), 7.24 (d, J = 7.2 Hz, 1H), 7.14 (m, 3H), 6.85 (m, 2H), 4.66 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 149.9, 147.9, 141.1, 137.4, 136.2, 134.2, 132.5, 131.4, 128.9, 128.7, 128.4, 128.3, 128.3, 126.3, 126.1, 126.0, 125.7, 125.5, 122.6, 42.1; HRMS (ESI) calcd for $C_{23}H_{18}N_2O$ $[M + H]^+$ 339.1492, found 339.1486.

*N-(8-Methylnaphthalen-1-yl)quinoline-2-carboxamide (**3j**).* 65 mg, 83% yield; light-yellow solid after purification by column chromatography (eluent, ethyl acetate/petroleum ether = 1/10 v/v); mp 173−174 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.92 (s, 1H), 8.44 (d, J = 8.8 Hz, 1H), 8.35 (d, J = 8.4 Hz, 1H), 8.21 (d, J = 7.2 Hz, 1H), 8.14 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.79 (t, J = 6.8 Hz, 1H), 7.72 (d, J = 8.0 Hz, 2H), 7.63 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 8.0 Hz, 1H), 7.34 (t, J = 6.8 Hz, 1H), 7.28 (d, J = 6.8 Hz, 1H), 3.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 149.9, 146.4, 137.9, 135.9, 133.4, 132.5, 130.4, 130.2, 129.7, 129.5, 128.2, 127.9, 127.8, 127.7, 127.2, 125.6, 125.4, 122.8, 119.0, 25.4; HRMS (ESI) calcd for $C_{21}H_{16}N_2O$ $[M + H]^+$ 313.1335, found 313.1330.

*N-(8-Propylnaphthalen-1-yl)quinoline-2-carboxamide (**3k**).* 65 mg, 76% yield; light-yellow solid after purification by column chromatography (eluent, ethyl acetate/petroleum ether = 1/10 v/v); mp 100−101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.73 (s, 1H), 8.47 (d, J = 8.4, 1H), 8.38 (d, J = 8.4 Hz, 1H), 8.18 (d, J = 8.4 Hz, 1H), 8.06 (d, J = 7.2 Hz, 1H), 7.92 (d, J = 7.6 Hz, 1H), 7.78 (m, 3H), 7.65 (t, J = 7.6 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.36 (m, 2H), 3.36 (t, J = 8.0 Hz, 2H), 1.76 (m, 2H), 0.74 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 150.0, 146.4, 137.9, 137.5, 136.2, 132.6, 130.4, 129.8, 129.7, 129.5, 128.2, 128.0, 127.9, 127.4, 125.4, 125.2, 124.5, 119.1, 39.5, 25.6, 14.0; HRMS (ESI) calcd for $C_{23}H_{20}N_2O$ $[M + H]^+$ 341.1648, found 341.1645.

*N-(8-Butylnaphthalen-1-yl)quinoline-2-carboxamide (**3l**).* 68 mg, 77% yield; light-yellow solid after purification by column chromatography (eluent, ethyl acetate/petroleum ether = 1/10 v/v); mp 101−102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.70 (s, 1H), 8.46 (d, J = 8.8 Hz, 1H), 8.37 (d, J = 8.8 Hz, 1H), 8.16 (d, J = 8.4 Hz, 1H), 8.04 (d, J = 7.6 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.82−7.73 (m, 3H), 7.64 (t, J = 7.6 Hz, 1H), 7.51 (t, J = 7.6 Hz, 1H), 7.39−7.31 (m, 2H), 3.38 (t, J = 7.6 Hz, 2H), 1.72−1.65 (m, 2H), 1.18−1.08 (m, 2H), 0.71 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 150.0, 146.4, 137.9, 137.7, 136.2, 132.6, 130.4, 129.6, 129.5, 128.2, 128.0, 127.9, 127.8, 127.6, 125.5, 125.2, 124.7, 119.1, 37.3, 34.6, 22.5, 14.0; HRMS (ESI) calcd for $C_{24}H_{22}N_2O$ $[M + H]^+$ 355.1805, found 355.1800.

*N-(8-(10-Iododecyl)naphthalen-1-yl)quinoline-2-carboxamide (**3m**).* 102 mg, 72% yield; light-yellow solid after purification by column chromatography (eluent, ethyl acetate/petroleum ether = 1/10 v/v); mp 159−160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.70 (s, 1H), 8.47 (d, J = 8.0 Hz, 1H), 8.39 (d, J = 8.8 Hz, 1H), 8.17 (d, J = 8.8 Hz, 1H), 8.04 (d, J = 7.2 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.77 (m, 3H), 7.66 (t, J = 8.0 Hz, 1H), 7.51 (t, J = 7.6 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 7.32 (d, J = 6.8 Hz, 1H), 3.36 (t, J = 8.0 Hz, 2H), 3.13 (t, J = 7.2 Hz, 2H), 1.68 (m, 4H), 1.22 (m, 2H), 1.04 (m, 6H), 0.90 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 150.1, 146.4, 137.9, 137.8, 136.2, 132.6, 130.3, 129.7, 129.6, 129.5, 128.2, 128.0, 127.9, 127.6, 125.5, 125.2, 124.7, 119.1, 37.7, 33.5, 32.5, 30.4, 29.6, 29.4, 29.3, 29.1, 28.4, 7.5; HRMS (ESI) calcd for $C_{30}H_{33}IN_2O$ $[M + H]^+$ 565.1710, found 565.1701.

Procedure for Hydrolysis of Amide 3c. *N*-(8-Butylnaphthalen-1-yl)picolinamide (**3c**) (0.2 mmol) and NaOH (256 mg, 6.4 mmol) were heated in ethanol (3 mL) for 18 h at 130 °C. After completion of the reaction, the mixture was diluted with ethyl acetate (3 mL), filtered through Celite, and concentrated in vacuo. The residue was purified by silica gel column chromatography with ethyl acetate/petroleum ether to afford the desired product.

*8-Butylnaphthalen-1-amine (**3p**).* 26 mg, 65% yield; brown oil after purification by column chromatography (eluent, ethyl acetate/petroleum ether = 1/20 v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 8.0 Hz, 1H), 7.27 (m, 2H), 7.19 (t, J = 8.0 Hz, 1H), 7.13 (d, J = 7.2 Hz, 1H), 6.67 (d, J = 7.6 Hz, 1H), 4.22 (s, 2H), 3.22 (t, J = 8.0 Hz, 2H), 1.73 (m, 2H), 1.47 (m, 2H), 0.96 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.1, 138.6, 136.7, 127.8, 127.6, 125.7, 125.3, 123.7, 120.4, 112.6, 37.1, 35.3, 22.8, 14.1; HRMS (ESI) calcd for $C_{14}H_{17}N$ $[M + H]^+$ 200.1434, found 200.1428.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H NMR and ^{13}C NMR spectra for all new compounds. 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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