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Note

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Iron-Catalyzed Regioselective Remote C(sp^2)-H Carboxylation of Naphthyl and Quinoline Amides

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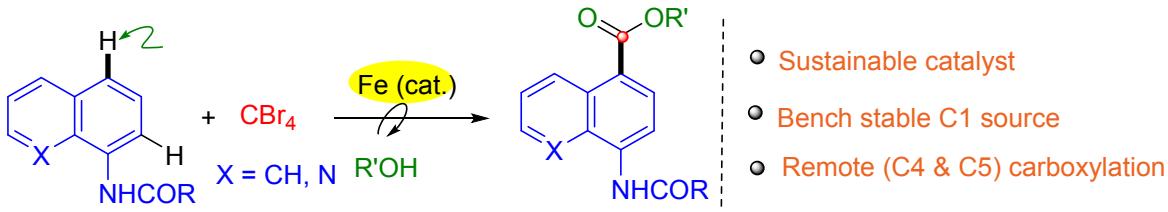


ABSTRACT: Iron(III)-catalyzed regioselective direct remote C-H carboxylation of naphthyl and quinoline amides has been developed using CBr_4 and alcohol. The reaction involves a radical pathway using a coordination activation strategy and single electron transfer process. The use of sustainable iron-catalysis, selectivity and the substrate scope are the important practical features.

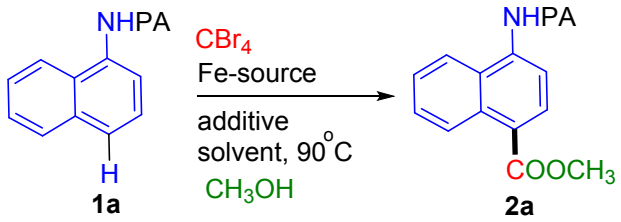
The selective carboxylation of pervasive C_{Ar}–H bonds is one of the most important transformations for the synthesis of aryl carboxylic acid derivatives, which are classified as the versatile building blocks in the construction of biologically active molecules, pharmaceuticals and fine chemicals.[1] Thus, the gases[2] such as CO_2, CO and their surrogates[3] are considerably studied using metal and metal-free conditions for this purpose. With the emergence of the directed C-H functionalization,[4] efforts are recently made to develop the site-selective C-H carboxylation of arenes. In this realm, Yu and co-workers reported a Pd-catalyzed *ortho*-selective carboxylation of aryl carboxylic acids and anilides using CO as the C1 source (See SI, Scheme S1a).[5] Soon after, Iwasawa and co-workers demonstrated a Rh-catalyzed *ortho*-selective carboxylation of 2-phenylpyridines employing CO_2 as the C1 source (Scheme S1a).[6] Later, Greaney and co-workers demonstrated a Ru-catalyzed *meta*-selective carboxylation of 2-phenylpyridines using CBr_4 as the C1 source

(Scheme S1b).[7,8] Naphthalenes and quinolines are the important structural scaffolds of functional materials, pharmaceuticals and agrochemicals (Figure S1).[9] Thereby, the functionalization of neighboring C2[10] and C8[11] positions of 1-naphthylamides has been achieved noticeably, while the remote C4 functionalization is underdeveloped. Recently, the coordination activation strategy[12] and single electron transfer (SET) guided remote C-H functionalization has emerged as an effective synthetic tool for the radical addition reactions.[13] The base metal, iron is relatively abundant, less expensive and omnipresent in enzymes, having the binding ability to *N*- and *O*-based ligands.[14] Substantial attention is thus focused on the development of sustainable iron-based catalytic systems.[15] Herein, we report an iron-catalyzed picolinamide (PA) assisted remote C-H carboxylation of 1-naphthylamides *via* the coordination activation strategy and SET[12] using CBr_4 as a masked carboxylate functionality (Scheme S1c). The scope can be expanded for the remote carboxylation of quinolinamides. The selectivity and substrate scope are the important practical features.

At the outset, optimization of the reaction condition was commenced utilizing *N*-(naphthalen-1-yl)picolinamide **1a** as a model substrate with a series of iron-catalysts, additives and solvents at varied temperature (Scheme 1, Table S1, see SI). To our delight, the remote C-4 carboxylation occurred to give the ester **2a** in 47% yield, when **1a** was stirred with 10 mol % $Fe(acac)_3$ and 3 equiv CBr_4 in a 1:1 mixture of methanol and 1,4-dioxane at 90 °C. The yield was increased to 51% using methanol as a solvent, whereas dimethylacetamide (DMA), CH_3CN, $(CH_2Cl)_2$, trifluoroethanol and water gave inferior results. In a set of iron catalysts screened, $Fe(acac)_3$, $FeCl_3$, $FeSO_4•7H_2O$, ferrocene and $Fe(NO_3)_3•9H_2O$, the former produced superior results. Subsequent screening using additives led to enhance the yield to 65% with PivOH, whereas 1-Ad-OH and $MesCO_2H$ gave <63% yield. Decreasing the catalyst loading (5 mol %) or CBr_4 or temperature

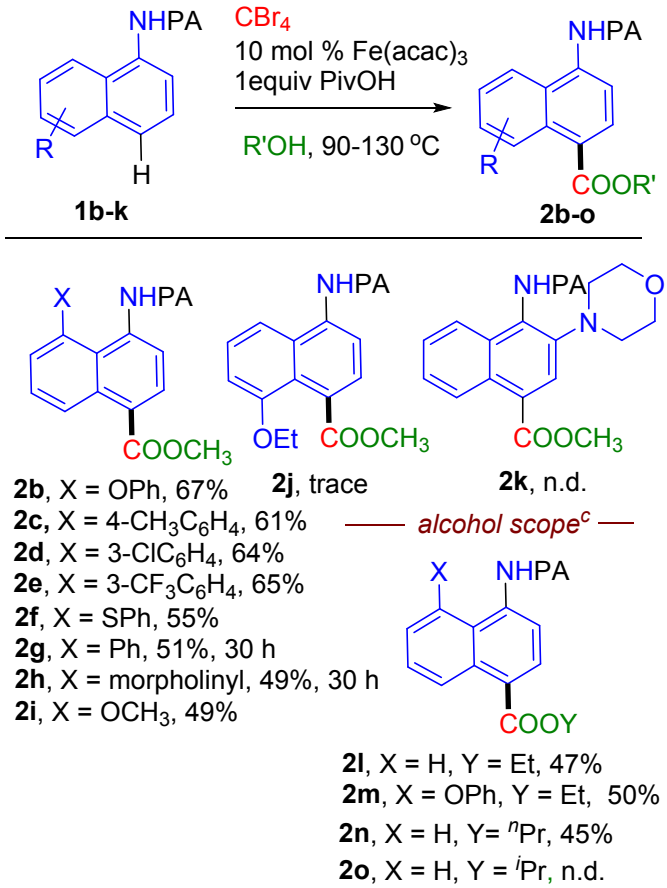
(60 °C) led to drop in the yield. Control experiment confirmed that no carboxylation was observed in the absence of the iron-catalyst.

Scheme 1. Optimization of Reaction Conditions



Next, the scope of the procedure was investigated for the esterification of a series of 1-naphthylamides (Scheme 2). The substrate **1b** having C-8 phenoxy substituent underwent reaction to give the methyl ester **2b** in 67% yield. Recrystallization of **2b** in CH_3CN yielded single crystal whose structure was determined using the X-ray analysis (see SI). The reaction of **1c** bearing C8 *p*-tolyoxy functionality produced **2c** in 61% yield, whereas the substrates having 3-chloro **1d** and 3-trifluoromethyl **1e** groups on the C-8 phenoxy ring gave **2d** and **2e** in 64 and 65% yields, respectively. In addition, the substrates containing C-8 thiophenyl **1f** and phenyl **1g** groups carboxylated to afford the esters **2f** and **2g** in 55 and 51% yield, respectively. Further, the reaction of the substrate **1h** having C-8 morpholine functionality provided the methyl ester **2h** in 49% yield. The reaction of C8-methoxy substrate **1i** gave **2i** in 49% yield, whereas 5-ethoxy **1j** and 2-morpholino **1k** substrates were incompatible to give the desired esters. Interestingly, the alkyl carboxylation scope was extended using ethanol and *n*-propanol as the alkyl source in place of methanol at 130 °C. For example, the reaction of 1-naphthylamides **1a** and **1b** having C-8 phenoxy substituent was carried out as the representative examples, in ethanol to give the ethyl esters **2l** and **2m** in 47 and 50% yields, respectively, while **1a** in *n*-propanol gave the *n*-propyl ester **2n** in 45% yield. In contrast, the reaction using isopropanol was unsuccessful, which may be due to the difficulty in alcoholysis via the nucleophilic substitution of the bulkier secondary alcohol.

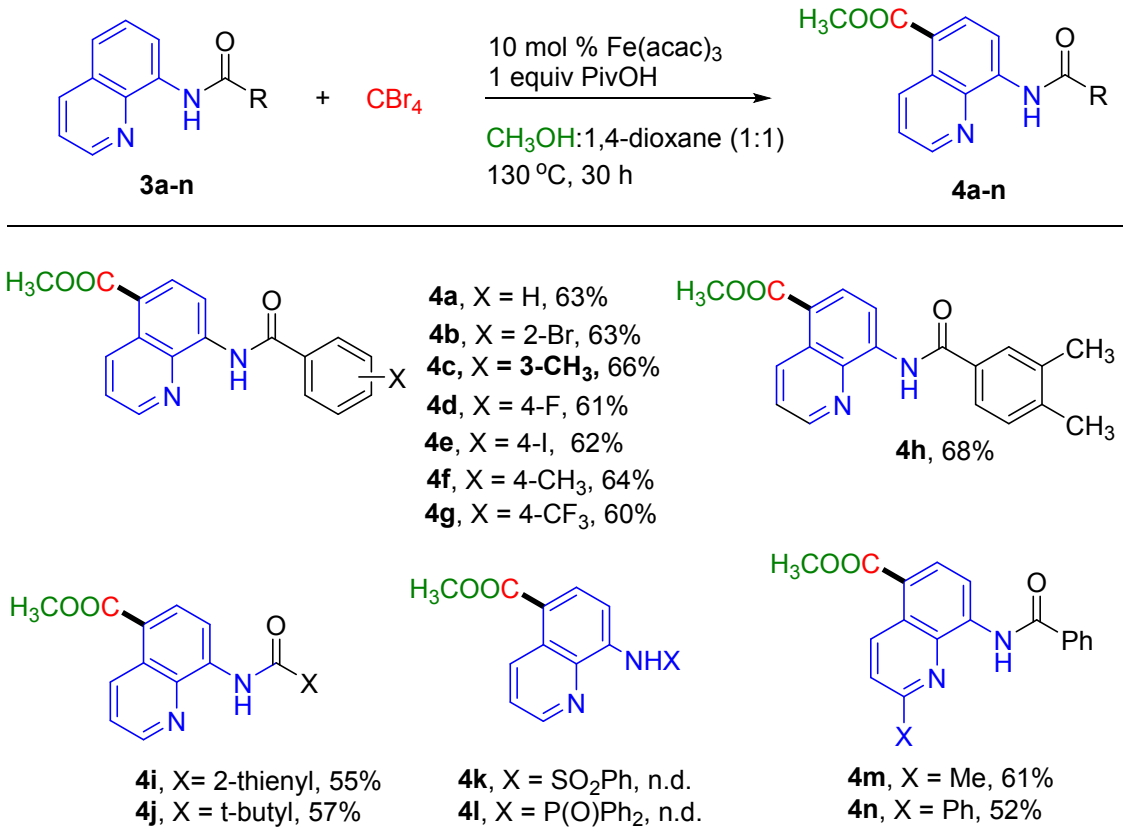
Scheme 2. Substrate Scope of 1-Naphthylamides[a,b]



[a]Reaction conditions: **1** (0.2 mmol), CBr_4 (0.6 mmol), ROH (1.5 mL), PivOH (0.2 mmol), $Fe(acac)_3$ (10 mol %), 90 °C, 24 h. [b]Isolated yield. [c]Reaction temperature 130 °C. n.d. = not detected.

The effect of archetypal chelating groups was investigated (Scheme S2). The substrates with bi-dentate chelating groups, pyrazine and isoquinoline were carboxylated to produce the methyl esters **2p** and **2q** in 57 and 58% yields, respectively, whereas the substrates having benzamide and *N*-methyl benzamide failed to produce the esters **2r** and **2s**, respectively, which suggest that the bidentate *N,N*-chelation and relative N-H acidity are crucial for the carboxylation.

Scheme 3. Substrate Scope of 8-Aminoquinolinamides.[a,b]



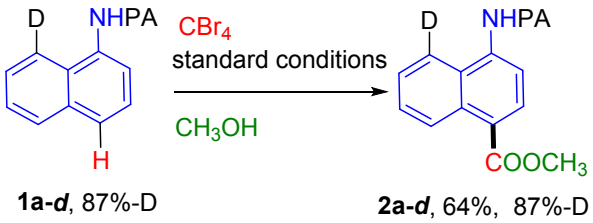
[a]Reaction conditions: **3a-n** (0.2 mmol), CBr_4 (0.8 mmol), $Fe(acac)_3$ (10 mol%), PivOH (0.2 mmol), CH_3OH:1,4-dioxane (1:1; 1.5 mL), 130 °C, 30 h. [b]Isolated yield. n.d. = not detected.

The scope of the protocol was extended for the remote C5 carboxylation of analogous 8-aminoquinolinamides (Scheme 3). The carboxylation occurred at an elevated temperature (130 °C) in a 1:1 mixture methanol and 1,4-dioxane. For example, the substrate **3a** having *N*-benzoyl substituent underwent reaction to provide the methyl ester **4a** in 63% yield. Similarly, the reaction of the substrates bearing electron-withdrawing and donating groups in the benzoyl ring can be accomplished. Thus, the substrate bearing 2-bromo group **3b** underwent carboxylation to give **4b** in 63% yield. Similar result was obtained with **3c** having 3-methyl group, giving **4c** in 66% yield.

The carboxylation of the substrates having 4-fluoro **3d**, 4-iodo **3e**, 4-methyl **3f** and 4-trifluoromethyl **3g** functional groups could be achieved in 60-64% yields. Likewise, **3h** having 3,4-dimethyl substituent underwent carboxylation to give the ester **4h** in 68% yield. Further, the substrate **3i** bearing *N*-2-thiophene carbonyl could be carboxylated to furnish the methyl ester **4i** in 55% yield, whereas **3j** having *N*-pivaloyl substituent afforded the desired ester **4j** in 57% yield. In contrast, *N*-sulfonyl **3k** and *N*-phosphonyl **3l** quinolinamides showed no carboxylation, which suggest that electronic nature of the amide is crucial for the chelation. While, quinolines bearing 2-methyl **3m** and 2-phenyl **3n** substituents underwent reaction to deliver the esters **4m** and **4n** in 61 and 51% yields, respectively.

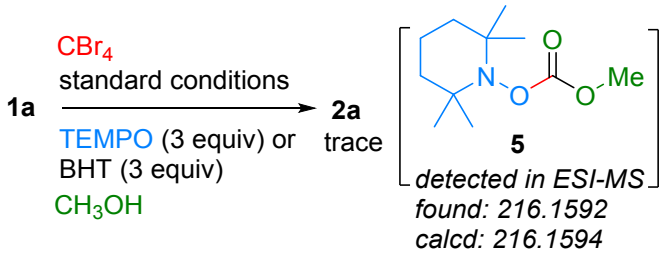
Scheme 4. Control Experiments

(a) Deuterium Scrambling Experiment



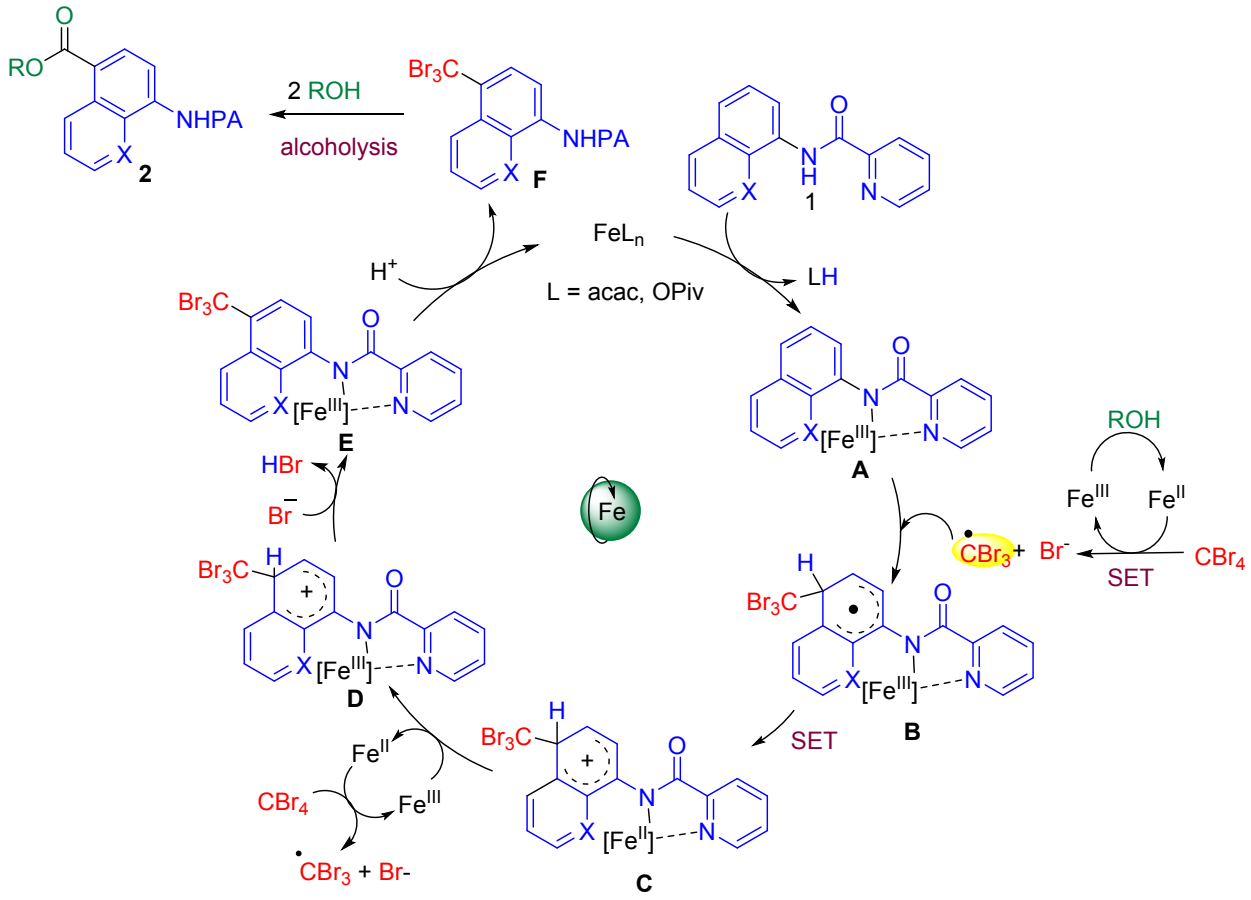
1a-*d*, 87%-D **2a-*d***, 64%, 87%-D

(b) Radical Scavenger Experiments



To gain insight into the catalytic cycle, the mode of chelation of the substrate was investigated. The *peri*-C-D bond in **1a-*d*** was intact, which suggests that no H/D exchange occurs and the remote C-H functionalization presumably dictated *via* the coordination activation strategy (Scheme 4a).

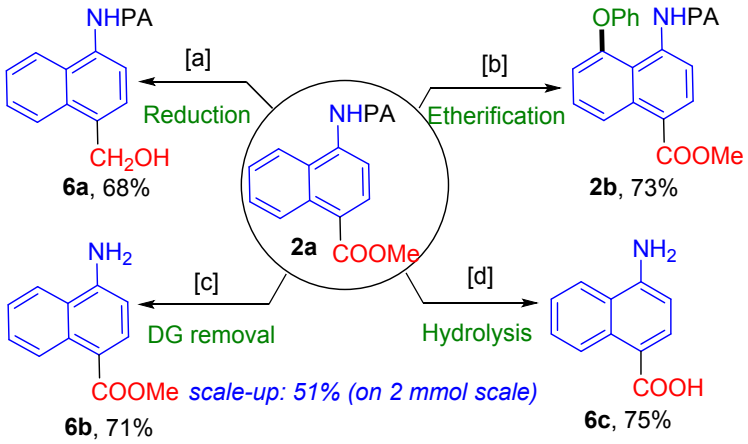
Scheme 5. Plausible Catalytic Cycle



The radical scavenger experiments employing 2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) and 2,6-di-*tert*-butyl-4-methyl-phenol (BHT) yielded a trace amount of **2a** (Scheme 4b).[7] In addition, the ESI-MS analysis of the reaction mixture revealed the formation of the TEMPO adduct **5** (See SI), which suggest that the reaction involves a radical pathway. Thus, $Fe(acac)_3$ with PivOH can give an active Fe(III) species, which can react with the substrate **1** to produce the complex **A** (Scheme 5). The CBr_3 radical can be generated from CBr_4[7] *via* SET[13] using Fe(II), which is *in-situ* yielded from Fe(III) reduction with alcohol.[16] The CBr_3 radical can react at the electrophilic carbon to produce the radical intermediate **B**, that can convert to **C** by SET. Disproportionation of **C** can give the Fe(III) species **D** and the imminent Fe(II) species can be oxidized to Fe(III) by CBr_4 present excess in the reaction. Deprotonation of **D** by bromide ion, that can be formed from CBr_4

using Fe(II), can lead to the formation of **E**. Protodemetalation can furnish **F** and regenerate the active Fe(III) catalyst. Alcoholysis[16] of **F** can give the target esters and the proposed catalytic cycle explains the use of excess CBr_4. PivOH may also help to reduce the pH to facilitate the reduction of Fe(III)[16b] along with the protodemetalation to realize the product formation.

Scheme 6. Synthetic Applications



Reaction conditions: [a] **2a** (0.1 mmol), $LiAlH_4$ (0.1 mmol), THF, 0-60 °C, 16 h, 68%; [b] **2a** (0.2 mmol), $PhB(OH)_2$ (0.4 mmol), $Cu(OAc)_2$ (0.3 mmol), Cs_2CO_3 (0.5 mmol), 130 °C, 10 h, air, DMSO (1 mL), 73%; [c] **2a** (0.1 mmol), NaOH (0.1 mmol), CH_3OH, 90 °C, 12 h, 71%; [d] **2a** (0.1 mmol), NaOH (0.4 mmol), CH_3OH, 90 °C, 24 h, 75%.

Finally, the synthetic utility was investigated using **2a** as a representative example (Scheme 6). The scale-up (2 mmol) reaction of **1a** was carried out and **2a** was obtained in 51% yield. The ester functional group can selectively be reduced utilizing $LiAlH_4$ to furnish the alcohol **6a** in 68% yield. In addition, the *peri*-selective etherification can be carried out using a Cu(II)-mediated C-H functionalization with phenylboronic acid to afford **2b** in 73% yield. Further, the amide hydrolysis

can selectively be performed using NaOH in methanol to afford **6b** in 71% yield, while the hydrolysis of both the amide and ester groups can be carried out using an excess NaOH in methanol to produce 4-amino-1-naphthoic acid **6c** in 75% yield.

In summary, we have developed an iron(III)-catalyzed direct carboxylation of the remote C-H bonds of 1-naphthylamine and 8-aminoquinoline derivatives using CBr_4 as the C1 source *via* a coordination activation strategy and SET process. The use of sustainable iron-catalyst and selectivity are the important practical features. Synthetic elaborations of the ester have also been accomplished.

EXPERIMENTAL SECTION

General Information. $Fe(acac)_3$, ferrocene, $FeCl_3$ and $Fe(NO_3)_3•9H_2O$ of Merck, and CBr_4 from Aldrich were utilized as received. The solvents were purchased from commercial sources and dried according to standard procedure. Purification of the reaction products was carried out on column chromatography using Merck silica gel (60-120 mesh). Analytical TLC was performed on Merck silica gel G/GF 254 plate. NMR spectra were recorded on Bruker 400 MHz and Bruker Avance III 600 MHz using $CDCl_3$ and DMSO-d_6 as solvent and Me_4Si as an internal standard. Chemical shifts (δ) were reported in ppm and spin-spin coupling constants (*J*) were given in Hz. Melting points were determined using Buchi B-540 apparatus and are uncorrected. FT-IR spectra were recorded using Thermo Fisher Scientific spectrometer. Mass spectra were recorded on a Q-TOF ESI-MS instrument (model HAB 273). Single crystal X-ray data were collected on Agilent single crystal X-ray diffractometer, equipped with Mo X-ray source (MoK_α), CCD detector (Eos) and the structure was solved by direct method using SHELXL-14 (Göttingen, Germany).

General Procedure for the Preparation of Amides. To a stirred solution of amine (1 mmol) and Et_3N (1.2 mmol) in CH_2Cl_2 (5 mL) at 0 °C was added acid chloride (1 mmol) in CH_2Cl_2 (5 mL)

drop wise. The mixture was allowed to warm upto room temperature and the starring was continued for 10-12 h. The progress of the reaction was monitored by TLC using ethyl acetate and hexane. After completion, the reaction mixture was diluted with CH_2Cl_2 (30 mL) and washed with brine (2 x 5 mL) and water (1 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on a short pad of silica gel column chromatography using ethyl acetate and hexane as an eluent. Naphthylamides **1a,**[11a] **1b-e**,[17] **1f**,[11b] **1g**,[12] **1h**,[11d] **1i**,[19d] **1k**,[11a] **1l-m**,[12] **1n-o**,[19c] and quinolinamides **3a**,[19a] **3b**,[19c] **3c-d**[11c] **3e**,[15b] **3f-g**,[19a] **3h**,[11d] **3i**,[19a] **3j**,[19c] **3k**,[19c] **3l**,[19b] and **3m-n**,[19c] are reported compounds and analyzed by comparing with the literature data. To show the purity, ^{1}H NMR spectra are provided.

General Procedure for the C4 Carboxylation of 1-Naphthylamides. 1-Naphthylamide **1** (0.2 mmol), CBr_4 (199 mg, 0.6 mmol), $Fe(acac)_3$ (7 mg, 0.02 mmol), PivOH (20.4 mg, 0.2 mmol) and alcohol (1.5 mL) were stirred in a sealed tube at 90-130 ^{o}C for the appropriate time in an oil bath. The progress of the reaction was monitored by TLC using *n*-hexane and ethyl acetate as an eluent. The reaction mixture was then cooled to room temperature and treated with water (5 mL), and the mixture was extracted using ethyl acetate (3 × 10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane and ethyl acetate as an eluent.

General Procedure for C5 Carboxylation of 8-Aminoquinolinamides. 8-Aminoquinolinamide **3** (0.20 mmol), CBr_4 (266 mg, 0.80 mmol), $Fe(acac)_3$ (7 mg, 0.02 mmol), PivOH (20.4 mg, 0.2 mmol), CH_3OH (0.75 mL) and 1,4-dioxane (0.75 mL) were stirred in a sealed tube at 130 ^{o}C for the appropriate time in an oil bath. The work up and purification processes were carried out as described above in general procedure for the carboxylation of 1-naphthylamides. Purification on silica gel column chromatography using n-hexane and ethyl acetate as an eluent afforded target esters.

Scale-up Synthesis of 2a. 1-Naphthylamide **1a** (496 mg, 2 mmol), CBr_4 (1.99 g, 6 mmol), $Fe(acac)_3$ (70.6 mg, 0.2 mmol), PivOH (204 mg, 2 mmol) and CH_3OH (10 mL) were stirred in a sealed tube at 90 °C for 24 h in an oil bath. The work-up was followed as reported in the general procedure. Purification on silica gel column chromatography using *n*-hexane and ethyl acetate (92/8) as an eluent afforded **2a** in 51% yield (312 mg).

***N*-(Naphthalen-1-yl)picolinamide 1a.**[11a] The compound **1a** was synthesized according to the reported procedure in 65% yield (161 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.77 (s, 1H), 8.73-8.71 (m, 1H), 8.39 (dd, *J* = 14.0, 7.6 Hz, 2H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.99-7.87 (m, 2H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.62-7.50 (m, 4H).

***N*-(8-Phenoxynaphthalen-1-yl)benzamide 1b**.[17] The compound **1b** was synthesized according to the reported procedure in 80% yield (272 mg). ^{1}H NMR (600 MHz, $CDCl_3$) δ 13.02 (s, 1H), 9.03-9.01 (m, 1H), 8.25 (d, *J* = 6.6 Hz, 2H), 7.85-7.80 (m, 1H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.62-7.54 (m, 2H), 7.42-7.37 (m, 2H), 7.36-7.31 (m, 2H), 7.25-7.20 (m, 2H), 7.17 (t, *J* = 7.8 Hz, 1H), 6.98-6.93 (m, 1H).

***N*-(8-(*p*-Tolyloxy)naphthalen-1-yl)benzamide 1c.**[17] The compound **1c** was synthesized according to the reported procedure in 70% yield (262 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.09 (s, 1H), 9.03-9.01 (m, 1H), 8.26-8.25 (m, 2H), 7.85-7.81 (m, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.59-7.52 (m, 2H), 7.38-7.28 (m, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 2H), 6.93-6.91 (m, 1H), 2.37 (s, 3H).

***N*-(8-(3-Chlorophenoxy)naphthalen-1-yl)benzamide 1d.**[17] The compound **1d** was synthesized according to the reported procedure in 63% yield (236 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.70 (s, 1H), 8.99-8.97 (m, 1H), 8.37 (d, *J* = 4.0 Hz, 1H), 8.26 (d, *J* = 7.6 Hz, 1H), 7.87-7.83 (m, 1H),

7.67-7.65 (m, 2H), 7.57 (t, *J* = 8.0 Hz, 1H), 7.42-7.38 (m, 2H), 7.28-7.27 (m, 2H), 7.12-7.09 (m, 1H), 7.04-7.01 (m, 2H).

***N*-(8-(3-(Trifluoromethyl)phenoxy)naphthalen-1-yl)benzamide 1e**.[17] The compound **1e** was synthesized according to the reported procedure in 71% yield (290 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.64 (s, 1H), 8.98-8.96 (m, 1H), 8.32 (d, *J* = 4.4 Hz, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 7.86-7.81 (m, 1H), 7.69-7.66 (m, 2H), 7.60-7.56 (m, 2H), 7.45-7.37 (m, 4H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.02-7.00 (m, 1H).

***N*-(8-(Phenylthio)naphthalen-1-yl)benzamide 1f.**[11b] The compound **1f** was synthesized according to the reported procedure in 73% yield (259 mg). ^{1}H NMR (600 MHz, $CDCl_3$) δ 12.25 (s, 1H), 8.66 (s, 1H), 8.37 (d, *J* = 7.2 Hz, 1H), 8.11 (d, *J* = 7.8 Hz, 1H), 7.97-7.96 (m, 1H), 7.85-7.80 (m, 3H), 7.60 (t, *J* = 7.8 Hz, 1H), 7.47-7.45 (m, 2H), 7.01-6.96 (m, 3H), 6.82-6.81 (m, 2H).

***N*-(8-Phenylnaphthalen-1-yl)benzamide 1g.**[12] The compound **1g** was synthesized according to the reported procedure in 71% yield (230 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.58 (s, 1H), 8.25 (d, *J* = 7.2 Hz, 1H), 8.17 (d, *J* = 4.4 Hz, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.77-7.73 (m, 1H), 7.59 (t, *J* = 8.0 Hz, 1H), 7.50-7.47 (m, 1H), 7.41 (d, *J* = 7.3 Hz, 2H), 7.33-7.29 (m, 2H), 7.18 (t, *J* = 8.0 Hz, 2H), 7.00 (t, *J* = 7.2 Hz, 1H).

***N*-(8-Morpholinonaphthalen-1-yl)benzamide 1h.**[11d] The compound **1h** was synthesized according to the reported procedure in 80% yield (266 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.85 (s, 1H), 9.14-9.11 (m, 1H), 8.74 (d, *J* = 4.4 Hz, 1H), 8.39 (d, *J* = 8.0 Hz, 1H), 7.96-7.92 (m, 1H), 7.67-7.64 (m, 1H), 7.62-7.60 (m, 1H), 7.54-7.49 (m, 2H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.39-7.37 (m, 1H), 4.27-4.21 (m, 2H), 3.86-3.83 (m, 2H), 3.20 (d, *J* = 12.0 Hz, 2H), 3.06-3.00 (m, 2H).

***N*-(8-Methoxynaphthalen-1-yl)picolinamide 1i.**[19d] The compound **1i** was synthesized according to the reported procedure in 65% yield (180 mg). ^{1}H NMR (600 MHz, $CDCl_3$) δ 13.24 (s, 1H),

8.99-8.98 (m, 1H), 8.71 (d, *J* = 4.2 Hz, 1H), 8.36 (d, *J* = 7.8 Hz, 1H), 7.94-7.91 (m, 1H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.52-7.48 (m, 2H), 7.46 (d, *J* = 8.4 Hz, 1H), 7.37 (t, *J* = 7.8 Hz, 1H), 6.93 (d, *J* = 7.8 Hz, 1H), 4.21 (s, 3H).

***N*-(5-Ethoxynaphthalen-1-yl)picolinamide 1j**. The compound **1j** was synthesized according to the reported procedure in 61% yield (178 mg). ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.73 (s, 1H), 8.70-8.69 (m, 1H), 8.43 (d, *J* = 7.8 Hz, 1H), 8.36 (d, *J* = 7.8 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 7.94-7.92 (m, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.54-7.50 (m, 2H), 7.47 (t, *J* = 7.8 Hz, 1H), 6.86 (d, *J* = 7.8 Hz, 1H), 4.22 (q, *J* = 6.0 Hz, 2H), 1.56 (t, *J* = 6.6 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 162.3, 155.4, 150.3, 148.2, 137.8, 132.2, 127.5, 126.59, 126.53, 125.2, 122.6, 119.2, 112.5, 105.0, 64.0, 14.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{17}N_2O_2$ 293.1285; found 293.1285.

***N*-(2-Morpholinonaphthalen-1-yl)picolinamide 1k**.[11a] The compound **1k** was synthesized according to the reported procedure in 65% yield (216 mg). ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.30 (s, 1H), 8.74 (d, *J* = 4.2 Hz, 1H), 8.36 (d, *J* = 7.8 Hz, 1H), 7.97-7.94 (m, 1H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.83-7.81 (m, 2H), 7.56-7.54 (m, 1H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.43-7.38 (m, 2H), 3.83-3.81 (m, 4H), 3.02-3.00 (m, 4H).

***N*-(Naphthalen-1-yl)pyrazine-2-carboxamide 1l.**[12] The compound **1i** was synthesized according to the reported procedure in 76% yield (189 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.34 (s, 1H), 9.58-9.57 (m, 1H), 8.86-8.84 (m, 1H), 8.68-8.67 (m, 1H), 8.37-8.35 (m, 1H), 8.04-8.02 (m, 1H), 7.92-7.90 (m, 1H), 7.75-7.73 (m, 1H), 7.61-7.52 (m, 3H).

***N*-(Naphthalen-1-yl)isoquinoline-1-carboxamide 1m.**[12] The compound **1j** was synthesized according to the reported procedure in 61% yield (181 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.07 (s, 1H), 9.82-9.79 (m, 1H), 8.64 (d, *J* = 5.2 Hz, 1H), 8.41-8.38 (m, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 7.91 (d, *J* = 7.2 Hz, 3H), 7.77-7.72 (m, 3H), 7.59-7.54 (m, 3H).

***N*-(Naphthalen-1-yl)benzamide 1n.**[19c] The compound **1k** was synthesized according to the reported procedure in 53% yield (131 mg). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.06 (s, 1H), 8.00 (d, *J* = 6.6 Hz, 2H), 7.92 (t, *J* = 6.6 Hz, 2H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.62-7.59 (m, 1H), 7.56-7.51 (m, 5H).

***N*-Methyl-*N*-(quinolin-8-yl)benzamide 1o**.[19c] The compound **1o** was synthesized according to the reported procedure in 81% yield (212 mg). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.98-8.97 (m, 1H), 8.12 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.43-7.41 (m, 1H), 7.38-7.33 (m, 2H), 7.28 (d, *J* = 7.2 Hz, 2H), 7.07 (t, *J* = 7.2 Hz, 1H), 6.97 (t, *J* = 7.2 Hz, 2H), 3.59 (s, 3H).

***N*-(Quinolin-8-yl)benzamide 3a.**[19a] The compound **3a** was synthesized according to the reported procedure in 65% yield (161 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.75 (s, 1H), 8.96-8.93 (m, 1H), 8.85-8.84 (m, 1H), 8.19 (d, *J* = 8.0 Hz, 1H), 8.10-8.08 (m, 2H), 7.62-7.53 (m, 5H), 7.49-7.46 (m, 1H).

2-Bromo-*N*-(quinolin-8-yl)benzamide 3b.[19c] The compound **3b** was synthesized according to the reported procedure in 63% yield (206 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.29 (s, 1H), 8.96-8.94 (m, 1H), 8.80-8.78 (m, 1H), 8.19 (d, *J* = 8.0 Hz, 1H), 7.73-7.68 (m, 2H), 7.63-7.56 (m, 2H), 7.48-7.43 (m, 2H), 7.37-7.33 (m, 1H).

3-Methyl-*N*-(quinolin-8-yl)benzamide 3c.[11c] The compound **3c** was synthesized according to the reported procedure in 61% yield (159 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.21 (s, 1H), 8.95 (d, *J* = 7.2 Hz, 1H), 8.78-8.77 (m, 1H), 8.19-8.17 (m, 1H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.62-7.54 (m, 2H), 7.47-7.44 (m, 1H), 7.42-7.38 (m, 1H), 7.33 (t, *J* = 7.2 Hz, 2H), 2.61 (s, 3H).

4-Fluoro-*N*-(quinolin-8-yl)benzamide 3d.[11c] The compound **3d** was synthesized according to the reported procedure in 59% yield (157 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.70 (s, 1H), 8.92-8.90

(m, 1H), 8.86-8.85 (m, 1H), 8.22-8.19 (m, 1H), 8.12-8.09 (m, 2H), 7.63-7.56 (m, 2H), 7.51-7.48 (m, 1H), 7.25-7.21 (m, 2H).

4-Iodo-*N*-(quinolin-8-yl)benzamide 3e.[15b] The compound **3e** was synthesized according to the reported procedure in 55% yield (205 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.71 (s, 1H), 8.91-8.89 (m, 1H), 8.85-8.84 (m, 1H), 8.19 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.4 Hz, 2H), 7.81 (d, J = 8.4 Hz, 2H), 7.62-7.56 (m, 2H), 7.50-4.47 (m, 1H).

4-Methyl-*N*-(quinolin-8-yl)benzamide 3f.[19a] The compound **3f** was synthesized according to the reported procedure in 67% yield (175 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.72 (s, 1H), 8.95-8.92 (m, 1H), 8.86-8.84 (m, 1H), 8.20-8.17 (m, 1H), 7.99 (d, J = 8.4 Hz, 2H), 7.59 (t, J = 8.0 Hz, 1H), 7.55-7.52 (m, 1H), 7.49-7.46 (m, 1H), 7.35 (d, J = 8.0 Hz, 2H), 2.46 (s, 3H).

***N*-(Quinolin-8-yl)-4-(trifluoromethyl)benzamide 3g.**[19a] The compound **3g** was synthesized according to the reported procedure in 65% yield (205 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.79 (s, 1H), 8.93-8.91 (m, 1H), 8.87-8.85 (m, 1H), 8.23-8.18 (m, 3H), 7.82 (d, J = 8.0 Hz, 2H), 7.64-7.57 (m, 2H), 7.52-7.49 (m, 1H).

3,4-Dimethyl-*N*-(quinolin-8-yl)benzamide 3h.[11d] The compound **3h** was synthesized according to the reported procedure in 63% yield (174 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.69 (s, 1H), 8.95-8.93 (m, 1H), 8.86-8.85 (m, 1H), 8.19-8.16 (m, 1H), 7.85 (s, 1H), 7.82-7.80 (m, 1H), 7.59 (t, J = 8.0 Hz, 1H), 7.54-7.51 (m, 1H), 7.48-7.45 (m, 1H), 7.30 (d, J = 8.0 Hz, 1H), 2.38 (s, 3H), 2.35 (s, 3H).

***N*-(Quinolin-8-yl)thiophene-2-carboxamide 3i.**[19a] The compound **3i** was synthesized according to the reported procedure in 59% yield (150 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.60 (s, 1H), 8.86-8.83 (m, 2H), 8.19-8.17 (m, 1H), 7.85-7.83 (m, 1H), 7.60-7.52 (m, 3H), 7.49-7.46 (m, 1H), 7.19-7.17 (m, 1H).

***N*-(Quinolin-8-yl)pivalamide 3j.**[19c] The compound **3j** was synthesized according to the reported procedure in 67% yield (153 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.6 Hz, 1H), 7.88-7.86 (m, 1H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.55-7.45 (m, 3H), 1.44 (s, 9H).

***N*-(Quinolin-8-yl)benzenesulfonamide 3k**.[19c] The compound **3k** was synthesized according to the reported procedure in 73% yield (270 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (s, 1H), 8.75-8.74 (m, 1H), 8.09-8.07 (m, 1H), 7.92-7.90 (m, 2H), 7.84-7.82 (m, 1H), 7.46-7.39 (m, 4H), 7.36 (t, *J* = 8.0 Hz, 2H).

***P,P*-Diphenyl-*N*-(quinolin-8-yl)phosphinic amide 3l**.[19b] The compound **3l** was synthesized according to the reported procedure in 71% yield (244 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77-8.75 (m, 1H), 8.13-8.10 (m, 1H), 8.02 (s, 1H), 7.98-7.92 (m, 4H), 7.57-7.53 (m, 2H), 7.50-7.45 (m, 4H), 7.44-7.37 (m, 2H), 7.33-7.24 (m, 2H).

***N*-(2-Methylquinolin-8-yl)benzamide 3m**.[19c] The compound **3m** was synthesized according to the reported procedure in 51% yield (133 mg).^{1}H NMR (600 MHz, $CDCl_3$) δ 10.82 (s, 1H), 8.90-8.89 (m, 1H), 8.09-8.05 (m, 3H), 7.60-7.55 (m, 3H), 7.53-7.49 (m, 2H), 7.35 (d, *J* = 8.4 Hz, 1H), 2.77 (s, 3H).

***N*-(2-Phenylquinolin-8-yl)benzamide 3n**.[19c] The compound **3n** was synthesized according to the reported procedure in 43% yield (139 mg). ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.96 (s, 1H), 8.94-8.93 (m, 1H), 8.25 (d, *J* = 8.4 Hz, 1H), 8.18 (d, *J* = 7.2 Hz, 2H), 8.12 (d, *J* = 7.2 Hz, 2H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.62-7.55 (m, 7H), 7.51 (t, *J* = 7.2 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 165.3, 155.2, 139.2, 138.5, 137.4, 135.4, 134.7, 131.9, 129.7, 129.1, 129.0, 127.48, 127.44, 127.3, 127.0, 121.5, 119.4, 116.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{22}H_{17}N_2O$ 325.1335; found 325.1335.

Methyl 4-(picolinamido)-1-naphthoate 2a. Light yellow solid; yield 65% (40 mg); analytical TLC on silica gel R_f 0.45 in 10% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 92/8); mp 166-168 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.07 (s, 1H), 9.12-9.10 (m, 1H), 8.74-8.72 (m, 1H), 8.60 (d, *J* = 8.2 Hz, 1H), 8.37 (d, *J* = 8.0, Hz, 1H), 8.31 (d, *J* = 8.0 Hz, 1H), 8.18-8.15 (m, 1H), 7.99-7.95 (m, 1H), 7.70-7.65 (m, 2H), 7.57-7.54 (m, 1H), 4.00 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.7, 162.4, 149.8, 148.3, 138.0, 136.9, 132.5, 131.4, 127.9, 127.0, 126.9, 126.6, 125.8, 123.0, 122.7, 120.4, 115.9, 52.2; IR (KBr) 3350, 2952, 1707, 1698, 1534, 1201 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{15}N_2O_3$ 307.1077; found 307.1092.

Methyl 5-phenoxy-4-(picolinamido)-1-naphthoate 2b. Colorless solid; yield 67% (53 mg); analytical TLC on silica gel R_f 0.47 in 10% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 92/8); mp 142-144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.36 (s, 1H), 9.08 (d, *J* = 8.4 Hz, 1H), 8.82-8.79 (m, 1H), 8.28 (d, *J* = 8.4 Hz, 1H), 8.26-8.20 (m, 2H), 7.85-7.81 (m, 1H), 7.48-7.39 (m, 3H), 7.37-7.33 (m, 1H), 7.24-7.18 (m, 3H), 7.01 (d, *J* = 8.0 Hz, 1H), 4.00 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.9, 163.2, 156.4, 154.6, 150.2, 147.9, 139.1, 137.5, 134.8, 132.2, 129.9, 127.5, 126.4, 124.4, 122.4, 122.2, 121.8, 120.3, 117.9, 115.1, 114.4, 52.2; IR (KBr) 3375, 2923, 1713, 1689, 1578, 1207 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{24}H_{19}N_2O_4$, 399.1339; found 399.1351.

Methyl 4-(picolinamido)-5-(*p*-tolyloxy)-1-naphthoate 2c. Colorless solid; yield 61% (50 mg); analytical TLC on silica gel R_f 0.45 in 10% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 92/8); mp 154-156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.44 (s, 1H), 9.08 (d, *J* = 8.5 Hz, 1H), 8.77 (d, *J* = 8.6 Hz, 1H), 8.28-8.24 (m, 3H), 7.87-7.82 (m, 1H), 7.46-7.42 (m, 1H), 7.38-7.35 (m, 1H), 7.21 (d, *J* = 8.3 Hz, 2H), 7.13-7.10 (m, 2H), 6.98 (d, *J* = 7.5 Hz, 1H), 3.99 (s, 3H), 2.37 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 168.0, 163.2, 155.1, 154.0, 150.3, 148.0, 139.2, 137.5, 134.9, 134.1, 132.2, 130.4, 127.5, 126.4, 122.4, 122.2, 121.5, 120.3, 117.8, 115.0, 113.9, 52.3,

20.9; IR (KBr) 3276, 2954, 1703, 1689, 1585, 1283 cm^{-1} ; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{25}H_{21}N_2O_4$ 413.1496; found 413.1500.

Methyl 5-(3-chlorophenoxy)-4-(picolinamido)-1-naphthoate 2d. Colorless solid; yield 64% (55 mg); analytical TLC on silica gel R_f 0.46 in 10% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 92/8); mp 152-154 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 13.08 (s, 1H), 9.07 (d, J = 8.4 Hz, 1H), 8.88-8.86 (m, 1H), 8.34-8.33 (m, 1H), 8.29-8.25 (m, 2H), 7.88-7.85 (m, 1H), 7.52-7.49 (m, 1H), 7.43-7.41 (m, 1H), 7.30-7.27 (m, 2H), 7.15-7.13 (m, 1H), 7.07 (d, J = 7.7 Hz, 1H), 7.04-7.02 (m, 1H), 4.00 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.8, 163.1, 157.5, 153.4, 150.1, 147.9, 138.7, 137.6, 135.2, 134.9, 132.3, 130.6, 127.5, 126.6, 124.4, 122.7, 122.6, 122.4, 120.6, 118.1, 117.7, 115.5, 52.3; IR (KBr) 3275, 2950, 1706, 1688, 1579, 1246 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{24}H_{18}ClN_2O_4$ 433.0950; found 433.0972.

Methyl 4-(picolinamido)-5-(3-(trifluoromethyl)phenoxy)-1-naphthoate 2e. Colorless solid; yield 65% (61 mg); analytical TLC on silica gel R_f 0.46 in 10% ethyl acetate/hexane; purification (n-hexane/ethyl acetate 92/8); mp 164-166 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 13.02 (s, 1H), 9.06 (d, J = 8.4 Hz, 1H), 8.91-8.88 (m, 1H), 8.30-8.28 (m, 2H), 8.26-8.24 (m, 1H), 7.88-7.84 (m, 1H), 7.59 (s, 1H), 7.54-7.50 (m, 1H), 7.48-7.44 (m, 1H), 7.42-7.39 (2H), 7.23-7.21 (m, 1H), 7.08-7.06 (m, 1H), 4.01 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.8, 163.1, 157.1, 153.2, 150.1, 147.8, 138.6, 137.7, 135.0, 134.2 ($J_{C\text{-}F}$ = 166 Hz), 132.3, 130.5, 127.5, 126.7, 123.0, 122.7 ($J_{C\text{-}F}$ = 25.0 Hz), 120.8 ($J_{C\text{-}F}$ = 3.7 Hz), 118.2, 117.2 ($J_{C\text{-}F}$ = 3.8 Hz), 115.75, 115.7, 52.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.58; IR (KBr) 3270, 2953, 1711, 1681, 1581, 1241 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{25}H_{18}F_3N_2O_4$ 467.1213; found 467.1228.

Methyl 5-(phenylthio)-4-(picolinamido)-1-naphthoate 2f. Colorless solid; yield 55% (46 mg); analytical TLC on silica gel R_f 0.45 in 10% ethyl acetate/hexane; purification (*n*-hexane/ethyl

acetate 92/8); mp 166-168 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.76 (s, 1H), 9.13-9.11 (m, 1H), 8.66-8.64 (m, 1H), 8.56 (d, *J* = 8.3 Hz, 1H), 8.23 (d, *J* = 8.3 Hz, 1H), 8.14-8.11 (m, 1H), 7.89-7.84 (m, 2H), 7.59-7.55 (m, 1H), 7.49-7.44 (m, 1H), 6.99-6.97 (m, 3H), 6.79-6.77 (m, 2H), 4.01(s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 168.0, 162.9, 150.3, 148.1, 138.9, 138.7, 137.7, 137.4, 134.8, 130.9, 128.95, 128.93, 127.2, 126.8, 126.7, 126.5, 125.9, 124.9, 124.7, 122.8, 120.5, 52.5; IR (KBr) 3453, 2960, 1713, 1686, 1571, 1233 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{24}H_{19}N_2O_3S$ 415.1111; found 415.1119.

Methyl 5-phenyl-4-(picolinamido)-1-naphthoate 2g. Colorless solid; yield 51% (39 mg); analytical TLC on silica gel R_f 0.47 in 10% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 92/8); mp 146-150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 1H), 9.04 (d, *J* = 8.6, 1H), 8.48 (d, *J* = 8.2 Hz, 1H), 8.27 (d, *J* = 8.2 Hz, 1H), 8.17-8.16 (m, 1H), 8.08 (d, *J* = 7.7 Hz, 1H), 7.79-7.75 (m, 1H), 7.64-7.60 (m, 1H), 7.44-7.40 (m, 3H), 7.34-7.31 (m, 1H), 7.25-7.21 (m, 2H), 7.06-7.03 (m, 1H), 4.03 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.1, 162.1, 149.5, 147.5, 142.5, 137.9, 137.5, 137.2, 133.8, 131.2, 130.8, 129.4, 128.4, 127.2, 126.7, 126.14, 126.11, 124.5, 124.4, 122.0, 119.5, 52.3; IR (KBr) 3346, 2949, 1713, 1685, 1575, 1276 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{24}H_{19}N_2O_3$ 383.1390; found 383.1404.

Methyl 5-morpholino-4-(picolinamido)-1-naphthoate 2h. Light yellow solid; yield 49% (38 mg); analytical TLC on silica gel R_f 0.43 in 15% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 85/15); mp 148-150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.20 (s, 1H), 9.14 (d, *J* = 8.5 Hz, 1H), 8.84-8.81 (m, 1H), 8.75-8.73 (m, 1H), 8.39-8.37 (m, 1H), 8.21 (d, *J* = 8.5 Hz, 1H), 7.98-7.93 (m, 1H), 7.58-7.53 (m, 2H), 7.44-7.42 (m, 1H), 4.26-4.20 (m, 2H), 3.98 (s, 3H), 3.86 (d, *J* = 11.2 Hz, 2H), 3.20 (d, *J* = 11.6 Hz, 2H), 3.05-2.99 (m, 2H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 168.2, 163.0, 153.0, 151.1, 149.9, 148.1, 137.8, 135.5, 134.4, 130.2, 128.1, 126.6, 123.5, 121.9, 119.3,

117.4, 114.3, 65.6, 54.0, 52.4; IR (KBr) 3451, 2954, 1712, 1682, 1520, 1239 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{22}H_{22}N_3O_4$ 392.1605; found 392.1616.

Methyl 5-methoxy-4-(picolinamido)-1-naphthoate 2i. Yellow liquid; yield 49% (33 mg); analytical TLC on silica gel R_f 0.46 in 10% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 94/6); ^1H NMR (400 MHz, $CDCl_3$) δ 13.55 (s, 1H), 9.05 (d, *J* = 8.4 Hz, 1H), 8.73-8.71 (m, 1H), 8.66-8.63 (m, 1H), 8.36 (d, *J* = 8.0 Hz, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 7.96-7.91 (m, 1H), 7.53-7.49 (m, 2H), 7.01 (d, *J* = 7.6 Hz, 1H), 4.23 (s, 3H), 3.97 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 168.0, 162.8, 156.4, 150.8, 148.0, 139.6, 137.6, 134.7, 131.9, 127.4, 126.3, 122.7, 122.0, 119.4, 116.6, 114.7, 106.3, 56.3, 52.0; IR (KBr) 3010, 2925, 1709, 1683, 1586, 1536, 1400, 1250 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{17}N_2O_4$ 337.1183; found 337.1186.

Ethyl 4-(picolinamido)-1-naphthoate 2l. Colorless solid; yield 47% (30 mg); analytical TLC on silica gel R_f 0.42 in 10% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 92/8); mp 122-124 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 11.06 (s, 1H), 9.11-9.09 (m, 1H), 8.74-8.72 (m, 1H), 8.59 (d, *J* = 8.0 Hz, 1H), 8.38-8.36 (m, 1H), 8.30 (d, *J* = 8.0 Hz, 1H), 8.17-8.15 (m, 1H), 7.99-7.95 (m, 1H), 7.68-7.65 (m, 2H), 7.58-7.54 (m, 1H), δ 4.47 (q, *J* = 7.1 Hz, 2H), 1.47 (t, *J* = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.4, 162.4, 149.8, 148.3, 138.0, 136.8, 132.5, 131.2, 127.8, 127.0, 126.9, 126.6, 125.9, 123.5, 122.7, 120.4, 116.0, 77.1, 61.1, 14.5; IR (KBr) 3436, 2985, 1705, 1622, 1534, 1286 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{17}N_2O_3$ 321.1234; found 321.1239.

Ethyl 5-phenoxy-4-(picolinamido)-1-naphthoate 2m. Colorless solid; yield 50% (41 mg); analytical TLC on silica gel R_f 0.43 in 10% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 94/6); mp 118-120 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 13.34 (s, 1H), 9.08 (d, *J* = 8.4 Hz, 1H), 8.81-8.78 (m, 1H), 8.28-8.21 (m, 3H), 7.86-7.82 (m, 1H), 7.48-7.34 (m, 4H), 7.23-7.17 (m,

3H), 7.02-7.00 (m, 1H), 4.47 (q, J = 7.2 Hz, 2H), 1.47 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 167.6, 163.2, 156.5, 154.6, 150.2, 147.9, 138.9, 137.5, 134.8, 132.0, 129.9, 127.4, 126.4, 124.4, 122.7, 122.4, 121.8, 120.3, 117.9, 115.1, 114.5, 61.1, 14.5; IR (KBr) 3469, 2925, 1689, 1690, 1580, 1245 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{25}H_{21}N_2O_4$ 413.1496; found 413.1510.

Propyl 5-phenoxy-4-(picolinamido)-1-naphthoate 2n. Colorless solid; yield 45% (30 mg); analytical TLC on silica gel R_f 0.41 in 10% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 92/8); mp 116-118 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 11.05 (s, 1H), 9.11-9.09 (m, 1H), 8.73-8.71 (m 1H), 8.58 (d, J = 8.2 Hz, 1H), 8.37-8.35 (m, 1H), 8.30 (d, J = 8.2 Hz, 1H), 8.16-8.14 (m, 1H), 7.98-7.94 (m, 1H), 7.67-7.64 (m, 2H), 7.56-7.53 (m, 1H), 4.37 (t, J = 6.7 Hz, 2H), 1.87 (q, J = 7.1 Hz, 2H), 1.08 (t, J = 7.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.4, 162.4, 149.8, 148.3, 138.0, 136.8, 132.5, 131.2, 127.8, 127.0, 126.9, 126.6, 125.9, 123.5, 122.7, 120.4, 116.0, 66.7, 22.3, 10.8; IR (KBr) 3436, 2924, 1746, 1701, 1536, 1236 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{20}H_{19}N_2O_3$ 335.1390; found 335.1406.

Methyl 4-(pyrazine-2-carboxamido)-1-naphthoate 2p. Colorless solid; yield 57% (35 mg); analytical TLC on silica gel R_f 0.41 in 10% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 92/8); mp 158-162 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 10.6 (s, 1H), 9.59 (s, 1H), 9.12-9.09 (m, 1H), 8.89 (d, J = 2.5 Hz, 1H), 8.71-8.70 (m, 1H), 8.56 (d, J = 8.2 Hz, 1H), 8.31 (d, J = 8.2 Hz, 1H), 8.12-8.08 (m, 1H), 7.69-7.67 (m, 2H), 4.01 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.6, 161.1, 148.1, 145.0, 144.4, 142.7, 136.2, 132.4, 131.2, 128.0, 127.1, 126.8, 125.8, 123.7, 120.0, 116.6, 52.3; IR (KBr) 3466, 2924, 1712, 1682, 1580, 1289 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{14}N_3O_3$ 308.1030; found 308.1045.

Methyl 4-(isoquinoline-1-carboxamido)-1-naphthoate 2q. Light yellow solid; yield 58% (41 mg); analytical TLC on silica gel R_f 0.41 in 10% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 92/8); mp 156-158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.48 (s, 1H), 9.81-9.79 (m, 1H), 9.13-9.10 (m, 1H), 8.63-8.61 (m, 2H), 8.33 (d, *J* = 8.2 Hz, 1H), 8.21-8.19 (m, 1H), 7.93-7.91 (m, 2H), 7.78-7.75 (m, 2H), 7.68-7.65 (m, 2H), 4.01 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.8, 163.9, 147.1, 140.1, 137.9, 137.3, 132.5, 131.4, 130.9, 129.3, 127.9, 127.8, 127.6, 127.1, 126.9, 126.5, 126.1, 125.5, 122.9, 120.6, 115.9, 52.2; IR (KBr) 3469, 2924, 1712, 1691, 1581, 1242 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{22}H_{17}N_2O_3$ 357.1234; found 357.1249.

Methyl 8-benzamidoquinoline-5-carboxylate 4a. Colorless solid; yield 63% (39 mg); analytical TLC on silica gel R_f 0.48 in 5% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 96/4); mp 188-190 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.05 (s, 1H), 9.54 (dd, *J* = 1.6 Hz, 1H), 8.94 (d, *J* = 8.4 Hz, 1H), 8.89-8.87 (m, 1H), 8.42 (d, *J* = 8.4 Hz, 1H), 8.11-8.08 (m, 2H), 7.63-7.54 (m, 4H), 3.99 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.8, 165.8, 148.3, 139.1, 138.5, 135.4, 134.8, 133.1, 132.3, 129.0, 127.5, 127.4, 123.2, 119.9, 114.7, 52.2; IR (KBr) 3442, 2924, 1707, 1687, 1574, 1281 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{15}N_2O_3$ 307.1077; found 307.1086.

Methyl 8-(2-bromobenzamido)quinoline-5-carboxylate 4b. Colorless solid; yield 63% (49 mg); analytical TLC on silica gel R_f 0.47 in 5% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 95/5); mp 156-158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.61 (s, 1H), 9.53-9.50 (m, 1H), 8.94 (d, *J* = 8.0 Hz, 1H), 8.82-8.80 (m, 1H), 8.42 (d, *J* = 8.4 Hz, 1H), 7.74-7.70 (m, 2H), 7.60-7.57 (dd, *J* = 8.8 Hz, 1.6 Hz, 1H), 7.48-7.45 (m, 1H), 7.40-7.37 (m, 1H), 4.00 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.8, 166.2, 148.4, 138.7, 138.3, 138.0, 135.3, 133.9, 133.0, 131.9, 129.8, 127.8, 127.4, 123.3, 120.4, 119.8, 115.1, 52.2; IR (KBr) 3297, 2921, 1709, 1676, 1527, 1279 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{14}BrN_2O_3$ 385.0182; found 385.0184.

Methyl 8-(3-methylbenzamido)quinoline-5-carboxylate 4c. Colorless solid; yield 66% (42 mg); analytical TLC on silica gel R_f 0.48 in 5% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 96/4); mp 146-148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.52 (s, 1H), 9.53-9.50 (m, 1H), 8.93 (d, *J* = 8.0 Hz, 1H), 8.80-8.79 (m, 1H), 8.41 (d, *J* = 8.4 Hz, 1H), 7.71-7.68 (m, 1H), 7.58 (dd, *J* = 8.8 Hz, 4.4 Hz, 1H), 7.44-7.40 (m, 1H), 7.36-7.32 (m, 2H), 3.99 (s, 3H), 2.61 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.4, 166.8, 148.3, 139.2, 138.3, 137.1, 136.2, 135.3, 133.0, 131.6, 130.8, 127.4, 126.2, 123.2, 119.9, 114.6, 52.2, 20.4; IR (KBr) 3339, 2953, 1711, 1686, 1574, 1279 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{17}N_2O_3$ 321.1234; found 321.1251.

Methyl 8-(4-fluorobenzamido)quinoline-5-carboxylate 4d. Colorless solid; yield 61% (40 mg); analytical TLC on silica gel R_f 0.47 in 5% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 95/5); mp 167-168 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.00 (s, 1H), 9.55-9.53 (m, 1H), 8.91 (d, *J* = 8.3 Hz, 1H), 8.89-8.87 (m, 1H), 8.42 (d, *J* = 8.3 Hz, 1H), 8.13-8.10 (m, 2H), 7.62 (dd, *J* = 8.8, 4.2 Hz, 1H), 7.27 (s, 1H), 7.24-7.22 (m, 1H), 3.99 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.8, 164.6 ($J_{C\text{-}F}$ = 251.5 Hz), 148.4, 138.9, 138.5, 135.5, 133.1, 131.0, 130.0 (($J_{C\text{-}F}$ = 9.0 Hz), 127.4, 123.3, 120.0, 116.2 ($J_{C\text{-}F}$ = 21.9 Hz), 116.0, 114.7, 52.3; ^{19}F NMR (565 MHz, $CDCl_3$) δ -106.83; IR (KBr) 3341, 2924, 1712, 1679, 1573, 1223 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{14}FN_2O_3$ 325.0983; found 325.1001.

Methyl 8-(4-iodobenzamido)quinoline-5-carboxylate 4e. Colorless solid; yield 62% (54 mg); analytical TLC on silica gel R_f 0.47 in 5% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 95/5); mp 156-158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.03 (s, 1H), 9.55-9.53 (m, 1H), 8.91 (d, *J* = 8.3 Hz, 1H), 8.90-8.88 (m, 1H), 8.42 (d, *J* = 8.3 Hz, 1H), 7.94-7.92 (m, 1H), 7.83-7.80 (m, 2H), 7.62 (dd, *J* = 8.7, 4.2 Hz, 1H), 4.00 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.8, 165.0, 148.4, 138.7, 138.4, 138.3, 135.5, 134.2, 133.0, 129.0, 127.4, 123.3, 114.8, 99.6, 52.2; IR

(KBr) 3437, 2924, 1712, 1686, 1527, 1280 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[M+H]^+$ $C_{18}H_{14}IN_2O_3$ 433.0044; found 433.0056.

Methyl 8-(4-methylbenzamido)quinoline-5-carboxylate 4f. Colorless solid; yield 64% (41 mg); analytical TLC on silica gel R_f 0.48 in 5% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 96/4); mp 159-161 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 11.03 (s, 1H), 9.55-9.52 (m, 1H), 8.93 (d, *J* = 8.3 Hz, 1H), 8.89-8.87 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.42 (d, *J* = 8.3 Hz, 1H), 8.00-7.98 (m, 2H), 7.61 (dd, *J* = 8.8 Hz, 4.2 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 3.99 (s, 3H), 2.46 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.9, 165.8, 148.3, 142.9, 139.2, 138.4, 135.4, 133.2, 132.0, 129.7, 127.6, 127.4, 123.2, 119.6, 114.6, 52.2, 21.7; IR (KBr) 3470, 2952, 1708, 1682, 1527, 1283 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{17}N_2O_3$ 321.1234; found 321.1240.

Methyl 8-(4-(trifluoromethyl)benzamido)quinoline-5-carboxylate 4g. Colorless solid; yield 60% (45 mg); analytical TLC on silica gel R_f 0.48 in 5% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 96/4); mp 168-170 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 11.08 (s, 1H), 9.56-9.53 (m, 1H), 8.92 (d, *J* = 8.4 Hz, 1H), 8.89-8.88 (m, 1H), 8.42 (d, *J* = 8.4 Hz, 1H), 8.21-8.18 (m, 2H), 7.85-7.82 (m, 2H), 7.63 (dd, *J* = 8.8 Hz, 4.2 Hz, 1H), 4.00 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.7, 164.4, 148.4 , 138.5, 138.3, 138.0, 135.6, 134.4 (J_{C-F} = 26.6 Hz), 133.8, 133.0, 128.0, 127.8 (J_{C-F} = 270.9 Hz), 126.1 (J_{C-F} = 3.6 Hz), 123.4, 120.4, 115.0, 52.3; ^{19}F NMR (565 MHz, $CDCl_3$) δ -62.96; IR (KBr) 3342, 2924, 1712, 1683, 1527, 1283 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{14}F_3N_2O_3$ 375.0951; found 375.0978.

Methyl 8-(3,4-dimethylbenzamido)quinoline-5-carboxylate 4h. Colorless solid; yield 68% (46 mg); analytical TLC on silica gel R_f 0.45 in 5% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 94/6); mp 166-168 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 10.99 (s, 1H), 9.55-9.52 (m, 1H), 8.93 (d, *J* = 8.4 Hz, 1H), 8.89-8.88 (m, 1H), 8.42 (d, *J* = 8.4 Hz, 1H), 7.86 (s, 1H), 7.82-7.80 (m,

1H), 7.60 (dd, J = 8.8 Hz, 4 Hz, 1H), 7.31 (d, J = 7.6 Hz, 1H), 3.99 (s, 3H), 2.39 (s, 3H). 2.36 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.9, 166.0, 148.3, 141.6, 139.3, 138.5, 137.4, 135.4, 133.2, 132.4, 130.2, 128.8, 127.4, 124.8, 123.2, 119.6, 114.6, 52.1, 20.09, 20.06; IR (KBr) 3346, 2948, 1713, 1685, 1576, 1276 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{20}H_{19}N_2O_3$ 335.1390; found 335.1396.

Methyl 8-(thiophene-2-carboxamido)quinoline-5-carboxylate 4i. Colorless solid; yield 55% (35 mg); analytical TLC on silica gel R_f 0.48 in 5% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 95/5); mp 158-160 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 10.89 (s, 1H), 9.54-9.52 (m, 1H), 8.89-8.87 (m, 1H), 8.84 (d, J = 8.4 Hz, 1H), 8.40 (d, J = 8.4 Hz, 1H), 7.87-7.85 (m, 1H), 7.63-7.59 (m, 2H), 7.21-7.19 (m, 1H), 3.99 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.8, 160.3, 148.3, 139.7, 138.8, 138.2, 135.4, 133.1, 131.6, 129.0, 128.1, 127.4, 123.3, 119.8, 114.7, 52.2; IR (KBr) 3332, 2921, 1708, 1673, 1573, 1281 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{13}N_2O_3S$ 313.0641; found 313.0642.

Methyl 8-pivalamidoquinoline-5-carboxylate 4j. Colorless solid; yield 57% (33 mg); analytical TLC on silica gel R_f 0.48 in 5% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 95/5); mp 158-160 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 10.55 (s, 1H), 9.51-9.48 (m, 1H), 8.83-8.82 (m, 1H), 8.78 (d, J = 8.0 Hz, 1H), 8.35 (d, J = 8.4 Hz, 1H), 7.58-7.55(m, 1H), 3.96 (s, 3H), 1.43 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 177.7, 166.8, 148.2, 139.2, 138.4, 135.3, 133.1, 127.3, 123.1, 119.4, 114.3, 52.1, 40.6, 27.7; IR (KBr) 3355, 2961, 1705, 1684, 1520, 1281 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{19}N_2O_3$ 287.1390; found 287.1413.

Methyl 8-benzamido-2-methylquinoline-5-carboxylate 4m. Colorless solid; yield 61% (39 mg); analytical TLC on silica gel R_f 0.47 in 5% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 94/6); mp 189-190 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 11.14 (s, 1H), 9.40 (d, J = 8.4 Hz,

1H), 8.90 (d, *J* = 8.4 Hz, 1H), 8.35 (d, *J* = 7.8 Hz, 1H), 8.09 (d, *J* = 7.2 Hz, 2H), 7.63-7.60 (m, 1H), 7.57 (t, *J* = 7.8 Hz, 2H), 7.49 (d, *J* = 9.6 Hz, 1H), 3.98 (s, 3H), 2.79 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 166.8, 165.5, 157.2, 138.2, 137.8, 135.3, 134.8, 132.1, 131.9, 128.9, 127.3, 125.4, 123.9, 119.6, 114.6, 52.0, 25.1; IR (KBr) 3327, 1703, 1687, 1533, 1400, 1276 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{17}N_2O_3$ 321.1234; found 321.1237.

Methyl 8-benzamido-2-phenylquinoline-5-carboxylate 4n. Colorless solid; yield 52% (39 mg); analytical TLC on silica gel R_f 0.47 in 5% ethyl acetate/hexane; purification (*n*-hexane/ethyl acetate 94/6); mp 187-188 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 11.29 (s, 1H), 9.61 (d, *J* = 9.0 Hz, 1H), 8.95 (d, *J* = 8.4 Hz, 1H), 8.41 (d, *J* = 8.4 Hz, 1H), 8.21 (d, *J* = 7.2 Hz, 2H), 8.14 (d, *J* = 7.2 Hz, 2H), 8.10 (d, *J* = 9.0 Hz, 1H), 7.64-7.62 (m, 1H), 7.58 (t, *J* = 7.8 Hz, 4H), 7.55 (d, *J* = 7.2 Hz, 1H), 4.01 (s, 3H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 166.9, 165.6, 155.1, 139.0, 138.7, 138.2, 136.4, 135.0, 132.8, 132.4, 130.1, 129.2, 129.1, 127.5, 127.4, 126.3, 120.9, 119.8, 115.0, 77.3, 77.1, 76.9, 52.2; IR (KBr) 3339, 1712, 1676, 1525, 1400, 1261 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{24}H_{19}N_2O_3$ 383.1390; found 383.1389.

***N*-(4-(Hydroxymethyl)naphthalen-1-yl)picolinamide 6a**. $LiAlH_4$ (3.8 mg, 0.1 mmol) was suspended in THF (10 mL) and cooled to 0 °C in an ice bath in a 25 mL round bottom flask kept under nitrogen atmosphere.[18a] A solution of **2a** (30.6 mg, 0.1 mmol) in THF (5 mL) was added dropwise via syringe at 0 °C. The resultant mixture was stirred at 60 °C for 6 h in an oil bath. The reaction was then cooled to room temperature and quenched by addition of EtOAc (15 mL). The organic layer was separated and the solid was extracted with EtOAc (2 x 15 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using ethyl acetate and hexane (20/80) as eluent to give **6a**. White solid, yield 68% (19 mg), mp 186-188 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 10.79 (s, 1H), 8.73-8.71 (m, 1H),

8.37-8.35 (m, 2H), 8.24-8.22 (m, 1H), 8.15-8.13 (m, 1H), 7.98-7.95 (m, 1H), 7.64-7.53 (m, 4H), 5.15 (s, 2H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 162.4, 150.0, 148.2, 138.0, 133.3, 132.9, 132.1, 126.9, 126.7, 126.6, 126.4, 126.1, 124.9, 122.7, 121.2, 118.1, 63.9; IR (KBr) 3516, 3350, 2920, 1678, 1540, 1288 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{15}N_2O_2$ 279.1128; found 279.1124.

General Procedure for Copper-Mediated Etherification.[17] Compound **2a** (0.2 mmol, 61.2 mg), phenylboronic acid (48.8 mg, 0.4 mmol), Cs_2CO_3 (0.5 mmol, 163 mg), $Cu(OAc)_2$ (0.3 mmol, 55 mg) and DMSO (1.0 mL) were stirred in a preheated oil bath at 130 °C under air for 10 h in an oil bath. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as an eluent. After completion, the reaction mixture was cooled to room temperature, diluted with EtOAc (45 mL). The mixture was washed with aqueous ammonia (3mL), brine (5 mL) and water (5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane and ethyl acetate as an eluent (90/10) to give **2b** as white solid; yield 73% (58 mg,). The characterization data were identical to the reported.

Methyl 4-amino-1-naphthoate 6b. To a stirred solution of NaOH (0.1 mmol, 4 mg) in CH_3OH (1.5 mL), **2a** (30.6 mg, 0.1 mmol) was added. The reaction mixture was stirred at room temperature for 2 min and heated at 90 °C for 12 h. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as an eluent. After completion, the reaction mixture was allowed to cool to room temperature, diluted with EtOAc (20 mL). The solution was washed with 0.5 N HCl (4 × 5 mL), brine (5 mL) and water (5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane and ethyl acetate (90/10). White solid, 71% yield (14 mg); mp 168-170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.16-9.14 (m, 1H), 8.15 (d, *J*=8.4 Hz, 1H), 7.81(d, *J* = 8.4 Hz, 1H), 7.63-7.58 (m, 1H), 7.51-7.47 (m, 1H),

6.72 (d, J = 8.4 Hz, 1H), 3.93 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 168.0, 147.3, 133.3, 132.9, 128.0, 126.9, 125.1, 122.8, 120.8, 116.2, 107.6, 51.7; IR (KBr) 3491, 2960, 2924, 2853, 1681, 1261 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{12}H_{12}NO_2$ 202.0863; found 202.0889.

4-Amino-1-naphthoic acid 6c. The above described procedure for **6b** was followed prolonging the reaction to 24 h. purification (*n*-hexane/ethyl acetate 50/50); White solid, 75% yield (14 mg); mp 174-176 °C, lit[18b] 176 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 12.03 (s, 1H), 9.12 (d, J = 8.4 Hz, 1H), 8.15 (d, J = 8.3 Hz, 1H), 8.04 (d, J = 8.3 Hz, 1H), 7.53 (t, J = 7.1 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 6.64-6.62 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 168.4, 150.2, 133.6, 133.4, 127.4, 125.9, 123.6, 122.6, 121.8, 111.8, 105.5; IR (KBr) 3481, 2954, 2924, 2853, 1577, 1244 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $[M+H]^+$ $C_{11}H_{10}NO_2$ 188.0706; found 188.0733.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information having scheme S1, figure S1, table S1, Scheme S2, crystal structure of **2b** and NMR spectra of all the products is available free of charge on the ACS Publications website at DOI:

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Notes

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