Organic & Biomolecular Chemistry

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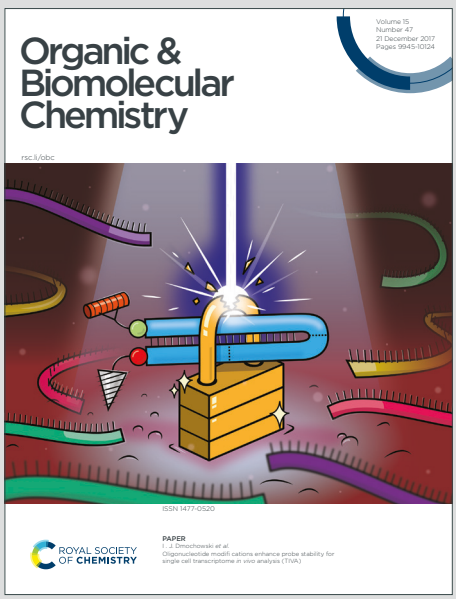

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DOI: 10.1039/D0OB00586J

ARTICLE

Palladium-Catalyzed C8-H Alkoxycarbonylation of 1-Naphthylamines with Alkyl Chloroformates

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Received 00th January 20xx,
Accepted 00th January 20xx

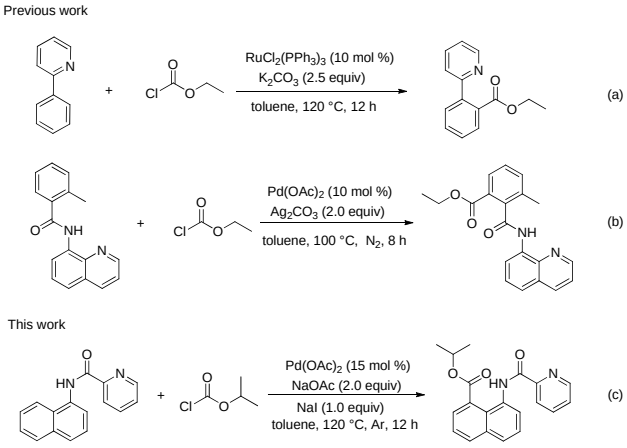
DOI: 10.1039/x0xx00000x

A simple and efficient protocol for palladium-catalyzed C8-H alkoxycarbonylation of 1-naphthylamine derivatives with alkyl chloroformates has been developed, exhibiting broad functional group tolerance, high regioselectivity, and oxidant-free conditions. Furthermore, the reaction features its ease of further functionalization and transformation. For example, the concise synthesis of one BET bromodomain inhibitor was accomplished *via* benz[cd]indol-2(1H)-one after multistep transformations from the obtained alkoxycarbonylation product. In addition, the control experiments suggest that the reaction might involve a radical process and the C-H bond cleavage might not be involved in the rate-determining step.

Introduction

Aromatic esters, as a type of important synthetic building blocks, are ubiquitous in many fields, such as pharmaceutical industries, natural products, and materials science.[1] Therefore, the synthesis of organic compounds containing such structural moiety has attracted synthetic chemists' efforts. The traditional synthetic methodologies for these compounds relied on either the reaction of activated acid derivatives with alcohols or the transition metal-catalyzed cross-coupling reaction of aryl halides with carbon monoxide.[2]

The C-H carbonylation/esterification reactions have been proven to be an important tool towards synthesis of amides/lactams, carboxylic acids, esters, ketones, and anhydrides involving carbon monoxide as a carbonyl source.[3] However, carbon monoxide as the carbonyl source have its drawbacks of high toxicity, flammability, explosibility, and difficult handling of gaseous carbon monoxide. Since Yu and co-workers developed the first palladium-catalyzed oxidative ethoxycarbonylation of aromatic C–H bonds with diethyl azodicarboxylate (DEAD),[4a] many groups have successfully achieved carbonylative transformations with azodicarboxylate.[4] Other esterification reagents also appeared, such as carbon dioxide,[5] glyoxylate,[6] α-keto esters,[7] di-*tert*-butyl decarbonate (Boc_2O),[8] formates,[9] and potassium oxalate.[10] Although the abovementioned carboxylation reagents have been widely utilized in the synthesis of ester compounds, investigating new avenues for direct C–H alkoxycarbonylation would be highly desirable.



Scheme 1. Ligand-directed regioselective C-H alkoxycarbonylation

In 2009, the ruthenium-catalyzed direct alkoxycarbonylation of the aromatic C–H bonds with alkyl chloroformates was described by Kakiuchi and co-workers (Scheme 1a).[11a] Subsequently, Shi disclosed the Pd(II)-catalyzed stereoselective alkoxycarbonylation of $C(sp^3)$–H bonds with alkyl chloroformates.[11b] And then, they realized the alkoxycarbonylation of aromatic C–H bonds using 8-aminoquinoline moiety (AQ) as a directing group (Scheme 1b).[11c] Despite these advances, the above alkoxycarbonylation protocols belong to the *ortho*-C-H functionalization, and the catalytic C8–H of 1-Naphthylamines alkoxycarbonylation remains rare.

Since Daugulis and co-workers introduced the picolinamide (PA) moiety as a bidentate directing group in 2005,[12] several catalytic versions for regioselective C-H functionalization of 1-naphthylamine have been achieved.[13] The research interest in our group mainly focuses on the remote C-H functionalization of arene derivatives at an unusual site, especially at the C4 or C5 site of 8-aminoquinoline derivatives[14] and the C4[15] or

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Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

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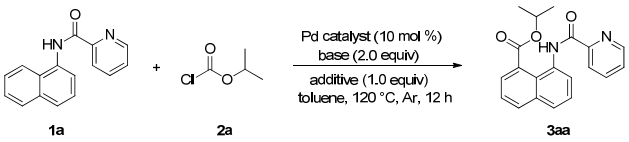
C8[13d,13j,13k] site of 1-naphthylamide derivatives. Just recently, an efficient palladium-catalyzed C8-H acylation of 1-naphthylamines was developed in our group.[13j] Inspired by abovementioned pioneering examples, herein we envisioned showcasing a simple and efficient protocol for direct C8–H alkoxycarbonylation of 1-naphthylamides with alkyl chloroformates (Scheme 1c).

Results and discussion

Initially, the $Pd(OAc)_2$-catalyzed reaction of N-(naphthalen-1-yl) picolinamide **1a** with isopropyl chloroformate **2a** was performed in the presence of NaOAc in toluene, and gratifyingly, the desired product **3aa** was obtained in 57% yield (Table 1, entry 1). However, other palladium species did not provide comparable yields of the product **3aa** (Table 1, entries 2-6). Then, various bases were examined, and NaOAc was the best base with high yield of 57% (Table 1, entry 1 *vs.* entries 7-12 and the ESI). Subsequently, different additives were examined, NaI exhibited the best activity for this reaction (Table 1, entries 13-16). However, a catalytic amount of NaI did not afford the products with better results (Table 1, entries 17 and 18 *vs.* entry 14). Finally, some control experiments were performed (Table 1, entries 19-23). Both the palladium catalyst and the base played important roles for this successful catalytic reaction (Table1, entries 19 and 20). When the catalyst loading was increased to 15 mol %, the product was obtained in a higher yield of 88% (Table 1, entry 21 *vs.* entry 14). However, when the temperature reduced to 100 °C, the yield of **3aa** was decreased to 48% (Table 1, entry 22 *vs.* entry 21). The reaction could also be conducted under air, albeit generating the product in a lower yield of 77% (entry 23 vs entry 21).

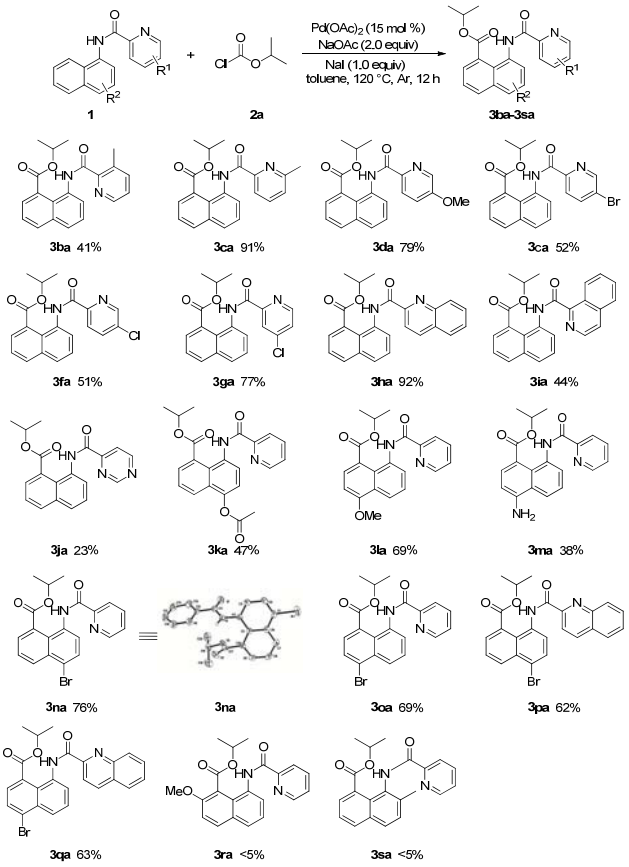
Table 1. Optimization of the reaction conditions[a]



1a 2a 3aa

entry	catalyst	base	additive	Yield (%)[b]
1	$Pd(OAc)_2$	NaOAc	-	57
2	$Pd(TFA)_2$	NaOAc	-	45
3	$PdCl_2$	NaOAc	-	43
4	$Pd(CH_3CN)_2Cl_2$	NaOAc	-	32
5	Pd_2dba_3	NaOAc	-	<5
6	PdI_2	NaOAc		26
7	$Pd(OAc)_2$	Na_2CO_3	-	40
8	$Pd(OAc)_2$	K_2CO_3	-	43
9	$Pd(OAc)_2$	Na_3PO_4	-	41
10	$Pd(OAc)_2$	Na_2HPO_4	-	35
11	$Pd(OAc)_2$	EtONa	-	44
12	$Pd(OAc)_2$	tBuONa	-	47
13	$Pd(OAc)_2$	NaOAc	I_2	<5
14	$Pd(OAc)_2$	NaOAc	NaI	81
15	$Pd(OAc)_2$	NaOAc	KI	73
16	$Pd(OAc)_2$	NaOAc	$AgSbF_6$	16
17[c]	$Pd(OAc)_2$	NaOAc	NaI	68
18[d]	$Pd(OAc)_2$	NaOAc	NaI	72
19	-	NaOAc	NaI	<5
20	$Pd(OAc)_2$	-	NaI	<5
21[e]	$Pd(OAc)_2$	NaOAc	NaI	88
22[e,f]	$Pd(OAc)_2$	NaOAc	NaI	48
23[e,g]	$Pd(OAc)_2$	NaOAc	NaI	77

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), Pd catalyst (10 mol %), base (0.2 mmol) and an additive in toluene (1.0 mL) at 120 °C under argon for 12 h. [b]Isolated yield based on **1a**. [c]With an additive loading of 30 mol %. [d]With an additive loading of 50 mol %. [e]With a catalyst loading of 15 mol %. [f]At 100 °C. [g]Under air.



Scheme 2. Scope of 1-(Naphthalenyl)picolinamides

With the optimized reaction conditions in hand, the substrate scope of N-(naphthalen-1-yl)picolinamide derivatives with isopropyl chloroformate **2a** was explored, and the results are summarized in Scheme 2. Generally, the reaction could tolerate various electron-donating and -withdrawing substituents in the pyridine ring or the naphthalene moiety, affording the corresponding products in moderate to good yields (**3ba-3qa**). Comparatively, substrates bearing electron-donating groups could result in products in slightly higher yields of than those of substrates bearing electron-withdrawing groups in the pyridine ring (**3ca** and **3da** *vs.* **3ea-3ga**). Substrates bearing an *ortho*-substituent in the pyridine ring would lead to lower yields (**3ba** *vs.* **3ca**), which may be attributed to the *ortho*-steric effect. Notably, the AQ directing group possessing a benzene ring moiety would accelerate reaction, affording the product **3ha** in a high yield of 92%. However, the similar result of **3ia** was obtained to that of **3ba** probably due to the steric effect of the C8-H bond in the isoquinoline moiety. The electron-poor directing group did not have advantage to this reaction and result in the product **3ja** in a low yield of 23%. The substrates bearing electron-donating or -withdrawing groups at the C4 or C5 site in the naphthalene ring could afford the desired products

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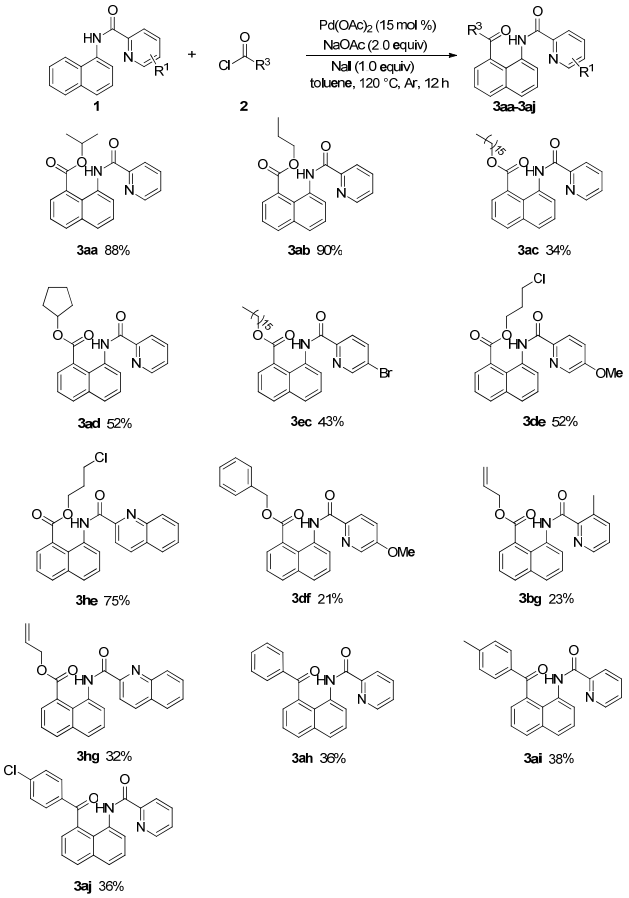
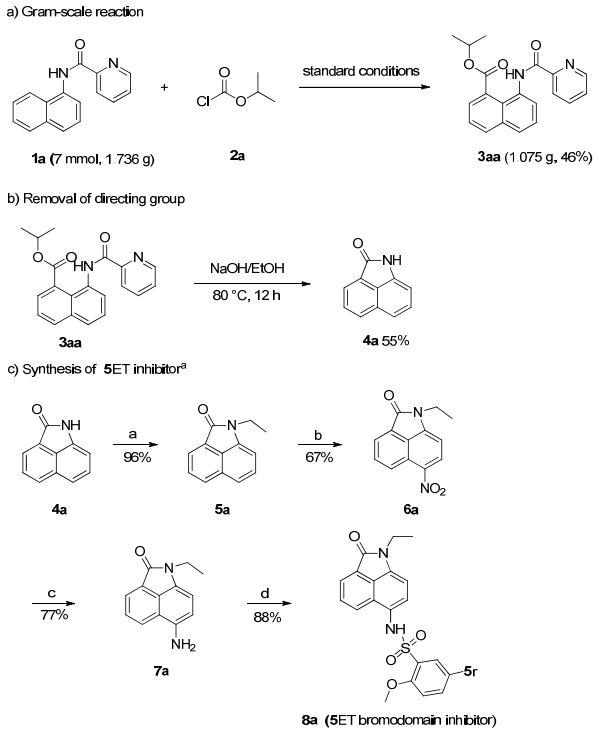


Scheme 3. Scope of Various Chloroformates

in moderate yields (**3ka-3oa**). Especially, the molecular structure of **3na** was unambiguously confirmed by single-crystal X-ray diffraction study.[18] However, when there was a substituent at the C7 or C2 site in the naphthalene ring, the reactivity was switched off and few products **3ra** and **3sa** can be obtained due to the strong steric hindrance.

Subsequently, the substrate scope of chloroformates and aryl chlorides were also explored under the standard reaction conditions (Scheme 3). Chloroformates containing a wide range of aliphatic groups were employed in this reaction, affording the desired products in mostly moderate yields (**3ab-3ec**). Moreover, the 3-chloropropyl chloroformate **2e** could also tolerated in this reaction, providing the product in moderate yields of 52% and 75%, respectively (**3de** and **3he**). However, in the case of benzyl chloroformate **2f** as an esterification reagent, the desired product **3df** was obtained in a lower yield of 21%. In addition, allyl chloroformate **2g** was also checked in this reaction, albeit generating the target products in lower yields of 23% and 32%, respectively (**3bg** and **3hg**). Finally, the reaction was also suitable to traditional aryl chlorides, although providing the target products in relatively lower yields, which is attributed to the electron-poor property of the aryl chlorides (**3ah-3aj**).



[a]Reagents and conditions: (a) CH_3CH_2I, NaH, DMF, rt; (b) HNO_3, AcOH, 0-50 °C, 1 h; (c) Fe, NH_4Cl, AcOH, 50 °C, 30 min; (d) 5-Bromo-2-methoxybenzenesulfonyl chloride, CH_2Cl_2, pyridine, rt.

Scheme 4. Synthetic Applications

In order to demonstrate the synthetic utility of this protocol, a gram scale reaction and some potential applications of the esterification product were completed (Scheme 4). A gram scale reaction of **1a** (7 mmol, 1.736 g) was investigated under the standard conditions, affording the product **3aa** (1.075 g) in a moderate yield of 46% (Scheme 4a). The experiment of removal of the directing group was carried out, and benz[cd]indol-2(1H)-one **4a** was successfully obtained in 55% yield *via* the hydrolysis process of **3aa** (Scheme 4b). Benz[cd]indol-2(1H)-one **4a** as a significant skeleton is frequently found in pharmaceuticals, natural products, and biologically active compounds, and notably, the BET inhibitor is a new class of potent BET bromodomain inhibitor with anti-tumor and anti-inflammatory activities.[16] Herein its facile synthesis was successfully achieved from benz[cd]indol-2(1H)-one **4a**. First, alkyl substitution product **5a** was obtained by nucleophilic substitution of **4a** with iodoalkane in 96% yield. Then, nitration reaction of **5a** with nitric acid took place to afford the product **6a** in 67% yield, followed by a nitro reduction in the presence of iron and AcOH to form **7a** in 77% yield. Finally, the sulfonamidation occurred to provide the BET bromodomain inhibitor **8a** in a high yield of 88% (Scheme 4c).

In order to gain insight into the mechanism, several control experiments were conducted (Scheme 5). Some designed substrates (**A–D**) were first explored under the standard reaction conditions, but no esterification products were

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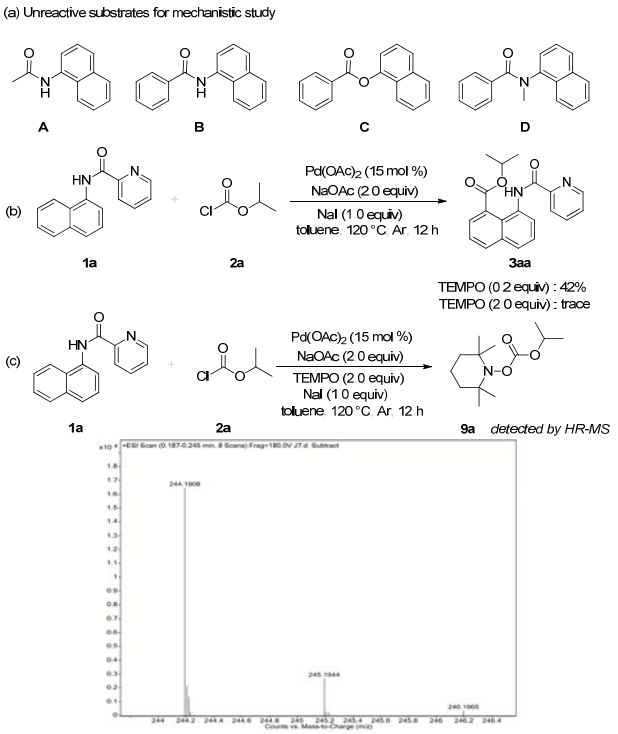
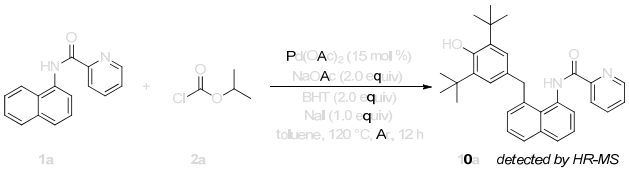
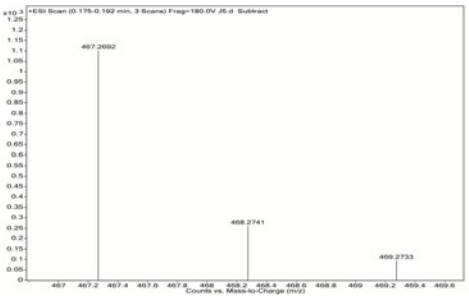
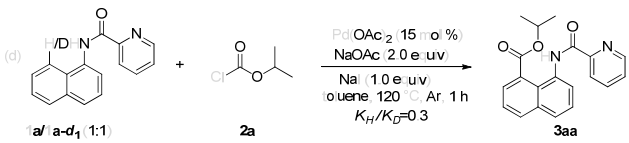


HRMS (ESI$^+$) for **9a**: calcd for $C_{13}H_{26}NO_3$ $[M+H]^+$: 244.1907, found: 244.1908.





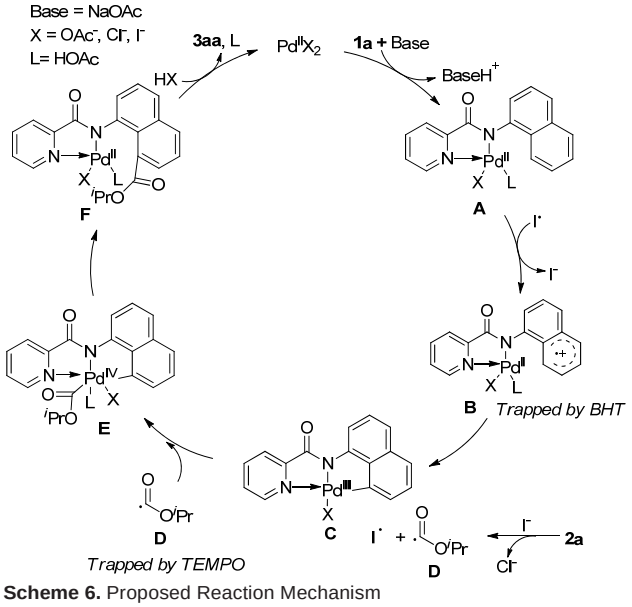
HRMS (ESI$^+$) for **10a**: calcd for $C_{31}H_{35}N_2O_2$ $[M+H]^+$: 467.2693, found: 467.2692.



Scheme 5. Control Experiments

observed, demonstrating that the N,N-bidentate directing group may be essential in this transformation (Scheme 5a). The addition of radical scavenger of 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) successfully suppressed the reaction (Scheme 5b). When the reaction were performed in the presence of TEMPO or 2,6-di-tert-butyl-4-methylphenol (BHT), an adduct of TEMPO and isopropyl chloroformate **2a** as the product **9a** and an adduct of BHT and N-(naphthalen-1-yl) picolinamide **1a** as the product **10a** could be detected by HR-MS, respectively (Scheme 5c). These results suggested that the reaction might involve a radical process. Finally, the experiment of the kinetic isotope effect (KIE) was carried out, and the result (KIE = 0.3) may imply that the C–H bond cleavage might not be involved in the rate-determining step (Scheme 5d).

Based on the above experimental results and previous reports,[13] a plausible mechanism is proposed in Scheme 6. First, the coordination of the substrate **1a** to the Pd(II) species with the help of a base occurs to afford a bischelated metallacyclic Pd(II) intermediate **A**. The isopropyl chloroformate **2a** reacts with iodine anion to generate an intermediate radical **D** and an iodine radical under the standard heating conditions. Subsequently, the reaction of the intermediate **A** with the iodine radical undergoes a single electron transfer (SET) process to generate iodine anion and
an intermediate radical **B**, followed by an intramolecular SET process to generate a Pd(III) intermediate **C**.[17] Next, the oxidative addition of the intermediate radical **D** to the intermediate **C** forms a Pd(IV) intermediate **E**, the reductive elimination of which takes place to afford a Pd(II) intermediate **F**. Finally, the ligand dissociation of the resulting Pd(II) intermediate **F** occurs to provide the corresponding naphthyl ester **3aa** and regenerate the catalytically active Pd(II) species to fulfil the catalytic cycle.



Scheme 6. Proposed Reaction Mechanism

Conclusions

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In conclusion, we have developed an efficient and convenient protocol for palladium-catalyzed regioselective C8-H bond alkoxycarbonylation of 1-naphthylamine derivatives with chloroformates. The reaction proceeded smoothly under oxidant-free conditions, which showed broad functional group tolerance and high regioselectivity. Remarkably, the reaction offered a convenient alternative to the concise synthesis of one BET bromodomain inhibitor.

Experimental section

General Information

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-400 spectrometer with $CDCl_3$ as the solvent and TMS as an internal standard. Melting points were measured using a WC-1 microscopic apparatus and are uncorrected. High resolution mass spectra were ensured on an Agilent Technologies 1290-6540 UHPLC/Accurate-Mass Quadrupole Time-of-Flight LC/MS. All solvents were used directly without further purification. Dichloromethane, ethyl acetate, and hexane were used for column chromatography. The commercials were obtained from commercial sources and used as-received without further purification unless otherwise noted. Chemical shift multiplicities are represented as follows: s = singlet, d = doublet, t = triplet, m = multiplet, dd = double doublet, td = three doublets. Unless otherwise mentioned, all materials were commercially obtained and used without further purification.

Preparation of Naphthalene. A 100 mL two-necked round-bottom flask was equipped with a magnetic stir bar and charged with 1-naphthylamine (20 mmol, 2.86 g), picolinic acid (1.1 equiv, 2.70 g), N,N-dimethyl-4-aminopyridine (DMAP, 0.1 equiv, 0.244 g) in 30 mL anhydrous CH_2Cl_2 at 0 ºC. After EDCI (4.20 g, 1.1 equiv) in CH_2Cl_2 (20 mL) was added dropwise to the solution under a nitrogen atmosphere, the reaction was then warmed to room temperature, stirred for 12 h and quenched with water (30 mL). The reaction mixture was extracted with CH_2Cl_2 (3 × 20 mL), and the combined organic solvent was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (hexane/ethyl acetate = 3:1) (V/V) to afford the pure product **1a** as a white solid (4.42 g, 89%).

All amides were prepared from the corresponding 1-naphthylamine derivatives and 2-picolinic acid according to the reported procedure.[19]

General Experimental Procedure for alkoxycarbonylation reaction. A Schlenk tube was equipped with a magnetic stir bar and charged with N-(naphthalen-1-yl)picolinamide **1a** (0.1 mmol, 24.8 mg), **2a** (0.3 mmol, 41 µL), NaOAc (0.2 mmol, 16 mg), $Pd(OAc)_2$ (0.015 mmol, 3.3 mg), NaI (0.1 mmol, 15 mg) in toluene (1.0 mL). The resulting mixture was sealed under argon, heated at 120 ºC for 12 h, and cooled to room temperature. Upon completion, CH_2Cl_2 (20 mL) was added to the reaction system, and the resulting mixture was filtered through a pad of Celite. After the organic material was concentrated in vacuum, the product was purified by column chromatography on silica gel (100–200 mesh) using hexane/EtOAc as an eluent (5:1, V/V) to afford the pure product **3aa.**

General Procedures for the Deprotection of Directing Groups. A mixture of **3aa** (66.8 mg, 0.2 mmol, 1.0 equiv) and NaOH (240 mg, 6 mmol, 30 equiv) was heated in ethanol (3.0 mL) for 12 h at 80 ºC. After the mixture was cooled to room temperature and diluted with water (3.0 mL), the solution of diluted hydrochloric acid was added until it was acidic. The saturated $NaHCO_3$ solution was then added until the pH value was about 7. The mixture was then extracted with CH_2Cl_2 and dried over anhydrous Na_2SO_4. After the organic material was concentrated in vacuum, the product was purified by column chromatography on silica gel (100–200 mesh) using hexane/EtOAc as an eluent (3:1, V/V) to afford the pure product **4a**.

General Procedures for the BET bromodomain inhibitor. To a solution of **4a** (169 mg, 1.0 mmol, 1.0 equiv) in DMF (2.5 mL), NaH (36 mg, 1.5 mmol, 1.5 equiv) was added at 0 ºC. After stirred for 10 min at 0 ºC, iodoethane (96 µL, 1.2 mmol, 1.2 equiv) was added dropwise into the solution and the reaction mixture was stirred at room temperature. After the reaction was completed, the resulting mixture was poured into H_2O and extracted with ethyl acetate. The organic material was dried over Na_2SO_4 and concentrated in vacuum, and the product was purified by column chromatography on silica gel (100–200 mesh) using hexane/EtOAc as an eluent (5:1, V/V) to afford the pure product **5a**.

To a solution of **5a** (189 mg, 0.96 mmol, 1.0 equiv) in AcOH (2.5 mL), HNO_3 (61 mg, 0.96 mmol, 1.0 equiv) was added at 0 ºC and then the reaction mixture was stirred at 50 ºC for 1 h. After the reaction was completed, the reaction mixture was cooled to room temperature. The mixture was extracted with ethyl acetate, dried over anhydrous Na_2SO_4 and concentrated in vacuo, and the product was purified by column chromatography on silica gel (100–200 mesh) using hexane/EtOAc as an eluent (5:1, V/V) to afford the pure product **6a**.

A mixture of iron powder (179 mg, 3.2 mmol, 5.0 equiv) and NH_4Cl (68 mg, 1.28 mmol, 2.0 equiv) in a mixture of AcOH/water (2 mL/8 mL) was heated at 50 °C for 5 min. Subsequently, **6a** (155 mg, 0.64 mmol, 1.0 equiv) was dissolved in DMF (2 mL) and added to the reaction mixture. After completion, the mixture was cooled to room temperature, extracted with ethyl acetate. After the organic layer was washed with brine, dried over Na_2SO_4 and filtered, the filtrate was concentrated in vacuo. The product was purified by column chromatography on silica gel (100–200 mesh) using hexane/EtOAc as an eluent (3:1, V/V) to afford the pure product **7a**.

A mixture of **7a** (105 mg, 0.5 mmol, 1.0 equiv) and 5-bromo-2-methoxybenzenesulfonyl chloride (170 mg, 0.6 mmol, 1.2 equiv) in CH_2Cl_2 (10 mL) was added in pyridine (0.5 mL) and stirred at room temperature for 2 h. The mixture was extracted with CH_2Cl_2, and the organic layer was washed with brine, dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated in vacuo, and the product was purified by column chromatography on silica gel (100–200 mesh) using hexane/EtOAc as an eluent (2:1, V/V) to afford the pure product **8a**.[16]

A Gram scale Synthesis. A oven-dried, 500 mL round-bottom flask with Condensing return pipe was equipped with a magnetic stir bar and charged with N-(naphthalen-1-yl)picolinamide **1a** (7.0 mmol, 1.736 g), **2a** (21.0 mmol, 2.5 mL), NaOAc (14.0 mmol, 1.1 g),

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$Pd(OAc)_2$ (10.5 mmol, 231.0 mg), NaI (7.0 mmol, 1.0 g) in toluene (150 mL). The resulting mixture was sealed under argon, heated at 120 ºC for 12 h, and cooled to room temperature. Upon completion, CH_2Cl_2 (150 mL) was added to the reaction system. After the organic material was concentrated in vacuum, the product was purified by column chromatography on silica gel (100–200 mesh) using hexane/EtOAc as an eluent (5:1, V/V) to afford the pure product **3aa**.

Characterization Data of the Products. Isopropyl 8-(picolinamido)-1-naphthoate, 3aa: yellow solid (29.4 mg, 88%); mp 110-112 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.37 (s, 1H), 8.72-8.70 (m, 1H), 8.30-8.28 (m, 1H), 7.98 (dd, J_1 = 8.24 Hz, J_2 = 1.12 Hz, 1H), 7.92-7.88 (m, 2H), 7.84 (d, J = 7.20 Hz, 1H), 7.67-7.62 (m, 2H), 7.49-7.45 (m, 2H), 5.15-5.09 (m, 1H), 1.20 (d, J = 6.28 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 163.5, 150.2, 148.1, 137.5, 135.1, 131.9, 131.7, 129.4, 128.3, 127.5, 126.7, 126.5, 126.4, 125.7, 124.6, 122.8, 69.5, 21.6; HRMS (ESI$^+$): calcd for $C_{20}H_{19}N_2O_3$ $[M+H]^+$: 335.1390, found: 335.1391.

Isopropyl 8-(3-methylpicolinamido)-1-naphthoate, 3ba: colorless solid (14.3 mg, 41%); mp 113-115 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.39 (s, 1H), 8.55 (dd, J_1 = 4.56 Hz, J_2 = 1.04 Hz, 1H), 7.97 (dd, J_1 = 8.24 Hz, J_2 = 1.12 Hz, 1H), 7.88-7.82 (m, 2H), 7.65-7.59 (m, 3H), 7.49-7.45 (m, 1H), 7.40-7.37 (m, 1H), 5.04-4.98 (m, 1H), 2.76 (s, 3H), 1.16 (d, J = 6.28 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 165.1, 147.3, 145.5, 141.0, 136.2, 135.1, 132.1, 131.7, 130.0, 128.0, 127.3, 126.8, 126.3, 126.0, 124.5, 69.3, 21.5, 20.7; HRMS (ESI$^+$): calcd for $C_{21}H_{21}N_2O_3$, $[M+H]^+$: 349.1547, found: 349.1549.

Isopropyl 8-(6-methylpicolinamido)-1-naphthoate, 3ca: yellow solid (31.7 mg, 91%); mp 109-110 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.43 (s, 1H), 8.09 (d, J = 7.64 Hz, 1H), 7.97 (d, J = 8.08 Hz, 1H), 7.90 (d, J = 7.40 Hz, 1H), 7.83-7.75 (m, 2H), 7.65-7.58 (m, 2H), 7.46 (t, J = 7.62 Hz, 1H), 7.34 (d, J = 7.68 Hz, 1H), 5.09-5.02 (m, 1H), 2.70 (s, 3H), 1.13 (d, J = 6.28 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 163.8, 157.3, 149.4, 137.6, 135.1, 132.0, 129.5, 128.1, 127.4, 126.6, 126.4, 126.2, 125.8, 124.5, 119.8, 69.1, 24.1, 21.6; HRMS (ESI$^+$): calcd for $C_{21}H_{21}N_2O_3$ $[M+H]^+$: 349.1547, found: 349.1548.

Isopropyl 8-(5-methoxypicolinamido)-1-naphthoate, 3da: brown solid (28.8 mg, 79%); mp 76-79 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.18 (s, 1H), 8.36 (d, J = 2.80 Hz, 1H), 8.24 (d, J = 8.64 Hz, 1H), 7.90 (dd, J_1 = 8.24 Hz, J_2 = 1.12 Hz, 1H), 7.89 (d, J = 7.44, Hz, 1H), 7.83-7.81 (m, 1H), 7.66-7.58 (m, 2H), 7.48-7.45 (m, 1H), 7.33 (dd, J_1 = 8.68 Hz, J_2 = 2.84 Hz, 1H), 5.15-5.09 (m, 1H), 3.93 (s, 3H), 1.22 (d, J = 6.28 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 163.4, 158.1, 142.8, 136.4, 135.1, 131.9, 131.8, 129.5, 128.1, 127.3, 126.7, 126.4, 125.8, 124.5, 124.1, 120.3, 69.5, 55.8, 21.6; HRMS (ESI$^+$): calcd for $C_{21}H_{21}N_2O_4$ $[M+H]^+$: 365.1496, found: 365.1498.

Isopropyl 8-(5-bromopicolinamido)-1-naphthoate, 3ea: yellow solid (21.4 mg, 52%); mp 85-87 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.28 (s, 1H), 8.77 (dd, J_1 = 2.22 Hz, J_2 = 0.58 Hz, 1H), 8.18 (dd, J_1 = 8.32 Hz, J_2 = 0.56 Hz, 1H), 8.04 (dd, J_1 = 8.32 Hz, J_2 = 2.28 Hz, 1H), 7.99 (dd, J_1 = 8.24 Hz, J_2 = 1.12 Hz, 1H), 7.90 (d, J = 7.48 Hz, 1H), 7.84 (d, J = 8.16 Hz, 1H), 7.69 (dd, J_1 = 7.10 Hz, J_2 = 1.26 Hz, 1H), 7.61 (t, J = 7.84 Hz, 1H), 7.50-7.46 (m, 1H), 5.18-5.11 (m, 1H), 1.24 (d, J = 6.28 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 162.8, 149.2, 148.7, 140.2, 135.1, 132.1, 131.4, 129.2, 128.6, 127.7, 126.7, 126.3, 125.6, 124.6, 124.4, 124.3, 69.5, 21.6; HRMS (ESI$^+$): calcd for $C_{20}H_{18}BrN_2O_3$ $[M+H]^+$: 413.0495, found: 413.0497.

Isopropyl 8-(5-chloropicolinamido)-1-naphthoate, 3fa: yellow solid (18.8 mg, 51%); mp 102-104 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.27 (s, 1H), 8.66 (d, J = 2.09 Hz, 1H), 8.25 (d, J = 8.27 Hz, 1H), 8.00 (dd, J_1 = 8.19 Hz, J_2 = 0.88 Hz, 1H), 7.91-7.84 (m, 3H), 7.69 (dd, J_1 = 7.11 Hz, J_2 = 1.26 Hz, 1H), 7.62 (t, J = 7.83 Hz, 1H), 7.50-7.46 (m, 1H), 5.18-5.11 (m, 1H), 1.24 (d, J = 6.28 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 162.6, 148.4, 147.1, 137.2, 135.4, 135.1, 132.1, 131.5, 129.2, 128.6, 127.7, 126.7, 126.3, 125.6, 124.6, 123.9, 69.5, 21.6; HRMS (ESI$^+$): calcd for $C_{20}H_{18}ClN_2O_3$ $[M+H]^+$: 369.1000, found: 369.0998.

Isopropyl 8-(4-chloropicolinamido)-1-naphthoate, 3ga: white solid (28.3 mg, 77%); mp 146-148 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.35 (s, 1H), 8.61 (d, J = 5.24 Hz, 1H), 8.29 (d, J = 1.92 Hz, 1H), 8.00-7.98 (m, 1H), 7.91 (d, J = 7.44 Hz, 1H), 7.85 (d, J = 8.00 Hz, 1H), 7.70-7.68 (m, 1H), 7.62 (t, J = 7.82 Hz, 1H), 7.52-7.47 (m, 2H), 5.17-5.11 (m, 1H), 1.23 (d, J = 6.28 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 162.4, 151.7, 149.0, 146.0, 135.1, 132.2, 131.4, 129.1, 128.7, 127.7, 126.7, 126.4, 125.6, 124.6, 123.5, 69.5, 21.6; HRMS (ESI$^+$): calcd for $C_{20}H_{18}ClN_2O_3$ $[M+H]^+$: 369.1000, found: 369.1002.

Isopropyl 8-(quinoline-2-carboxamido)-1-naphthoate, 3ha: yellow solid (35.3 mg, 92%); mp 93-95 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.67 (s, 1H), 8.40-8.32 (m, 3H), 7.99-7.97 (m, 2H), 7.90 (dd, J_1 = 8.06 Hz, J_2 = 1.02 Hz, 1H), 7.84-7.79 (m, 2H), 7.68-7.60 (m, 3H), 7.49-7.45 (m, 1H), 5.09-5.03 (m, 1H), 1.01 (d, J = 6.28 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 163.7, 149.9, 146.5, 137.7, 135.2, 131.9, 130.3, 129.9, 129.5, 129.4, 128.3, 128.2, 127.8, 127.5, 126.6, 126.4, 125.8, 124.6, 119.1, 69.3, 21.5; HRMS (ESI$^+$): calcd for $C_{24}H_{21}N_2O_3$ $[M+H]^+$: 385.1547, found: 385.1548.

Isopropyl 8-(isoquinoline-1-carboxamido)-1-naphthoate, 3ia: colorless solid (16.9 mg, 44%); mp 84-85 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.57 (s, 1H), 9.62-9.59 (m, 1H), 8.63 (d, J = 5.52 Hz, 1H), 8.01-7.97 (m, 2H), 7.89-7.84 (m, 3H), 7.75-7.63 (m, 4H), 7.50-7.46 (m, 1H), 5.00-4.94 (m, 1H), 1.08 (d, J = 6.28 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 165.1, 148.2, 140.2, 137.5, 135.2, 132.0, 131.9, 130.6, 129.5, 128.9, 128.2, 127.8, 127.5, 127.3, 126.9, 126.8, 126.4, 125.9, 124.8, 124.6, 69.4, 21.5; HRMS (ESI$^+$): calcd for $C_{24}H_{21}N_2O_3$ $[M+H]^+$: 385.1547, found: 385.1548.

Isopropyl 8-(pyrimidine-4-carboxamido)-1-naphthoate, 3ja: yellow oil (7.7 mg, 23%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.47 (s, 1H), 9.41 (d, J = 1.28 Hz, 1H), 9.04 (d, J = 5.00 Hz, 1H), 8.22 (dd, J_1 = 5.02 Hz, J_2 = 1.34 Hz, 1H), 8.02 (dd, J_1 = 8.22 Hz, J_2 = 1.06 Hz, 1H), 7.93 (d, J = 7.48 Hz, 1H), 7.87 (d, J = 8.08 Hz, 1H), 7.76 (dd, J_1 = 7.12 Hz, J_2 = 1.20 Hz, 1H), 7.63 (t, J = 7.84 Hz, 1H), 7.52-7.48 (m, 1H), 5.24-5.18 (m, 1H), 1.26 (d, J = 6.24 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 161.9, 159.4, 157.8, 156.8, 135.2, 132.5, 130.9, 129.2, 128.8, 128.1, 126.8, 126.3, 125.4, 124.7, 119.1, 69.7, 21.6; HRMS (ESI$^+$): calcd for $C_{19}H_{18}N_3O_3$ $[M+H]^+$: 336.1343, found: 336.1342.

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DOI: 10.1039/D0OB00586J

Isopropyl 5-acetoxy-8-(picolinamido)-1-naphthoate, 3ka: brown oil (18.4 mg, 47%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.28 (s, 1H), 8.70 (d, J = 4.52 Hz, 1H), 8.29 (d, J = 7.76 Hz, 1H), 8.06-8.04 (m, 1H), 7.92-7.87 (m, 2H), 7.66 (d, J = 6.28 Hz, 1H), 7.54-7.49 (m, 2H), 7.41 (d, J = 8.20 Hz, 1H), 5.11-5.05 (m, 1H), 2.47 (s, 3H), 1.19 (d, J = 6.28 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 169.3, 163.6, 149.9, 148.1, 145.2, 137.5, 129.9, 129.7, 128.5, 128.2, 126.8, 126.6, 126.4, 125.2, 124.6, 122.9, 118.9, 69.7, 21.5, 21.1; HRMS (ESI$^+$): calcd for $C_{22}H_{21}N_2O_5$ $[M+H]^+$: 393.1445, found: 393.1444.

Isopropyl 4-methoxy-8-(picolinamido)-1-naphthoate, 3la: brown solid (25.1 mg, 69%); mp 156-158 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.55 (s, 1H), 8.69 (d, J = 4.56 Hz, 1H), 8.31-8.26 (m, 2H), 7.96 (d, J = 7.32 Hz, 1H), 7.87 (t, = 7.70 Hz, 1H), 7.72 (d, J = 8.08 Hz, 1H), 7.61 (t, = 7.96 Hz, 1H), 7.48-7.45 (m, 1H), 6.76 (d, J = 8.04 Hz, 1H), 5.19-5.12 (m, 1H), 4.00 (s, 3H), 1.21 (d, J = 6.28 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 163.5, 158.3, 150.3, 148.1, 137.4, 131.7, 130.4, 127.3, 127.2, 127.0, 126.4, 125.7, 122.8, 121.3, 121.1, 102.3, 69.1, 55.9, 21.6; HRMS (ESI$^+$): calcd for $C_{21}H_{21}N_2O_4$ $[M+H]^+$: 365.1496, found: 365.1499.

Isopropyl 4-amino-8-(picolinamido)-1-naphthoate, 3ma: brown solid (13.3 mg, 38%); mp 130-133 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.78 (s, 1H), 8.72-8.71 (m, 1H), 8.43 (d, J = 7.48 Hz, 1H), 8.36 (d, J = 7.80 Hz, 1H), 8.00-7.89 (m, 3H), 7.74 (d, J = 8.56 Hz, 1H), 7.60-7.52 (m, 3H), 7.01 (s, 1H), 5.12-5.06 (m, 1H), 1.35 (d, J = 6.24 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 154.0, 149.9, 148.2, 137.8, 133.5, 133.0, 127.0, 126.6, 126.2, 126.1, 122.5, 118.7, 117.3, 116.9, 69.1, 22.2; HRMS (ESI$^+$): calcd for $C_{20}H_{20}N_3O_3$ $[M+H]^+$: 350.1499, found: 350.1051.

Isopropyl 5-bromo-8-(picolinamido)-1-naphthoate, 3na: yellow solid (31.3 mg, 76%); mp 114-116 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.26 (s, 1H), 8.70 (d, J = 4.48 Hz, 1H), 8.45 (dd, J_1 = 8.52 Hz, J_2 = 1.00 Hz, 1H), 8.28 (d, = 7.84 Hz, 1H), 7.93-7.88 (m, 2H), 7.75 (d, J = 8.12 Hz, 1H), 7.68 (dd, J_1 = 7.04 Hz, J_2 = 1.12 Hz, 1H), 7.61-7.57 (m, 1H), 7.52-7.49 (m, 1H), 5.11-5.04 (m, 1H), 1.18 (d, J = 6.28 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 163.5, 149.8, 148.1, 137.6, 133.1, 131.7, 130.9, 130.6, 130.1, 128.8, 127.2, 127.0, 126.7, 126.1, 122.9, 121.6, 69.8, 21.5; HRMS (ESI$^+$): calcd for $C_{20}H_{18}BrN_2O_3$ $[M+H]^+$: 413.0495, found: 413.0496.

Isopropyl 4-bromo-8-(picolinamido)-1-naphthoate, 3oa: yellow solid (28.4 mg, 69%); mp 114-116 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.27 (s, 1H), 8.71-8.69 (m, 1H), 8.34-8.28 (m, 2H), 7.93-7.88 (m, 2H), 7.80 (d, J = 7.68 Hz, 1H), 7.75-7.71 (m, 1H), 7.52-7.48 (m, 1H), 7.45 (d, J = 7.68 Hz, 1H), 5.07-5.01 (m, 1H), 1.17 (d, J = 6.28 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 163.6, 149.8, 148.1, 137.6, 133.4, 132.2, 129.6, 129.1, 127.9, 127.8, 127.7, 127.2, 126.8, 126.7, 126.6, 122.9, 69.8, 21.5; HRMS (ESI$^+$): calcd for $C_{20}H_{18}BrN_2O_3$ $[M+H]^+$: 413.0495, found: 413.0493.

Isopropyl 5-bromo-8-(quinoline-2-carboxamido)-1-naphthoate, 3pa: yellow solid (28.6 mg, 62%); mp 128-130 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.54 (s, 1H), 8.48 (dd, J_1 = 8.52 Hz, J_2 = 1.24 Hz, 1H), 8.38 (s, 2H), 8.33 (d, J = 8.44 Hz, 1H), 7.96-7.93 (m, 2H), 7.86-7.80 (m, 2H), 7.71-7.67 (m, 2H), 7.63-7.59 (m, 1H), 5.03-4.97 (m, 1H), 1.00 (d, J = 6.28 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 163.7, 149.5, 146.4, 137.8, 133.2, 131.9, 130.9, 130.6, 130.4, 130.2, 129.9, 129.5, 128.8, 128.3, 127.8, 127.3, 126.8, 126.1, 121.6, 119.0, 69.5, 21.0; HRMS (ESI$^+$): calcd for $C_{24}H_{20}N_2O_3$ $[M+H]^+$: 463.0652, found: 463.0653.

Isopropyl 4-bromo-8-(quinoline-2-carboxamido)-1-naphthoate, 3qa: yellow solid (29.1 mg, 63%); mp 137-139 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.54 (s, 1H), 8.37-8.31 (m, 4H), 7.99 (d, J = 7.44 Hz, 1H), 7.93-7.91 (m, 1H), 7.85-7.80 (m, 2H), 7.75-7.71 (m, 1H), 7.69-7.65 (m, 1H), 7.46 (d, J = 7.68 Hz, 1H), 5.00-4.94 (m, 1H), 0.99 (d, J = 6.28 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 163.8, 149.6, 146.4, 137.7, 133.4, 132.3, 130.4, 129.9, 129.7, 129.5, 129.1, 128.3, 127.9, 127.8, 127.7, 127.6, 127.3, 126.8, 126.6, 119.1, 69.6, 21.4; HRMS (ESI$^+$): calcd for $C_{24}H_{20}N_2O_3$ $[M+H]^+$: 463.0652, found: 463.0653.

Propyl 8-(picolinamido)-1-naphthoate, 3ab: yellow solid (30.1 mg, 90%); mp 108-110 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.31 (s, 1H), 8.72-8.70 (m, 1H), 8.31-8.28 (m, 1H), 7.99 (dd, J_1 = 8.28 Hz, J_2 = 1.16 Hz, 1H), 7.93-7.89 (m, 2H), 7.86-7.84 (m, 1H), 7.69 (dd, J_1 = 7.08 Hz, J_2 = 1.28 Hz, 1H), 7.62 (t, J = 7.82 Hz, 1H), 7.53-7.46 (m, 2H), 4.11 (t, J = 6.82 Hz, 2H), 1.66-1.57 (m, 2H), 0.83 (t, J = 7.44 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 163.5, 150.0, 149.1, 137.5, 135.1, 131.9, 131.6, 129.1, 128.3, 127.6, 126.8, 126.6, 126.4, 125.9, 124.6, 122.8, 67.6, 21.7, 10.3; HRMS (ESI$^+$): calcd for $C_{20}H_{19}N_2O_3$ $[M+H]^+$: 335.1390, found: 335.1393.

Hexadecyl 8-(picolinamido)-1-naphthoate, 3ac: yellow solid (17.5 mg, 34%); mp 66-68 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.32 (s, 1H), 8.71-8.70 (m, 1H), 8.30-8.28 (m, 1H), 7.99 (dd, J_1 = 8.28 Hz, J_2 = 1.08 Hz, 1H), 7.93-7.88 (m, 2H), 7.85-7.83 (m, 1H), 7.68 (dd, J_1 = 7.08 Hz, J_2 = 1.24 Hz, 1H), 7.62 (t, J = 7.84 Hz, 1H), 7.52-7.46 (m, 2H), 4.14 (t, J = 6.88 Hz, 2H), 1.60-1.55 (m, 2H), 1.25-1.20 (m, 26H), 0.87 (t, J = 6.68 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 163.5, 150.1, 148.1, 137.5, 135.1, 131.9, 131.7, 129.1, 128.3, 127.5, 126.7, 126.5, 126.4, 125.9, 124.6, 122.9, 66.3, 31.9, 29.7, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.2, 28.4, 25.9, 22.7, 14.1; HRMS (ESI$^+$): calcd for $C_{33}H_{45}N_2O_3$ $[M+H]^+$: 517.3425, found: 517.3427.

Cyclopentyl 8-(picolinamido)-1-naphthoate, 3ad: yellow solid (18.7 mg, 52%); mp 95-97 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.36 (s, 1H), 8.72 (d, J = 4.28 Hz, 1H), 8.29 (d, J = 7.80 Hz, 1H), 7.97 (dd, J_1 = 8.22 Hz, J_2 = 1.04 Hz, 1H), 7.92-7.88 (m, 2H), 7.83 (d, J = 8.08 Hz, 1H), 7.64-7.59 (m, 2H), 7.51-7.45 (m, 2H), 5.25-5.22 (m, 1H), 1.69-1.65 (m, 6H), 1.54-1.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 163.5, 150.1, 148.1, 137.5, 135.1, 131.9, 131.7, 129.4, 128.3, 127.5, 126.7, 126.5, 126.4, 125.8, 124.6, 122.8, 78.8, 32.6, 20.8; HRMS (ESI$^+$): calcd for $C_{22}H_{21}N_2O_3$ $[M+H]^+$: 361.1547, found: 361.1548.

Hexadecyl 8-(5-bromopicolinamido)-1-naphthoate, 3ec: yellow solid (25.5 mg, 43%); mp 65-68 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.23 (s, 1H), 8.76 (d, J = 1.76 Hz, 1H), 8.20-8.17 (m, 1H), 8.04 (dd, J_1 = 8.32 Hz, J_2 = 2.24 Hz, 1H), 8.00 (dd, J_1 = 8.24 Hz, J_2 = 1.00 Hz, 1H), 7.90-7.84 (m, 2H), 7.71 (dd, J_1 = 7.08 Hz, J_2 = 1.20 Hz, 1H), 7.62 (t, J = 7.84 Hz, 1H), 7.50-7.47 (m, 1H), 4.17 (t, J = 6.26 Hz, 2H), 1.64-1.55 (m, 2H), 1.25-1.22 (m, 26H), 0.88 (t, J = 6.80 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 162.7, 149.3, 148.6, 140.2, 135.1,

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DOI: 10.1039/D0OB00586J

132.1, 131.4, 128.9, 128.6, 127.7, 126.8, 126.4, 125.7, 124.6, 124.4, 124.3, 66.3, 31.9, 29.7, 29.7, 29.7, 29.7, 29.6, 29.5, 29.4, 29.3, 28.5, 25.9, 22.7, 14.2; HRMS (ESI$^+$): calcd for $C_{33}H_{44}BrN_2O_3$ $[M+H]^+$: 595.2530, found: 595.2531.

3-Chloropropyl 8-(5-methoxypicolinamido)-1-naphthoate, 3de: brown solid (20.7 mg, 52%); mp 93-95 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.07 (s, 1H), 8.37 (d, J = 2.68 Hz, 1H), 8.24 (d, J = 8.64 Hz, 1H), 7.99 (dd, J_1 = 8.24 Hz, J_2 = 1.00 Hz, 1H), 7.88-7.82 (m, 2H), 7.67-7.59 (m, 2H), 7.49-7.46 (m, 1H), 7.33 (dd, J_1 = 8.68 Hz, J_2 = 2.84 Hz, 1H), 4.30 (t, J = 6.24 Hz, 2H), 3.93 (s, 3H), 3.51 (t, J = 6.34 Hz, 2H), 2.08-2.02 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 163.4, 158.3, 142.5, 136.5, 135.0, 132.0, 131.8, 128.7, 128.2, 127.5, 126.9, 126.5, 126.0, 124.6, 124.1, 120.5, 62.8, 55.9, 41.2, 31.3; HRMS (ESI$^+$): calcd for $C_{21}H_{20}ClN_2O_4$ $[M+H]^+$: 399.1106, found: 399.1107.

3-Chloropropyl 8-(quinoline-2-carboxamido)-1-naphthoate, 3he: yellow solid (31.4 mg, 75%); mp 104-106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.54 (s, 1H), 8.41-8.36 (m, 2H), 8.32 (d, J = 8.44 Hz, 1H), 8.02 (dd, J_1 = 8.24 Hz, J_2 = 1.04 Hz, 1H), 7.97-7.92 (m, 2H), 7.87-7.82 (m, 2H), 7.70-7.62 (m, 3H), 7.52-7.48 (m, 1H), 4.19 (t, J = 6.22 Hz, 2H), 3.32 (t, J = 6.38 Hz, 2H), 1.90-1.83 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 163.6, 149.6, 146.4, 137.8, 135.1, 132.1, 131.8, 130.5, 129.8, 129.5, 128.7, 128.3, 128.3, 127.9, 127.6, 126.7, 126.6, 125.9, 124.6, 119.1, 62.6, 40.9, 31.2; HRMS (ESI$^+$): calcd for $C_{24}H_{20}ClN_2O_3$ $[M+H]^+$: 419.1157, found: 419.1159.

Benzyl 8-(5-methoxypicolinamido)-1-naphthoate, 3df: brown oil (8.7 mg, 21%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.17 (s, 1H), 8.31 (d, J = 2.76 Hz, 1H), 8.23 (d, J = 8.64 Hz, 1H), 7.98 (dd, J_1 = 8.26 Hz, J_2 = 1.10 Hz, 1H), 7.89 (d, J = 7.44 Hz, 1H), 7.83 (d, J = 8.16 Hz, 1H), 7.67-7.59 (m, 2H), 7.47-7.43 (m, 1H), 7.32-7.28 (m, 6H), 5.22 (s, 2H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 163.4, 158.2, 142.6, 136.4, 135.5, 135.0, 132.0, 131.8, 128.7, 128.5, 128.3 128.3, 128.0, 127.4, 126.8, 126.5, 126.0, 124.6, 124.2, 120.4, 67.6, 55.8; HRMS (ESI$^+$): calcd for $C_{25}H_{21}N_2O_4$ $[M+H]^+$: 413.1496, found: 413.1499.

Allyl 8-(3-methylpicolinamido)-1-naphthoate, 3bg: brown solid (8.0 mg, 23%); mp 119-121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.35 (s, 1H), 8.55-8.53 (m, 1H), 7.99 (dd, J_1 = 8.24 Hz, J_2 = 1.12 Hz, 1H), 7.87-7.83 (m, 2H), 7.68-7.60 (m, 3H), 7.50-7.46 (m, 1H), 7.42-7.38 (m, 1H), 5.89-5.79 (m, 1H), 5.23-5.12 (m, 2H), 4.57 (dt, J_1 = 5.77 Hz, J_2 = 1.26 Hz, 2H), 2.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 165.0, 147.0, 145.4, 141.1, 136.4, 135.1, 131.9, 131.8, 131.6, 128.9, 128.2, 127.4, 126.9, 126.4, 126.2, 126.1, 124.6, 118.6, 66.4, 20.8; HRMS (ESI$^+$): calcd for $C_{21}H_{19}N_2O_3$ $[M+H]^+$: 347.1390, found: 347.1392.

Allyl 8-(quinoline-2-carboxamido)-1-naphthoate, 3hg: brown solid (12.2 mg, 32%); mp 109-111 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.54 (s, 1H), 8.41-8.35 (m, 2H), 8.31 (d, J = 8.48 Hz, 1H), 8.02-7.92 (m, 3H), 7.87-7.81 (m, 2H), 7.73-7.62 (m, 3H), 7.52-7.48 (m, 1H), 5.78-5.67 (m, 1H), 5.05-4.95 (m, 2H), 4.55 (dt, J_1 = 5.76 Hz, J_2 = 1.36 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 163.6, 149.7, 146.4, 137.7, 135.1, 132.0, 131.8, 131.5, 130.4, 129.9, 129.5, 128.8, 128.4, 128.2, 127.8, 127.5, 126.6, 126.5, 125.9, 124.7, 119.2, 118.4, 66.4; HRMS (ESI$^+$): calcd for $C_{24}H_{19}N_2O_3$ $[M+H]^+$: 383.1390, found: 383.1392.

N-(8-benzoylnaphthalen-1-yl)picolinamide, 3ah: White solid (12.7 mg, 36%); mp 144-146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (s, 1H), 8.54-8.52 (m, 1H), 8.04-8.02 (m, 1H), 7.92 (d, J = 7.92 Hz, 1H), 7.80-7.78 (m, 1H), 7.74-7.68 (m, 2H), 7.64-7.60 (m, 1H), 7.56-7.52 (m, 1H), 7.50-7.48 (m, 2H), 7.42-7.32 (m, 3H), 7.14-7.10 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.4, 163.1, 149.2, 147.9, 137.0, 136.9, 136.0, 135.1, 133.2, 131.7, 130.5, 130.0, 128.0, 127.9, 127.8, 126.9, 126.6, 126.5, 126.2, 124.9, 122.1; HRMS (ESI$^+$): calcd for $C_{23}H_{16}N_2O_2$ $[M+H]^+$: 353.1285, Found: 353.1287.

N-(8-(4-methylbenzoyl)naphthalen-1-yl)picolinamide, 3ai: White solid (13.9 mg, 38%); mp 166-168 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (s, 1H), 8.55-8.53 (m, 1H), 8.03-8.00 (m, 1H), 7.91 (d, J = 8.20 Hz, 1H), 7.81-7.79 (m, 1H), 7.75-7.68 (m, 2H), 7.63-7.59 (m, 1H), 7.55-7.52 (m, 1H), 7.42-7.38 (m, 4H), 6.91 (d, J = 7.96 Hz, 2H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.2, 163.2, 149.3, 147.9, 144.1, 136.8, 136.2, 135.1, 134.6, 131.8, 130.4, 130.2, 128.6, 127.9, 127.7, 126.8, 126.5, 126.4, 126.2, 124.9, 122.1, 21.6; HRMS (ESI$^+$): calcd for $C_{24}H_{18}N_2O_2$ $[M+H]^+$: 367.1441, Found: 367.1442.

N-(8-(4-chlorobenzoyl)naphthalen-1-yl)picolinamide, 3aj: White solid (11.8 mg, 36%); mp 174-177 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (s, 1H), 8.54 (d, J = 4.72 Hz, 1H), 8.03 (d, J = 8.12 Hz, 1H), 7.92 (d, J = 8.04 Hz, 1H), 7.82-7. 81 (m, 1H), 7.77-7.73 (m, 1H), 7.71-7.69 (m, 1H), 7.64-7.61 (m, 1H), 7.56-7.53 (m, 1H), 7.44-7.37 (m, 4H), 7.07 (d, J = 8.56 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.2, 163.2, 149.1, 147.9, 139.7, 137.1, 135.4, 135.3, 135.1, 131.6, 131.3, 130.7, 128.2, 128.2, 128.0, 127.2, 126.7, 126.4, 126.4, 124.9, 122.2; HRMS (ESI$^+$): calcd for $C_{23}H_{15}ClN_2O_2$ $[M+H]^+$: 387.0895, Found: 387.0894.

Benzo[cd]indol-2(1H)-one, 4a: yellow solid (18.6 mg, 55%); mp 173-176 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.11 (d, J = 7.00 Hz, 1H), 8.05 (d, J = 8.08 Hz, 1H), 7.76-7.72 (m, 1H), 7.56 (d, J = 8.44 Hz, 1H), 7.48-7.44 (m, 1H), 7.03 (d, J = 7.00 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 137.2, 131.2, 129.4, 128.7, 126.8, 126.3, 124.5, 120.4, 106.7; HRMS (ESI$^+$): calcd for $C_{11}H_8NO$ $[M+H]^+$: 170.0600, found: 170.0599.

1-Ethylbenzo[cd]indol-2(1H)-one, 5a: yellow solid (189 mg, 96%); mp 65-68 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 6.96 Hz, 1H), 7.91 (d, J = 8.12 Hz, 1H), 7.64-7.60 (m, 1H), 7.45-7.37 (m, 2H), 6.83 (d, J = 6.88 Hz, 1H), 3.92 (q, J = 7.24 Hz, 2H), 1.34 (t, J = 7.24 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 139.0, 130.6, 129.0, 128.5, 128.4, 126.7, 125.1, 124.0, 120.1, 104.8, 34.9, 14.1; HRMS (ESI$^+$): calcd for $C_{13}H_{12}NO$ $[M+H]^+$: 198.0913, found: 198.0915.

1-Ethyl-6-nitrobenzo[cd]indol-2(1H)-one, 6a: yellow solid (155 mg, 67%); mp 158-161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (d, J = 8.52 Hz, 1H), 8.56 (d, J = 8.00 Hz, 1H), 8.06 (d, J = 6.96 Hz, 1H), 7.86 (t, J = 7.76 Hz, 1H), 6.92 (d, J = 8.00 Hz, 1H), 3.99 (q, J = 7.20 Hz, 2H), 1.40 (t, J = 7.20 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 145.6, 138.9, 131.9, 129.9,129.9, 126.0, 125.6, 125.3, 122.5,

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DOI: 10.1039/D0OB00586J

102.9, 35.2, 13.9; HRMS (ESI$^+$): calcd for $C_{13}H_{11}N_2O_3$ $[M+H]^+$: 243.0764, found: 243.0762.

1-Ethyl-6-nitrobenzo[cd]indol-2(1H)-one, 7a: red solid (105 mg, 77%); mp 181-183 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 7.00 Hz, 1H), 8.00 (d, J = 8.16 Hz, 1H), 7.69-7.65 (m, 1H), 6.73 (d, J = 7.44 Hz, 1H), 6.64 (d, J = 7.44 Hz, 1H), 3.94 (q, J = 7.24 Hz, 2H), 3.41 (s, 2H), 1.35 (t, J = 7.24 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 138.4, 131.1, 127.6, 127.4, 125.6, 125.3, 124.3, 121.5, 109.7, 106.5, 34.9, 14.1; HRMS (ESI$^+$): calcd for $C_{13}H_{13}N_2O$ $[M+H]^+$: 213.1022, found: 213.1023.

5-bromo-N-(1-ethyl-2-oxo-1,2-dihydrobenzo[cd]indol-6-yl)-2-methoxybenzenesulfonamide, 8a: yellow solid (202 mg, 88%); mp 209-211 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.28 Hz, 1H), 8.00 (d, J = 6.96 Hz, 1H), 7.80-7.79 (m, 2H), 7.69-7.65 (m, 1H), 7.53 (dd, J_1 = 8.80 Hz, J_2 = 2.48 Hz, 1H), 7.17 (d, J = 7.56 Hz, 1H), 6.90 (d, J = 8.88 Hz, 1H), 6.71 (d, J = 7.60 Hz, 1H), 4.06 (s, 3H), 3.88 (q, J = 7.20 Hz, 2H), 1.30 (t, J = 7.20 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 155.4, 138.1, 137.6, 133.2, 129.0, 128.2, 127.0, 126.8, 126.4, 126.1, 125.5, 124.8, 124.4, 113.9, 112.8, 104.8, 56.7, 35.0, 14.0; HRMS (ESI$^+$): calcd for $C_{20}H_{18}BrN_2O_4S$ $[M+H]^+$: 461.0165, found: 461.0167.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We are grateful to the National Natural Science Foundation of China (nos. 21102134, 21172200) for financial support.

Notes and references

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DOI: 10.1039/D0OB00586J

18 CCDC 1956109 (**3na**).† Crystal data for compound **3na**: $C_{20}H_{17}BrN_2O_3$, M = 413.26, monoclinic, a = 16.6385(13) Å, α = 90°, b = 14.3268(8) Å, β = 100.731(7)°, c = 7.7041(5) Å, γ = 90°, V = 1804.3(2) Å^3, T = 293(2) K, space group = $P2_1/c$, Z = 4, reflections collected = 6920, independent reflections = 3221, [R(int) = 0.0468], final R indices [$I > 2\sigma(I)$] R_1 = 0.0486, wR_2 = 0.1062, R indices (all data) R_1 = 0.0755, wR_2 = 0.1265.
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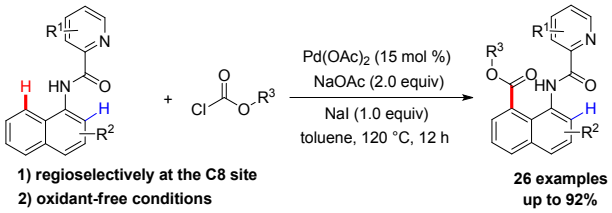
DOI: 10.1039/D0OB00586J

Palladium-Catalyzed C8-H Alkoxycarbonylation of 1-Naphthylamines with Alkyl Chloroformates



A simple and efficient protocol for palladium-catalyzed C8-H alkoxycarbonylation of 1-naphthylamine derivatives with alkyl chloroformates has been developed.