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Nickel(II)-Catalyzed Direct Arylation of C−H Bonds in Aromatic Amides Containing an 8-Aminoquinoline Moiety as a Directing Group

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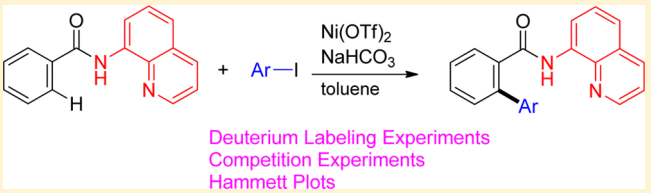
Supporting Information

ABSTRACT: Arylation via the cleavage of the ortho C−H bonds by a nickel-catalyzed reaction of aromatic amides containing an 8-aminoquinoline moiety with aryl iodides is reported. The reaction shows a high functional group compatibility. The reaction proceeds in a highly selective manner at the less hindered C−H bonds in the reaction of meta-substituted aromatic amides, irrespective of the electronic nature of the substituents. Electron-withdrawing groups on the aromatic amides facilitate the reaction. Various mechanistic experiments, such as deuterium labeling experiments, Hammett studies, competition experiments, and radical trap experiments, have been made for better understanding the reaction mechanism. It is found that the cleavage of C−H bonds is reversible on the basis of the deuterium labeling experiments. Both Ni(II) and Ni(0) show a high catalytic activity, but the results of mechanistic experiments suggest that a Ni(0)/Ni(II) catalytic cycle is not involved.



INTRODUCTION

The formation of C−C bonds by the catalytic functionalization of C(sp^2)−H bonds has been developed as an efficient and attractive synthetic strategy in transition-metal catalysis.[1] When a new substituent is introduced onto a substituted benzene derivative, the issue of regioselectivity is critical because organic molecules contain a wide variety and number of C−H bonds. In principle, it is not possible to discriminate between C−H bonds having similar electronic and steric properties. In 1993, Murai et al. reported on the use of olefins in the Ru-catalyzed alkylation of C−H bonds in aromatic ketones.[2] The formation of C−C bonds took place at the ortho position in a highly regioselective manner. A key to the success of the reaction is the utilization of a directing group. The coordination of the ketone moiety to the ruthenium center allows the catalyst to come into close proximity to the ortho C−H bonds, which are then cleaved. This observation represented a significant breakthrough in that it showed, for the first time, that the chelation-assisted functionalization of C−H bonds represented an efficient and valuable tool in organic synthesis. Since this seminal work on the use of a ketone moiety as a directing group in the alkylation of the ortho C−H bonds with olefins, the methodology has been extended to a variety of directing groups as well as to a wide variety of functionalization of C−H bonds. Chelation assistance is now one of the more reliable methods for the regioselective functionalization of C−H bonds. Although a wide variety of functional groups, such as ketones, aldehydes, carboxylic acids, esters, amides, cyano groups, pyridine, pyrazole, oxazoline, imine, carbamate, and amine derivatives, have been developed as directing groups in the functionalization of C−H bonds, the design of new types of directing groups continues to be an important issue. Yu recently reported on the development of a new, well-designed directing group which promotes meta-selective functionalization of C−H bonds, which promises to open up new possibilities in the area of chelation assistance.[3] The design of new directing groups is important in terms of exploring new functionalizations of C−H bonds that cannot be currently achieved using common directing groups. The successful pioneering example of N,N-bidentate directing group assisted functionalization of C−H bonds was reported by Daugulis, who discovered the Pd(II)-catalyzed arylation of C−H bonds in aliphatic amides that contain an 8-aminoquinoline and picolinamide moiety.[4] The reaction involves the catalytic activation of unactivated C(sp^3)−H bonds, which is, even now, a challenging issue. Following this pioneering finding, a number of reactions using 8-aminoquinoline and picolinamide-based bidentate directing groups have been developed.[5] Most of the examples reported so far involve the use of Pd(II) as a catalyst. If other transition metals could be used as catalysts, new types of functionalizations would be expected to be possible. In fact, the N,N-bidentate directing system was recently found to be applicable to other transition-metal-catalyzed functionalizations of C−H bonds. Various transition-metal complexes, including Cu,[6] Fe,[7] Ru,[8] and Ni,[9] have been recently used as catalysts. Some new types of functionalizations of C−H bonds that are not catalyzed by Pd(II) catalysts have

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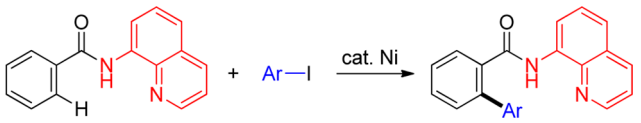
also been reported. However, examples of transition metals other than palladium, which is applicable to the N,N-bidentate chelation system, continue to be limited.

One of the pioneering examples of chelation-assisted C−H bond activation was achieved using a nickel complex via the cyclometalation of azobenzene with Cp_2Ni.[10] However, the chelation-assisted functionalization of C−H bonds catalyzed by nickel complexes are limited to C−H bonds in specific aromatic systems, such as pyridine derivatives, highly perfluorinated benzene, and azole derivatives.[11] On the other hand, examples of the nickel-catalyzed activation of C−H bonds in benzene ring are rare.[12] Recently, we found that Ni complexes also show a high catalytic activity in the directed activation of C−H bonds using a N,N-bidentate chelation system.[9b,c] We report here on the experimental details regarding the Ni(II)-catalyzed arylation of aromatic amides containing a N,N-bidentate directing group via the cleavage of C(sp^2)−H bonds (Scheme 1).

Scheme 1. Nickel-Catalyzed Direct Arylation in Aromatic Amides Involving the Cleavage of the Ortho C−H Bonds

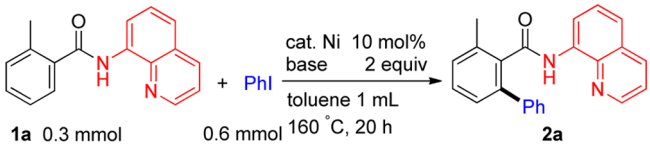


RESULTS AND DISCUSSION

The reaction of amide **1a** (0.3 mmol) with phenyl iodide (0.6 mmol) in the presence of $Ni(OTf)_2$ (0.03 mmol) as a catalyst and Na_2CO_3 (0.6 mmol) as a base in toluene (1 mL) at 160 °C for 20 h gave the arylation product **2a** in 80% NMR yield (75% isolated yield) along with the recovery of 5% of unreacted **1a**, and no evidence of any byproducts (entry 1 in Table 1). In a previous study, we observed that reactions using a bidentate chelation assisted system were quite sensitive to the nature of bases.[8e,f,9b,c] To investigate this issue further, we screened a variety of bases. Among the bases examined, $NaHCO_3$ and $KHCO_3$ also gave **2a** in high yield, but the others were not effective (entries 1−10). The addition of phosphine dramatically decreased the yield of **2a** (entries 11 and 12), similar to the case of the Ni-catalyzed arylation of C(sp^3)−H bonds in aliphatic amides.[9c] However, unlike the arylation of C(sp^3)−H bonds,[9c] the addition of a sterically bulky 2-PhC_6H_4COOH failed to improve the product yield (entry 13). Curiously, various nickel complexes involving both Ni(II) and Ni(0) showed a high catalytic activity, resulting in high yields of the arylation product (entries 16−19). The following conditions were finally selected as standard reaction conditions: the amide **1a** (0.3 mmol) was reacted with phenyl iodide (0.6 mmol) in the presence of $Ni(OTf)_2$ (0.015 mmol) and $NaHCO_3$ (0.6 mmol) in toluene (1 mL) at 160 °C for 20 h and gave **2a** in 94% isolated yield (entry 14).

We next examined the effect of directing groups (Figure 1). No phenylation took place when *N*-2-naphthyl benzamide (**3**) and the corresponding ester **4** were used as the substrate in place of **1a**. Furthermore, the use of *N*-methyl amide **5** also failed to result in the formation of the phenylation product, indicating that the presence of a proton on the amide nitrogen is required for the reaction to proceed, although NH is not included in the product formation at first sight. The use of 2-pyridinylmethylamine, as in **6**, resulted in no formation of a phenylation product. The reaction appears to be more efficient

Table 1. Nickel-Catalyzed Phenylation of 1a



entry	catalyst	ligand (amt, mol %)	base	yield of **2a**/**1a**,[a] %
1	$Ni(OTf)_2$	none	Na_2CO_3	80 (75)/5
2	$Ni(OTf)_2$	none	$NaHCO_3$	92 (87)/3
3	$Ni(OTf)_2$	none	$KHCO_3$	98 (86)/1
4	$Ni(OTf)_2$	none	K_2CO_3	45/12
5	$Ni(OTf)_2$	none	Cs_2CO_3	46/14
6	$Ni(OTf)_2$	none	Li_2CO_3	5/89
7	$Ni(OTf)_2$	none	NaOAc	11/94
8	$Ni(OTf)_2$	none	KOAc	3/>99
9	$Ni(OTf)_2$	none	Na_2HPO_4	5/90
10	$Ni(OTf)_2$	none	Et_3N	0/79
11	$Ni(OTf)_2$	PPh_3 (20)	$NaHCO_3$	2/5
12	$Ni(OTf)_2$	PCy_3 (20)	$NaHCO_3$	6/12
13	$Ni(OTf)_2$	2-PhC_6H_4COOH (20)	$NaHCO_3$	12/4
14[b]	$Ni(OTf)_2$	none	$NaHCO_3$	99 (94)/2
15[c]	$Ni(OTf)_2$	none	$NaHCO_3$	63/19
16[b]	$Ni(OAc)_2$	none	$NaHCO_3$	99 (92)/−
17[b]	$NiCl_2$	none	$NaHCO_3$	99/−
18[b]	NiI_2	none	$NaHCO_3$	95/−
19[b]	$Ni(cod)_2$	none	$NaHCO_3$	92/−

[a]NMR yield. Values in parentheses are the isolated yields of **2a**. [b]Nickel complexes (5 mol %) were used. [c]$Ni(OTf)_2$ (2.5 mol %) was used.

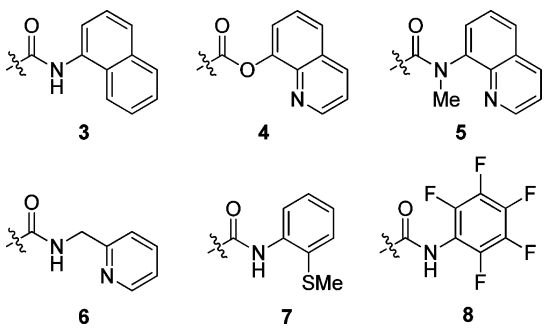


Figure 1. Ineffective directing groups.

for the 8-aminoquinoline motif. Directing groups, such as **7** and **8** which have been extensively used in the Pd-catalyzed functionalization of C−H bonds, were also ineffective.[13] The presence of an NH bond as well as the quinoline nitrogen is crucial for the success of the reaction.

With the optimized reaction conditions in hand, we examined the scope of the reaction. Table 2 shows the results for reactions of various aromatic amides with phenyl iodide under the standard reaction conditions. A variety of functional groups were tolerated in the reaction. The reaction of meta-substituted substrates resulted in selective phenylation exclusively at the less hindered C−H bonds, irrespective of the electronic nature of the substituent, indicating that the regioselectivity of the reaction was controlled by the steric nature of the substituent groups, as in **1e−l** and **9**. The reaction was sensitive to the steric factors. In fact, the reaction of **13** did not give **14** because the ortho C−H bond is highly congested.

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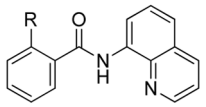
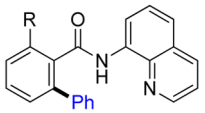
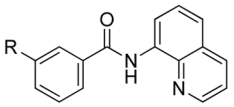
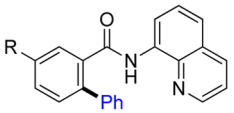
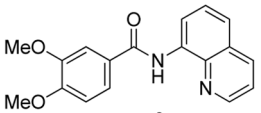
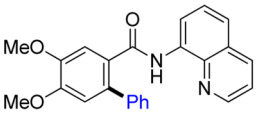
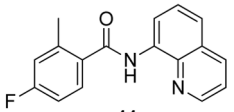
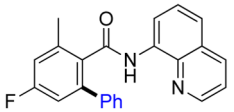
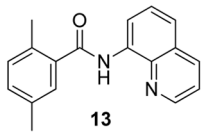
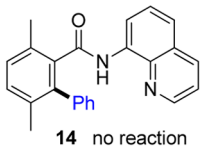
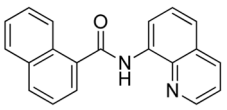
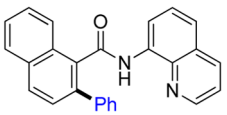
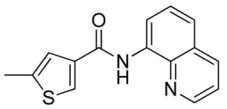
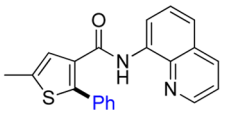
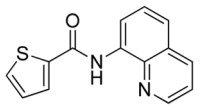
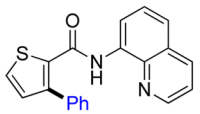
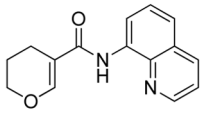
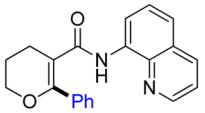
Table 2. Nickel-Catalyzed Phenylation of Aromatic Amides[a]

amide	product[b]
	
R = Ph (**1b**) F (**1c**) CF_3 (**1d**)	**2b** 73%[c] **2c** 59%[c] **2d** 63%[c]
	
R = NMe_2 (**1e**) OMe (**1f**) Me (**1g**) Ph (**1h**) Cl (**1i**) Br (**1j**) $C(O)CH_3$ (**1k**) CF_3 (**1l**)	**2e** 53%[d] **2f** 66%[d] **2g** 69%[d] **2h** 65%[d] **2i** 68%[d] **2j** 70%[d] **2k** 60%[d] **2l** 68%[d]
 **9**	 **10** 65%[d]
 **11**	 **12** 96%
 **13**	 **14** no reaction
 **15**	 **16** 57%[d]
 **17**	 **18** 62%[d]
 **19**	 **20** 57%[c,d,e]
 **21**	 **22** 54%[c,d,f]

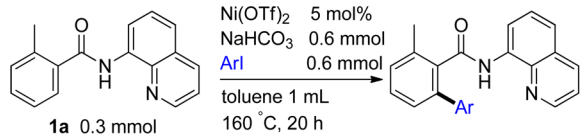
[a]Reaction conditions: amide (0.3 mmol), phenyl iodide (0.6 mmol), $Ni(OTf)_2$ (0.015 mmol), $NaHCO_3$ (0.6 mmol) in toluene (1 mL) at 160 °C for 20 h. [b]Isolated yield. [c]$Ni(OTf)_2$ (0.03 mmol) was used. [d]Isolated by GPC after column chromatography. [e]Run for 72 h. [f]Run for 48 h.

Table 2. continued

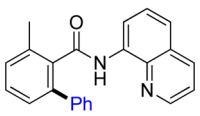
The reaction was also applicable to the C−H bond in a thiophene ring, as in **17** and **19**, and an olefinic C−H bond, as in **21**.

A variety of aryl iodides were applicable to the arylation reaction, as shown in Table 3. However, phenyl bromide, chloride, and triflate were not effective as coupling partners. Various functional groups, such as methoxy, chloro, bromo, ester, ketone, trifluoromethyl, and even iodide groups, were tolerated in the reaction. Some heteroaromatic halides, such as 7-iodo-1*H*-indole and 2-iodothiophene, also participated in the present arylation reaction of C−H bonds as coupling partners to give **25** and **26**, respectively.

Table 3. Nickel-Catalyzed Arylation of 1a

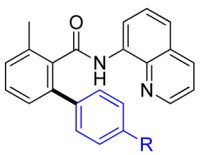


1a 0.3 mmol

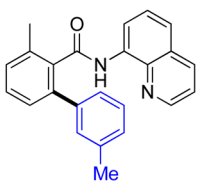


2a

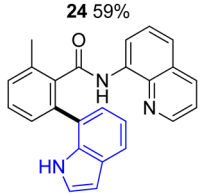
PhI	94%
PhBr	7%[a]
PhCl	0%
PhOTf	0%



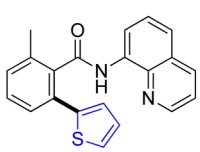
R = NH_2 (**23a**)	21%[b]
R = OMe (**23b**)	94%
R = Me (**23c**)	93%
R = Bu (**23d**)	96%
R = Ph (**23e**)	41%
R = Cl (**23f**)	73%[b]
R = Br (**23g**)	60%[b]
R = I (**23h**)	67%
R = CO_2Me (**23i**)	91%
R = COMe (**23j**)	65%
R = CF_3 (**23k**)	87%



24 59%



25 67%



26 98%

[a]NMR yield. [b]Isolated by GPC after column chromatography.

To gain insights into the mechanism for the reaction, deuterium labeling experiments were carried out (Scheme 2). We observed the H/D exchange between the ortho C−H bond (the D content dropped from >98% to 79% (21% H)) and N−H bond in the recovered amide when $Ni(OTf)_2$ was used as the catalyst. Even in the absence of 4-iodoanisole, a H/D exchange again occurred at the ortho position (the D content dropped from >98% to 73%), indicating that the cleavage of the C−H bonds is reversible. However, the rate of H/D exchange was not as fast in comparison with the Ru(II)-catalyzed reaction that we observed in the past.[8e] In the Ni(0) catalytic system,

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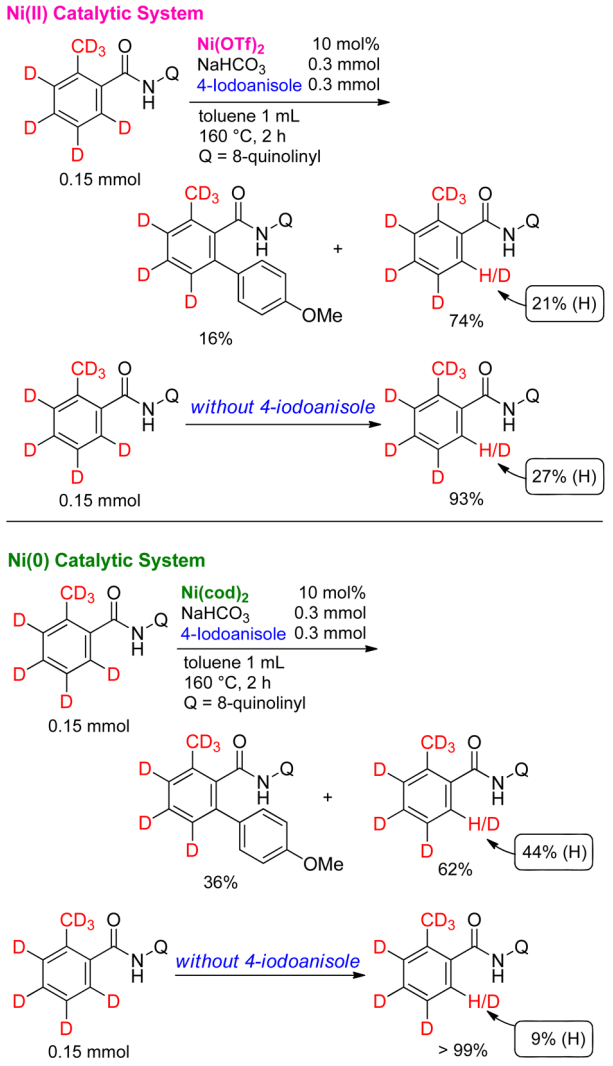
Scheme 2. Deuterium Labeling Experiments



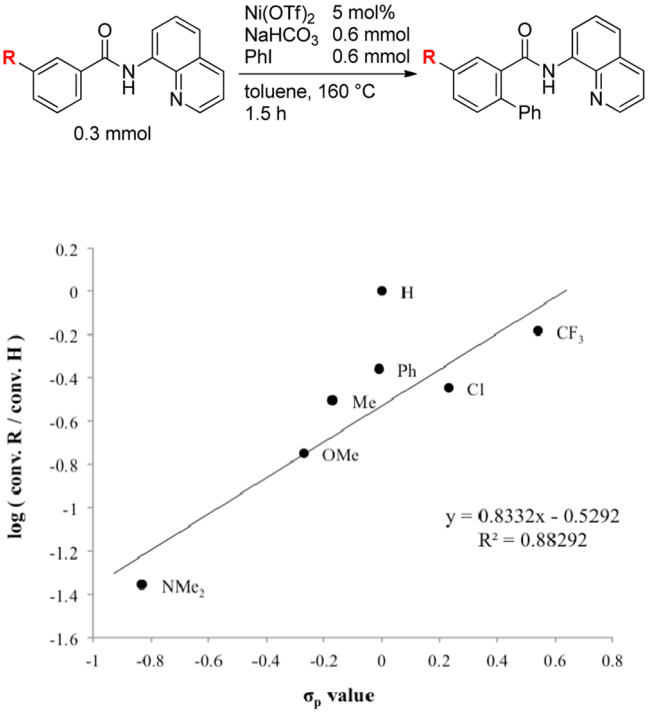
only 9% of the protons were introduced at the ortho position in the absence of aryl iodide, indicating that the presence of 4-iodoanisole was important for efficient H/D exchange to take place when Ni(0) was used as the catalyst. The difference between Ni(II) and Ni(0) systems will be discussed later.

To probe electronic effects on the arylation, we prepared a Hammett plot in which the reaction of an electronically different set of meta-substituted aromatic amides with PhI was compared (Scheme 3). A linear correlation from the conversion of amides vs Hammett σ_p led to a positive value of ρ = 0.88, indicating that the rate-determining transition state is more stabilized by electron-withdrawing substituents.

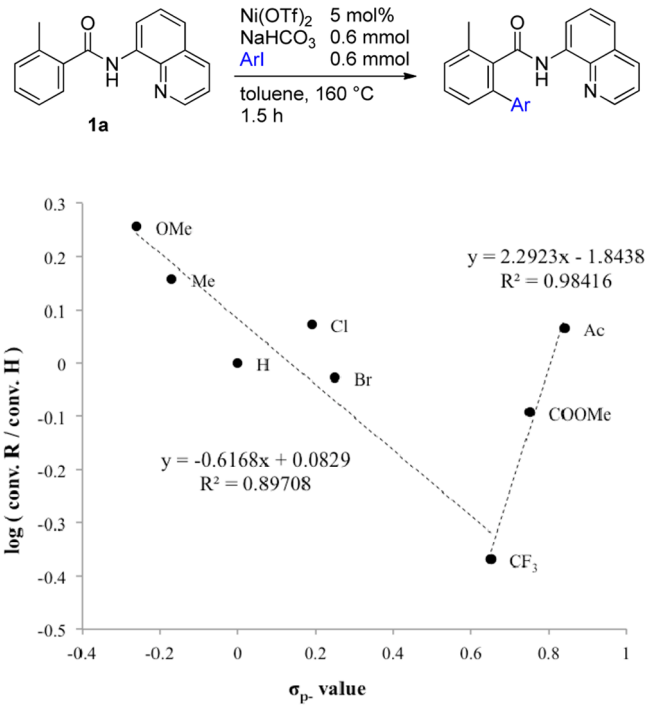
We next carried out the reaction of **1a** with an electronically different set of para-substituted aryl iodides (Scheme 4). Although the Hammett showed a low correlation, the trend was similar to that observed in the $RuCl_2$-catalzyed arylation of aromatic amides,[8e] in which a V-shaped Hammett plot was observed.[14] Thus, both electron-donating groups, such as methoxy and methyl groups, and electron-withdrawing groups, such as ketones and esters, facilitate the reaction and a CF_3 group was the least reactive substituent.

Competition experiments also were performed, in order to gain additional information regarding the electronic effects of the substituents on both aromatic amides and aryl iodides on

Scheme 3. Hammett Plots of *m*-R-C_6H_4CONHQ (Q = 8-Quinolinyl) with PhI



Scheme 4. Hammett Plots of *o*-Me-C_6H_4CONHQ (Q = 8-Quinolinyl) 1a with Para-Substituted ArI



the reaction (Scheme 5). A 1:1 mixture of **1e** and **1l** was reacted with four different aryl iodide derivatives. Irrespective of the electronic nature of the substituents on the aryl iodides, the electron-deficient amide **1l** reacted much faster than the electron-rich amides **1e**. Thus, products **b** were the major products in all cases, indicating that the presence of an electron-withdrawing group on the aromatic amides facilitates the

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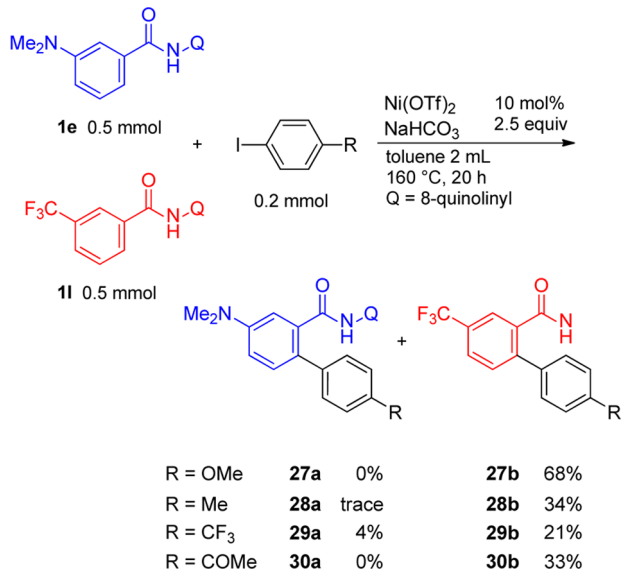
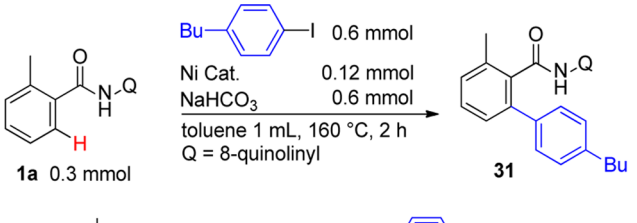
Scheme 5. Competition Experiments



reaction, as observed in Scheme 3. These series of mechanistic results (Scheme 2−5) suggest that the mechanism of the Ni-catalyzed arylation of C(sp^2)−H bonds is similar to that proposed for the $RuCl_2$-catalyzed arylation of aromatic amides with aryl halides.[8e]

Both Ni(II) and Ni(0) showed a high catalytic activity in the present catalytic system, as shown in Table 1. The product distribution at the early stage of the reaction was examined in order to develop a better understanding of the difference between the Ni(II)- and Ni(0)-catalyzed reactions (Scheme 6).

Scheme 6. Product Distribution

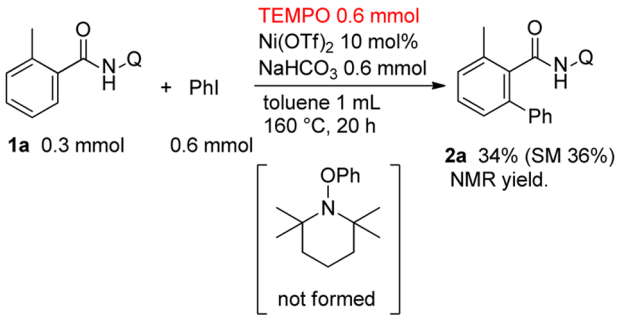


	31	recovery of iodide	Bu−H	Ar−Ar
$Ni(OTf)_2$	53% (8%)	50%	2%/Ni	trace
$Ni(cod)_2$	19% (49%)	49%	49%/Ni	3%/Ni

In the reaction of **1a** with 4-butyl-1-iodobenzene in the presence of 40 mol % of $Ni(OTf)_2$, the arylation product **31** was obtained in 53% NMR yield, with 8% of the starting amide being recovered. In contrast, when $Ni(cod)_2$ was used as the catalyst, **31** was obtained in 19% NMR yield with 49% of the starting amide **1a** being recovered, and butylbenzene was produced in 49% yield on the basis of $Ni(cod)_2$ used. Most importantly, only trace amount of a biaryl derivative was detected. It is known that Ni(0) complexes react with ArX to give homocoupling products Ar−Ar with the generation of a Ni(II) complex;[15] however, the results shown in Scheme 6 suggest that such a reaction did not take place under the present reaction conditions. Instead, the results suggest that the Ni(0) complex was oxidized to Ni(II) by 4-butyl-1-iodobenzene with the generation of butylbenzene.[16]

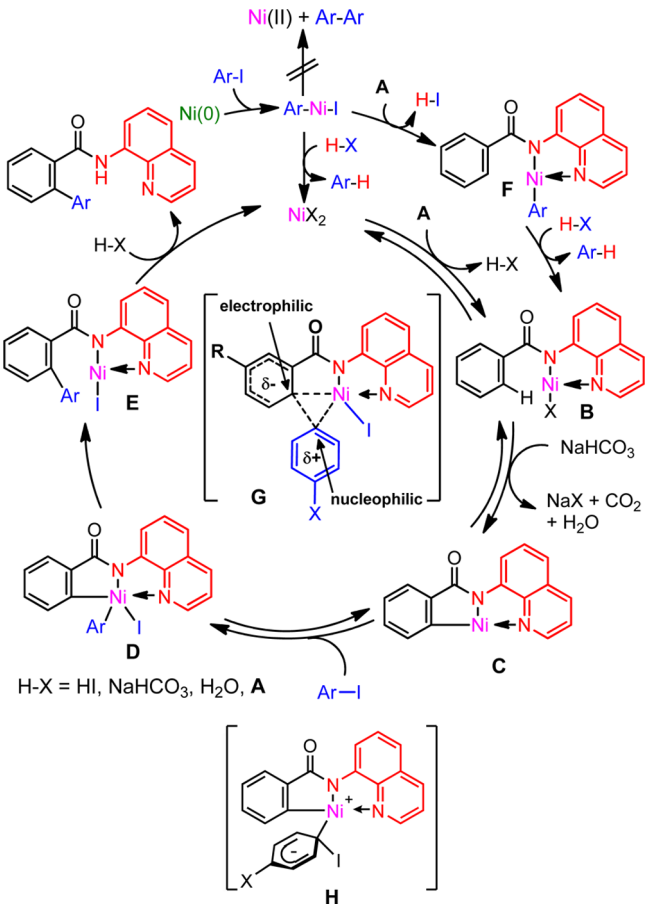
The reaction of **1a** was carried out in the presence of TEMPO (2 equiv). The yield of **2a** decreased and some unidentified products were produced, but the reaction was not completely inhibited and the corresponding TENPO ether was not obtained (Scheme 7).

Scheme 7. Radical Trap Experiment



A proposed mechanism for the reaction is shown in Scheme 8. Amide **A** coordinates to the nickel center followed by a ligand exchange with the generation of HX, which is accelerated by a base, to give the nickel complex **B**. The complex **B** then undergoes a cyclometalation to give complex **C** via a concerted metalation−deprotonation (CMD) mechanism. The oxidative addition of ArI leading to Ni(IV) species **D** followed by a

Scheme 8. Proposed Mechanism



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reductive elimination gives **E**, which is then protonated to afford the final arylation product with the regeneration of nickel(II). As shown in Scheme 2, C−H bond cleavage appears to be reversible and is not the rate-determining step in this reaction. The Hammett plots shown in Scheme 3, the region on the left in Scheme 4, and the results of competition experiments shown in Scheme 5 suggest that reductive elimination is the rate-determining step and that it proceeds through the transition state **G**, in which a developing negative charge is stabilized by the electron-withdrawing groups R on the aromatic amides and a developing positive charge is stabilized by the electron-donating group X on the aryl iodides. However, the reaction is also accelerated by the electron-withdrawing nature of the substituent X (X = COOMe, $C(O)CH_3$) in the aryl iodides, as shown in the region on the right in Scheme 4. This suggests that the oxidative addition proceeds through a nucleophilic substitution mechanism, as in **H**. The equilibrium position can be shifted to **D** from **C** by the appropriate use of electron-withdrawing groups, such as an ester or a ketone functional group on the ArI molecule. On the basis of the results shown in Scheme 6, Ni(0) is oxidized to Ni(II) under the reaction conditions. Although Ni(0) complexes are known to react with ArX to give homocoupling products Ar−Ar with the generation of a Ni(II) complex,[15] the results shown in Scheme 6 suggest that such a reaction did not take place under the present reaction conditions. When Ni(0) was used as the catalyst, the oxidative addition of an aryl iodide to Ni(0) generates Ar−Ni−I, which reacts with **A** with the generation of HI to give **F**. The protonation of **F** gives **B**, which now enters the main catalytic cycle of the Ni(II)-catalyzed reaction. Protonation of Ar−Ni−I species also may generate Ni(II) species. The proposed mechanism involves a Ni(II)/Ni(IV) catalytic cycle (Scheme 8).[17,18]

CONCLUSIONS

The regioselective arylation at the ortho position of aromatic amides with aryl iodides has been achieved using Ni catalysts in conjunction with an 8-aminoquinoline directing group. A variety of functional groups are tolerated in the reaction. The reaction proceeds in a highly selective manner at the less hindered C−H bonds in the reaction of meta-substituted aromatic amides, irrespective of the electronic nature of the substituents. It is found that the cleavage of C−H bonds is reversible based on the deuterium labeling experiments. Both Ni(II) and Ni(0) shows a high catalytic activity, but, based on various mechanistic experiments, it appears that that Ni(II) is the key catalytic species and Ni(0) is converted to Ni(II) under the reaction conditions. The proposed mechanism involves a Ni(II)/Ni(IV) catalytic cycle.

EXPERIMENTAL SECTION

General Comments. ^{1}H NMR and ^{13}C NMR spectra were recorded were recorded at 400 and 100 MHz in $CDCl_3$ with tetramethylsilane as the internal standard. Data are reported as follows: chemical shift in ppm, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br s = broad singlet, and m = multiplet), coupling constant (Hz), and integration. For infrared spectra (IR), absorptions are reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra were obtained with ionization voltages of 70 eV. High-resolution mass spectra (HRMS) were obtained by EI using a double-focusing mass spectrometer. Analytical gas chromatography (GC) was carried out with a flame ionization detector. Column chromatography was performed with SiO_2 (Silicycle SiliaFlash F60 (230−400 mesh)). Some compounds were purified by gel permeation chromatography (GPC).

General Procedure for the Preparation of Starting Amide. 3-Bromo-*N*-(quinolin-8-yl)benzamide (**1j**) and *N*-(quinolin-8-yl)-thiophene-2-carboxamide (**19**) were prepared by the reaction of the corresponding acid chlorides with 8-aminoquinoline. Other starting amides was prepared by our previously reported procedure.[8e,9b]

In an oven-dried 100 mL three-necked flask, 3-bromobenzoic acid (3.0 g, 15 mmol), DMF (5 drops), and DCM (30 mL) were added under a N_2 atmosphere. Oxalyl chloride (1.5 mL, 18 mmol, 1.2 equiv) was added dropwise at 0 °C, resulting in vigorous bubbling. The mixture was stirred for 3 h at room temperature, and the solvent was then removed in vacuo. The resulting acid chloride was used immediately without further purification. In another oven-dried 100 mL three-necked flask, 8-aminoquinoline (2.9 g, 20 mmol, 1.3 equiv), Et_3N (4.1 mL, 30 mmol, 2 equiv) and DCM (30 mL) were added. A solution of the acid chloride in DCM (10 mL) was added dropwise to the solution at 0 °C, and the solution was then warmed to room temperature. After it was stirred overnight, the reaction system was quenched with saturated aqueous $NaHCO_3$ (30 mL) and the organic layer was separated. The aqueous layer was extracted with DCM (2 × 15 mL). The combined organic layers were washed with 1 M aqueous HCl (30 mL) and brine (30 mL), dried over $MgSO_4$, filtered, and evaporated in vacuo. The resulting crude amide was purified by column chromatography on silica gel (eluent: hexane/EtOAc 5/1) to afford the desired amide as a white solid.

*3-Bromo-N-(quinolin-8-yl)benzamide (**1j**):* R_f = 0.26 (hexane/EtOAc 5/1); white solid; mp 104 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 7.44 (t, *J* = 7.6 Hz, 1H), 7.51 (dd, *J* = 8.4, 4.4 Hz, 1H), 7.57−7.63 (m, 2H), 7.70−7.73 (m, 1H), 8.01 (dd, *J* = 7.6, 1.2, 1H), 8.20−8.23 (m, 2H), 8.87 (dd, 4.0, 1.6 Hz, 1H), 8.91 (dd, *J* = 7.6, 1.2 Hz, 1H), 10.71 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 121.9, 122.2, 123.2, 125.9, 127.6, 128.1, 130.5, 130.8, 134.3, 134.9, 136.6, 137.2, 138.8, 148.5, 164.1; IR (neat) 3345 w, 3053 w, 1782 w, 1670 m, 1596 w, 1565 w, 1526 s, 1485 m; MS *m*/*z* (relative intensity, %) 326 (M^+, 91), 185 (93), 183 (97), 171 (100), 144 (2); HRMS calcd for $C_{16}H_{11}BrN_2O$ 326.0055, found 326.0056.

*N-(Quinolin-8-yl)thiophene-2-carboxamide (**19**):* R_f = 0.19 (hexane/EtOAc 5/1); white solid; mp 95 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 7.19 (t, *J* = 4.4 Hz, 1H), 7.48 (dd, *J* = 8.4, 4.4 Hz, 1H), 7.53−7.60 (m, 3H), 7.85 (d, *J* = 3.6 Hz, 1H), 8.19 (dd, *J* = 8.4, 1.2 Hz, 1H), 8.84−8.86 (m, 2H), 10.607 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 116.6, 121.8, 121.8, 127.6, 128.0, 128.1, 128.5, 131.1, 134.4, 136.5, 138.6, 140.2, 148.4, 160.1; IR (neat) 3342 w, 3069 w, 1658 m, 1595 w, 1525 s, 1483 s; MS *m*/*z* (relative intensity, %) 254 (M^+, 61), 171 (6), 144 (1), 111 (100). HRMS calcd for $C_{14}H_{10}N_2OS$ 254.0514, found 254.0515.

General Procedure for Direct Arylation: Ni-Catalyzed Reaction of Amide 1a with PhI. In an oven-dried 5 mL screw-capped vial in a glovebox 2-methyl-*N*-(8-quinolinyl)benzamide (**1a**; 79 mg, 0.3 mmol), iodobenzene (122 mg, 0.6 mmol), $Ni(OTf)_2$ (5 mg, 0.015 mmol), $NaHCO_3$ (50 mg, 0.6 mmol), and toluene (1 mL) were added. The mixture was stirred for 20 h at 160 °C followed by cooling. The mixture was filtered through a Celite pad and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluent: hexane/EtOAc 10/1) to afford the desired arylated product **2a** (97 mg, 94%) as a colorless oil.

*3-Methyl-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**2a**):* R_f = 0.23 (hexane/EtOAc 5/1); colorless oil; yield 97 mg, 94%; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.53 (s, 3H), 7.08 (t, *J* = 8.0 Hz, 1H), 7.19−7.24 (m, 2H), 7.28−7.33 (m, 3H), 7.38−7.54 (m, 5H), 8.04 (d, *J* = 8.4 Hz, 1H), 8.59 (d, *J* = 4.0 Hz, 1H), 8.77 (d, *J* = 7.6 Hz, 1H), 9.64 (br s, 1H); ^{13}C NMR ($CDCl_3$, 400 MHz) 19.94, 116.5, 121.6, 121.8, 127.3, 127.4, 127.7, 127.9, 128.3, 128.8, 129.3, 129.6, 134.5, 135.9, 136.2, 137.0, 138.5, 139.8, 140.5, 148.1, 168.4; HRMS calcd for $C_{23}H_{18}N_2O$ 338.1419, found 338.1422.

*N-(Quinolin-8-yl)-[1,1′:3′,1″-terphenyl]-2′-carboxamide (**2b**):* R_f = 0.23 (hexane/EtOAc 5/1); white solid; yield 88 mg, 73%; mp 205−206 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 7.13 (t, *J* = 7.6 Hz, 2H), 7.22−7.25 (m, 4H), 7.30 (dd, *J* = 4.0, 8.4 Hz, 1H), 7.35−7.41 (m, 2H), 7.46

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(d, J = 7.6 Hz, 2H), 7.53−7.57 (m, 5H), 8.01 (dd, J = 1.6, 8.4 Hz, 1H), 8.52 (dd, J = 2.8, 6,4 Hz, 1H), 8.55 (dd, J = 1.6, 4.0 Hz, 1H), 9.63 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 116.4, 121.5, 121.5, 127.3, 127.5, 127.5, 127.7, 128.8, 129.4, 129.5, 134.4, 136.1, 136.3, 138.4, 140.5, 140.7, 147.9, 167.6; IR (neat) 3350 w, 2311 w, 1672 m, 1575 w, 1517 s, 1480 m; MS m/z (relative intensity, %) 400 (M^+, 27), 257 (100), 171 (1), 144 (2); HRMS calcd for $C_{28}H_{20}N_2O$ 400.1576, found 400.1573.

3-Fluoro-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**2c**): R_f = 0.14 (hexane/EtOAc 8/1); white solid; yield 63 mg, 59%; mp 140 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 7.09−7.15 (m, 2H), 7.18−7.22 (m, 3H), 7.31 (dd, J = 8.0, 4.8 Hz, 1H), 7.39−7.46 (m, 5H), 8.04 (dd, J = 8.0, 1.6 Hz, 1H), 8.57 (dd, J = 4.0, 2.0 Hz, 1H), 8.71 (dd, J = 7.2, 2.0 Hz, 1H), 9.85 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 115.0 (d, J = 22.0 Hz), 117.1, 121.7, 122.2, 125.1 (d, J = 17.3 Hz), 126.1, 127.5, 127.9, 128.0, 128.6, 128.7, 131.2, 134.2, 136.6, 138.2, 139.1, 142.5, 148.1, 159.9 (d, J = 250.2 Hz), 163.4; IR (neat) 3340 w, 3058 w, 2251 w, 1677 m, 1608 w, 1565 w, 1522 s, 1484 s; MS m/z (relative intensity, %) 342 (M^+, 37), 199 (100), 171 (27), 144 (9); HRMS calcd for $C_{22}H_{15}FN_2O$ 342.1168, found 342.1165.

N-(Quinolin-8-yl)-3-(trifluoromethyl)-[1,1′-biphenyl]-2-carboxamide (**2d**): R_f = 0.20 (hexane/EtOAc 5/1); white solid; yield 75 mg, 63%; mp 143 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 7.13 (t, J = 7.2 Hz, 1H), 7.21−7.26 (m, 2H), 7.37 (dd, J = 8.4, 4.0 Hz, 1H), 7.46−7.51 (m, 4H), 7.61−7.67 (m, 2H), 7.79 (dd, J = 7.2, 2.0 Hz, 1H), 8.09 (dd, J = 8.0, 2.0 Hz, 1H), 8.63 (dd, J = 4.0, 2.0 Hz, 1H), 8.69 (dd, J = 6.4, 2.4 Hz, 1H), 9.74 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 116.8, 121.6, 122.1, 123.9 (q, J = 274.0 Hz), 125.5 (q, J = 4.8 Hz), 127.4, 127.9, 128.1, 128.2 (q, J = 31.6 Hz), 128.4, 128.4, 128.8, 129.6, 134.1, 135.0, 136.3, 138.4, 139.0, 141.5, 148.2, 165.3; IR (neat) 3338 w, 3059 w, 2251 w, 1679 m, 1596 w, 1580 w, 1522 s, 1484 m; MS m/z (relative intensity, %) 392 (M+, 49) 249 (100), 171 (8.8), 144 (8); HRMS calcd for $C_{23}H_{15}F_3N_2O$ 392.1136, found 392.1133

4-(Dimethylamino)-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**2e**): R_f = 0.20 (hexane/EtOAc 5/1); pale yellow solid; yield 61 mg, 53%; ^{1}H NMR ($CDCl_3$, 400 MHz) 3.05 (s, 6H), 6.91 (m, 1H), 7.07 (t, J = 7.6 Hz, 1H), 7.20−7.25 (m, 3H), 7.31 (dd, J = 8.4, 4.0 Hz, 1H), 7.37 (d, J = 8.8 Hz, 1H), 7.42 (d, J = 8.4 Hz, 1H), 7.47−7.53 (m, 3H), 8.04 (dd, J = 8.4, 1.2 Hz, 1H), 8.47 (dd, J = 4.0, 1.6 Hz, 1H), 8.83 (d, J = 7.2 Hz, 1H), 9.76 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 40.7, 113.0, 114.6, 116.3, 121.5, 126.8, 127.4, 127.8, 128.1, 128.3, 129.1, 131.7, 134.8, 136.0, 136.8, 138.6, 140.3, 147.8, 149.9, 168.8; HRMS calcd for $C_{24}H_{21}N_3O$ 367.1685, found 367.1687.

4-Methoxy-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**2f**): R_f = 0.17 (hexane/EtOAc 5/1); white solid; yield 75 mg, 66%; mp 144 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 3.90 (s, 3H), 7.08−7.13 (m, 2H), 7.23−7.26 (m, 2H), 7.38−7.52 (m, 6H), 7.31 (dd, J = 8.4, 4.0 Hz, 1H), 8.04 (d, J = 8.4 Hz, 1H), 8.48 (dd, J =4.0, 1.6 Hz, 1H), 8.81 (d, J = 7.6 Hz, 1H), 9.78 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 55.7, 113.8, 116.4, 117.1, 121.5, 121.7, 127.3, 127.8, 128.4, 129.1, 132.1, 132.8, 134.5, 136.1, 137.0, 138.4, 139.8, 147.8, 159.1, 167.7; IR (neat) 3325 w, 2359 w, 2251 w, 1662 w, 1604 w, 1524 m, 1482 w; MS m/z (relative intensity, %) 354 (M^+, 32), 211 (100), 171 (3), 144 (8). HRMS calcd for $C_{23}H_{18}N_2O_2$ 354.1368, found 354.1371.

4-Methyl-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**2g**): R_f = 0.29 (hexane/EtOAc 5/1); white solid; yield 72 mg, 69%; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.47 (s, 3H), 7.14 (t, J = 7.6 Hz, 1H), 7.24−7.28 (m, 2H), 7.34(dd, J = 8.4, 4.0, 1H), 7.38−7.39 (m, 2H), 7.43−7.53 (m, 4H), 7.72 (s, 1H), 8.06 (dd, J = 8.4, 1.6 Hz, 1H), 8.51 (dd, J = 4.0, 1.2 Hz, 1H), 8.81 (dd, J = 7.2, 1.6 Hz,1H), 9.75 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 21.2, 116.3, 121.5, 121.5, 127.4, 127.5, 127.8, 128.4, 129.1 129.9, 130.7, 131.4, 134.7, 136.0, 137.5, 137.6, 138.5, 140.1, 147.8, 168.1; HRMS calcd for $C_{23}H_{18}N_2O$ 338.1419, found 338.1420.

N-(Quinolin-8-yl)-[1,1′:4′,1″-terphenyl]-2′-carboxamide (**2h**): R_f = 0.40 (hexane/EtOAc 5/1); white solid; yield 79 mg, 65% ^{1}H NMR ($CDCl_3$, 400 MHz) 7.18 (t, J = 7.6 Hz, 1H), 7.28−7.32 (m, 2H), 7.35−7.42 (m, 2H), 7.47−7.59 (m, 7H), 7.72 (dd, J = 3.2, 1.6 Hz, 2H), 7.80 (dd, J = 8.0, 2.0 Hz, 1H), 8.10 (d, J = 8.4 Hz, 1H), 8.15 (d, J = 1.6 Hz, 1H), 8.53 (dd, J = 4.0, 2.0 Hz, 1H), 8.83 (dd, J = 7.6, 1.2 Hz, 1H), 9.88(br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 116.8, 121.5, 121.8, 127.3, 127.5, 127.8, 127.9, 128.0, 128.5, 129.06, 129.09, 129.2, 131.3, 134.4, 136.49, 136.47, 136.6, 138.2, 139.2, 139.7, 140.0, 140.6, 147.7, 168.0; HRMS calcd for $C_{28}H_{20}N_2O$ 400.1576, found 400.1573.

4-Chloro-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**2i**): R_f = 0.29 (hexane/EtOAc 5/1); white solid; yield 77 mg, 68%; mp 150 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 7.17 (t, J = 7.2 Hz, 1H), 7.25−7.30 (m, 2H), 7.35 (dd, J = 8.4, 4.0 Hz, 1H), 7.41 (d, J = 8.4 Hz, 1H), 7.45−7.54 (m, 5H), 7.90 (d, J = 7.9 Hz, 1H), 8.07 (dd, J = 8.0, 1.6 Hz, 1H), 8.51 (dd, J = 4.0, 2.0 Hz, 1H), 8.77 (dd, J = 7.2, 1.2 Hz, 1H), 9.76 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 116.5, 121.6, 121.9, 127.4, 127.8, 128.1, 128.7, 129.0, 129.4, 130.7, 132.2, 133.9, 134.3, 136.2, 137.5, 138.5, 138.8, 139.0, 148.0, 166.4; IR (neat) 3326 w, 2984 w, 2359 w, 1737 s, 1670 m, 1595 w, 1522 s, 1483 m; MS m/z (relative intensity, %) 358 (M^+, 49), 215 (100), 171 (11), 144 (23). HRMS calcd for $C_{22}H_{15}ClN_2O$ 358.0873, found 358.0870.

4-Bromo-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**2j**): R_f = 0.29 (hexane/EtOAc 5/1); white solid; yield 85 mg, 70%; mp 136 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 7.18 (t, J = 7.6 Hz, 1H), 7.26−7.30 (m, 2H), 7.34−7.36 (m, 2H), 7.45−7.53 (m, 4H), 7.68 (dd, J =8.4, 1.6 Hz, 1H), 8.06 (dd, J = 6.4, 1.2 Hz, 1H), 8.08 (d, J = 1.2 Hz, 1H), 8.52 (dd, J = 4.4, 1.6 Hz, 1H), 8.77 (dd, J = 7.6, 1.2 Hz, 1H), 9.75 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 116.6, 121.6, 121.9, 121.9, 127.4, 127.8, 128.1, 128.7, 128.9, 132.2, 132.4, 133.6, 134.3, 136.2, 137.7, 138.0, 138.3, 139.0, 139.2, 139.6, 147.9, 166.3; IR (neat) 2984 w, 1738 s, 1676 w, 1525 w, 1483 w; MS m/z (relative intensity, %) 404 (57), 403 (42), 402 (M^+, 58), 171 (18), 152 (100), 144 (40); HRMS calcd for $C_{22}H_{15}BrN_2O$ 402.0368, found 402.0370.

4-Acetyl-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**2k**): R_f = 0.08 (hexane/EtOAc 5/1). Colorless oil. yield 66 mg, 60%; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.71 (s, 3H), 7.21 (t, J = 8.0 Hz, 1H), 7.29−7.37 (m, 3H), 7.47−7.55 (m, 4H), 7.60 (d, J = 7.6 Hz, 1H), 8.09 (d, J = 8.0 Hz, 1H), 8.16 (dd, J = 7.6, 2.0 Hz, 1H), 8.49−8.52 (m, 2H), 8.80 (d, J = 7.6 Hz, 1H), 9.81 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 27.0, 116.5, 121.6, 122.0, 127.4, 127.8, 128.5, 128.7, 129.0, 129.9, 130.0, 131.3, 134.4, 136.2, 136.3, 136.5, 138.4, 139.0, 144.8, 148.0, 167.0, 197.3; IR (neat) 3322 w, 3057 w, 2348 w, 1681 s, 1598 m, 1523 s, 1484 m; MS m/z (relative intensity, %) 366 (M^+, 53), 223 (100), 171 (7), 144 (11); HRMS calcd for $C_{24}H_{18}N_2O_2$ 366.1368, found 366.1369.

N-(Quinolin-8-yl)-4-(trifluoromethyl)-[1,1′-biphenyl]-2-carboxamide (**2l**): R_f = 0.26 (hexane/EtOAc 5/1); white solid; yield 80 mg, 68%; ^{1}H NMR ($CDCl_3$, 400 MHz) 7.21 (t, J = 8.8 Hz, 1H), 7.29−7.36 (m, 3H), 7.46−7.54 (m, 4H), 7.61 (d, J = 8.4 Hz, 1H), 7.80 (dd, J = 8.0, 1.6 Hz, 1H), 8.07 (dd, J = 8.4, 1.6 Hz, 1H), 8.20 (s, 1H), 8.50 (dd, J = 4.0, 2.0 Hz, 1H), 8.79 (dd, J = 8.0, 1.2 Hz, 1H), 9.78 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 116.5, 121.6, 122.0, 124.0 (q, J = 272.2 Hz), 126.7, 127.2, 127.3, 127.8, 128.5, 128.8, 129.0, 130.1 (q, J = 32.7 Hz), 131.4, 134.2, 136.2, 136.7, 138.4, 138.7, 143.7, 148.0, 166.4; HRMS calcd for $C_{23}H_{15}F_3N_2O$ 392.1136, found 392.1134.

4,5-Dimethoxy-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**10**): R_f = 0.09 (hexane/EtOAc 5/1); white solid; yield 79 mg, 65%; ^{1}H NMR ($CDCl_3$, 400 MHz) 3.97 (s, 3H), 4.01 (s, 3H), 6.92 (s, 1H), 7.15 (t, J = 7.2 Hz, 1H), 7.26−7.33 (m, 3H), 7.43 (d, J = 8.4 Hz, 1H), 7.49−7.54 (m, 4 H), 8.04 (d, J = 8.4 Hz, 1H), 8.43 (d, J = 4.4 Hz, 1H), 8.82 (d, J = 7.6 Hz, 1H), 9.69 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 56.17, 56.22, 112.6, 113.3, 116.1, 121.4, 127.3, 127.6, 127.7, 128.0, 128.3, 128.5, 129.4, 133.8, 134.7, 135.9, 138.4, 140.0, 147.6, 148.4, 150.6, 167.3; HRMS calcd for $C_{24}H_{20}N_2O_3$ 384.1474, found 384.1469.

5-Fuoro-3-methyl-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**12**): R_f = 0.31 (hexane/EtOAc 5/1); colorless oil; yield 103 mg, 96%; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.53 (s, 3H), 6.99−7.02 (m, 2H), 7.09 (t, J = 7.2 Hz, 1H), 7.22 (dd, J = 15.2, 18.0 Hz, 2H), 7.35 (dd, J = 8.4, 4.0 Hz, 1H), 7.44−7.51 (m, 4H), 8.06 (dd, J = 8.0, 1.6 Hz, 1H), 8.60 (dd, J = 4.4, 1.2 Hz, 1H), 8.75 (dd, J = 7.2, 1.2 Hz, 1H), 9.61 (br s,1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 20.1, 114.4 (d, J = 22.0 Hz), 116.2, 116.4, 116.6, 121.8 (d, J = 32.6 Hz), 127.4, 127.9, 128.5 (d, J = 13.4 Hz), 131.8 (d, J = 151.4 Hz), 133.2, 134.3, 136.3, 138.3, 139.1 (d,

dx.doi.org/10.1021/jo501697n | J. Org. Chem. XXXX, XXX, XXX−XXX

J = 8.6 Hz), 139.4, 142.2, 148.1, 161.3, 163.8, 167.7; HRMS calcd for $C_{23}H_{17}FN_2O$ 356.1325, found 356.1328.

*2-Phenyl-N-(quinolin-8-yl)-1-naphthamide (**16**):* R_f = 0.26 (hexane/EtOAc 5/1); white solid; yield 65 mg, 57%; ^{1}H NMR ($CDCl_3$, 400 MHz) 7.13 (t, J = 8.0 Hz, 1H), 7.24−7.32 (m, 3H), 7.47 (d, J = 8.0 Hz, 1H), 7.51−7.66 (m, 6 H), 7.90−7.93 (m, 1H), 8.00 (d, J = 8.0 Hz, 1H), 8.05 (dd, J = 8.4, 2.0 Hz, 1H), 8.23 (dd, J = 6.0, 3.2 Hz, 1H), 8.52 (dd, J = 4.0, 1.6 Hz, 1H), 8.92 (dd, J = 7.2, 1.6 Hz, 1H), 9.83 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 116.7, 121.6, 122.0, 125.8, 126.5, 127.4, 127.6, 127.6, 127.87, 127.89, 128.2, 128.5, 129.1, 129.8, 130.6, 132.7, 133.8, 134.6, 136.2, 137.1, 138.4, 140.4, 148.1, 168.0; HRMS calcd for $C_{26}H_{18}N_2O$ 374.1419, found 374.1418.

*5-Methyl-2-phenyl-N-(quinolin-8-yl)thiophene-3-carboxamide (**18**):* R_f = 0.26 (hexane/EtOAc 5/1); white solid; yield 65 mg, 62%; mp 125 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.52 (s, 3H), 7.28−7.42 (m, 5H), 7.44 (d,J = 1.6 Hz, 1H), 7.48−7.57 (m, 3H), 8.04 (dd, J = 8.4, 2.0 Hz, 1H), 8.37 (dd, J = 4.0, 2.0 Hz, 1H), 8.83 (dd, J = 7.2, 1.6 Hz, 1H), 9.94 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 15.1, 116.2, 121.3, 127.3, 127.4, 127.7, 128.5, 128.7, 129.9, 132.9, 133.6, 134.7, 135.9, 138.4, 139.0, 143.3, 147.6, 162.4; IR (neat) 2984 w, 2362 w, 1738 s, 1525 w, 1446 w; MS m/z (relative intensity, %) 344 (M^+, 25), 201 (100), 171 (5), 144 (1); HRMS calcd for $C_{21}H_{16}N_2OS$ 344.0983, found 344.0984.

*3-Phenyl-N-(quinolin-8-yl)thiophene-2-carboxamide (**20**):* R_f = 0.24 (hexane/EtOAc 5/1); white solid; yield 57 mg, 57%; mp 106−107 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 7.10 (d, J = 5.2 Hz, 1H), 7.29 (dd, J = 8.8, 4.0 Hz, 1H), 7.42−7.57 (m, 8 H), 8.03 (dd, J = 8.8, 1.2 Hz, 1H), 8.28 (dd, J = 4.0, 2.0 Hz, 1H), 8.82 (d, J = 7.6 Hz, 1H), 10.06 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 116.6, 121.4, 121.6, 127.4, 127.8, 128.4, 129.2, 129.5, 129.7, 131.6, 134.6, 135.3, 135.9, 136.0, 138.6, 143.2, 147.6, 160.8; IR (neat) 3298 w, 3053 w, 2983 w, 2362 w, 1735 m, 1648 m, 1596 w, 1576 w, 1523 s, 1483 s; MS m/z (relative intensity, %) 330 (M^+, 33), 187 (100), 171 (2), 144(1); HRMS calcd for $C_{20}H_{14}N_2OS$ 330.0827, found 330.0829.

*6-Phenyl-N-(quinolin-8-yl)-3,4-dihydro-2H-pyran-5-carboxamide (**22**):* R_f = 0.13 (hexane/EtOAc 5/1); white solid; yield 54 mg, 54%; mp 158 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.04 (t, J =6.0, 4.4 Hz, 2H), 2.68 (t, J = 6.0 Hz, 2H), 4.26 (t, J = 5.2 Hz, 2H), 7.13−7.21 (m, 3H), 7.27 (dd, J = 8.4, 4.0 Hz, 1H), 7.37 (d, J = 8.4 Hz, 1H), 7.47 (t, J = 7.6 Hz, 1H), 7.53 (d, 7.6 Hz, 2H), 8.01 (dd, J = 8.4, 1.2 Hz, 1H), 8.37 (dd, J = 3.6, 1.6 Hz, 1H), 8.73 (d, J = 7.6 Hz, 1H), 9.43 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 22.2, 22.9, 67.3, 109.6, 115.8, 120.9, 121.3, 127.4, 127.8, 128.3, 129.2, 129.5, 135.0, 135.5, 136.0, 138.5, 147.5, 158.0, 168.4; IR (neat) 2984 w, 2362 w, 1737 s, 1658 w, 1521 w, 1483 w; MS m/z (relative intensity, %) 330 (M^+, 17), 187 (100), 171 (2), 144 (4); HRMS calcd for $C_{21}H_{18}N_2O_2$ 330.1368, found 330.1366.

*4′-Amino-3-methyl-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**23a**):* R_f = 0.37 (hexane/EtOAc 1/1); pink oil; yield 23 mg, 21%; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.50 (s, 3H), 6.54 (d, J = 6.4 Hz, 2H), 7.25 (q, J = 7.2 Hz, 2H), 7.31−7.39 (m, 4H), 7.45−7.54 (m, 2H), 8.09 (dd, J = 8.4, 2.0 Hz, 1H), 8.62 (dd, J = 4.0, 2.0 Hz, 1H), 8.81 (dd, J = 7.6, 1.2 Hz, 1H), 9.65 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 19.9, 115.1, 116.6, 121.6, 121.7, 127.4, 127.6, 127.9, 128.8, 129.2, 129.7, 130.8, 134.6, 135.8, 136.2, 136.8, 138.5, 139.7, 145.7, 148.1, 168.9; IR (neat) 3458 w, 3347 w, 3056 w, 2246 w, 1666 m, 1621 m, 1518 s, 1482 s; MS m/z (relative intensity, %) 353 (M^+, 29), 210 (100), 171 (1), 144 (2); HRMS calcd for $C_{23}H_{19}N_3O$ 353.1528, found 353.1526.

*4′-Methoxy-3-methyl-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**23b**):* R_f = 0.20 (hexane/EtOAc 5/1); white solid; yield 105 mg, 95%; mp 148−149 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.51 (s, 3H), 3.57 (s, 3H), 6.74 (d, J = 8.8 Hz, 2H), 7.22−7.30 (m, 3H), 7.34−7.42 (m, 2H), 7.45−7.50 (m, 3H), 8.00 (d, J = 8.4 Hz, 1H), 8.57 (dd, J = 4.8, 1.2 Hz, 1H), 8.80 (d, J = 8.0 Hz, 1H), 9.65 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 19.9, 55.1, 113.8, 116.5, 121.5, 121.7, 127.3, 127.7, 127.9, 129.2, 129.2, 129.8, 132.9, 134.5, 135.8, 136.1, 136.9, 138.4, 139.3, 148.0, 159.0, 168.6; IR (neat) 3342 w, 2957 w, 2837 w, 2249 w, 1668 m, 1610 w, 1517 s, 1482 m; MS m/z (relative intensity, %) 368 (M^+, 25), 225 (100), 171(1), 144 (2); HRMS calcd for $C_{24}H_{20}N_2O_2$: 368.1525, found 368.1527.

*3,4′-Dimethyl-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**23c**):* R_f = 0.29 (hexane/EtOAc 5/1); white solid; yield 99 mg, 93%; mp 118 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.14 (s, 3H), 2.52 (s, 3H), 7.01 (d, J = 8.0 Hz, 2H), 7.24−7.29 (m, 2H), 7.33 (dd, J = 8.4, 4.4 Hz, 1H), 7.36−7.45 (m, 4H), 7.50 (t, J = 8.0 Hz, 1H), 8.05 (d, J = 8.4 Hz, 1H), 8.60 (dd, J = 4.4, 1.6 Hz, 1H), 8.78 (d, J = 8.2 Hz, 1H), 9.66 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 19.9, 21.1, 116.7 121.6, 121.8, 127.4, 127.8, 127.9, 128.6, 129.1, 129.3, 129.4, 134.6, 135.8, 136.2, 136.9, 137.0, 137.6, 138.5, 139.8, 148.1, 168.6; IR (neat) 2984 w, 1738 s, 1523 w, 1482 w; MS m/z (relative intensity, %) 352 (M^+, 26), 209 (100), 171 (1), 144 (3); HRMS calcd for $C_{24}H_{20}N_2O$ 352.1576, found 352.1577.

*4′-Butyl-3-methyl-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**23d**):* R_f = 0.33 (hexane/EtOAc 5/1); yellow oil; yield 114 mg, 96%; ^{1}H NMR ($CDCl_3$, 400 MHz) 0.70 (t, J = 3.2 Hz, 3H), 0.99 (qt, J = 7.3, 7.2 Hz, 2H), 1.25 (tt, J = 7.6, 7.2 Hz, 2H), 2.36 (t, 7.6 Hz, 2H), 2.53 (s, 3H), 7.23−7.30 (m, 3H), 7.35−7.50 (m, 5H), 8.01 (d, J = 8.0 Hz, 1H), 8.56 (d, J = 4.0 Hz, 1H), 8.77 (d, J = 7.6 Hz, 1H), 9.58 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 13.9, 19.9, 22.0, 33.3, 35.1, 116.5, 121.5, 121.6, 127.3, 127.6, 127.8, 128.3, 128.6, 129.3, 129.4, 134.5, 136.0, 136.1, 136.9, 137.8, 138.4, 139.9, 141.9, 147.9, 168.5; IR (neat) 3341 w, 2957 w, 2929 w, 2858 w, 2248 w, 1669 w, 1593 w, 1521 s, 1483 m; MS m/z (relative intensity, %) 394 (M^+, 54), 251 (100), 195 (85), 171 (2), 144 (8); HRMS calcd for $C_{27}H_{26}N_2O$ 394.2045, found 394.2044.

*3-Methyl-N-(quinolin-8-yl)-[1,1′:4′,1″-terphenyl]-2-carboxamide (**23e**):* R_f = 0.34 (hexane/EtOAc 5/1); white solid; yield 51 mg, 41%; mp 188 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.55 (s, 3H), 7.23−7.27 (m, 1H), 7.29−7.45 (m, 11H), 7.50 (t, J = 7.6 Hz, 1H), 7.60 (d, J = 8.4 Hz, 2H), 8.04 (dd, J = 8.4, 1.2 Hz, 1H), 8.59 (dd, J = 4.4, 1.6 Hz, 1H), 8.79 (dd, J = 7.6, 1.2 Hz, 1H), 9.70 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 20.0, 116.7, 121.6, 121.9, 126.7, 127.1, 127.3, 127.4, 127.7, 127.9, 128.5, 128.7, 128.9, 129.2, 129.4, 129.7, 134.5, 136.1, 136.2, 136.9, 138.5, 139.3, 139.5, 140.1, 140.7, 148.1, 168.5; IR (neat) 3342 w, 3058 w, 2247 w, 1672 m, 1594 w, 1520 s, 1482 s; MS m/z (relative intensity, %) 414 (M^+, 30), 271 (100), 171 (1), 144 (4); HRMS calcd for $C_{29}H_{22}N_2O$ 414.1732, found 414.1727.

*4′-Chloro-3-methyl-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**23f**):* R_f = 0.24 (hexane/EtOAc 5/1). Colorless oil. yield 81 mg, 73%; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.53 (s, 3H), 7.17−7.7.21 (m, 2H), 7.26 (d, J = 7.6 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.35- 7.42 (m, 2H), 7.44- 7.54 (m, 4H), 8.09 (dd, J = 8.4, 1.2 Hz, 1H), 8.61(dd, J = 4.8, 1.2 Hz, 1H), 8.77 (dd, J = 7.6, 1.6 Hz, 1H), 9.67 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 19.9, 116.8, 121.7, 122.1, 127.4, 127.6, 127.9, 128.5, 129.4, 129.9, 130.1, 133.5, 134.2, 136.1, 136.4, 136.9, 138.4, 138.9, 148.2, 168.2; IR (neat) 3340 w, 3059 w, 2248 w, 1671 m, 1595 w, 1519 s, 1482 s; MS m/z (relative intensity, %) 372 (M^+, 36), 229 (100), 171 (2), 144 (3); HRMS calcd for $C_{23}H_{17}ClN_2O$ 372.1029, found 372.1026.

*4′-Bromo-3-methyl-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**23g**):* R_f = 0.34 (hexane/EtOAc 5/1); white solid; yield 76 mg, 60%; mp 138−139 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.52 (s, 3H), 7.24- 7.42 (m, 8H), 7.47−7.54 (m, 2H), 8.10 (dd, J = 8.4, 1.2 Hz, 1H), 8.61 (dd, J = 4.8, 1.2 Hz, 1H), 8.76 (dd, J = 6.8, 2.0 Hz, 1H), 9.65 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 19.9, 116.8, 121.7, 121.8, 122.1, 127.4, 127.6, 128.0, 129.4, 130.0, 130.5, 130.7, 131.5, 134.3, 136.1, 136.3, 136.9, 137.4, 138.48, 138.54, 139.5, 148.2, 168.1; IR (neat) 2984 w, 2359 w, 1737 s, 1680 w, 1523 w, 1482 w; MS m/z (relative intensity, %) 416 (M^+, 41), 194 (100), 171 (3), 165 (49), 144 (7); HRMS calcd for $C_{23}H_{17}BrN_2O$ 416.0524, found 416.0518.

*4′-Iodo-3-methyl-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**23h**):* R_f = 0.23 (hexane/EtOAc 5/1); white solid; yield 94 mg, 67%; mp 124−125 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.53 (s, 3H), 7.24−7.28 (m, 3H), 7.31 (d, J = 7.6 Hz, 1H), 7.38−7.43 (m, 2H), 7.49−7.55 (m, 4H), 8.12 (dd, J = 8.4, 1.2 Hz, 1H), 8.62 (dd, J = 4.4, 1.2 Hz, 1H), 8.76 (dd, J = 7.2, 2.0 Hz, 1H), 9.65 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 19.9, 93.6, 116.8, 121.7, 122.1, 127.3, 127.5, 127.9, 129.5, 130.0, 130.6, 134.3, 136.1, 136.3, 136.7, 137.4, 138.5, 140.0, 148.2, 168.1; IR (neat) 2983 w, 2361 w, 1737 s, 1680 w, 1523 w, 1483

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w; MS *m*/*z* (relative intensity, %) 464 (M^+, 54), 194 (100), 171 (2), 144 (5); HRMS calcd for $C_{23}H_{17}IN_2O$ 464.0386, found464.0389.

*Methyl 3′-methyl-2′-(quinolin-8-ylcarbamoyl)-[1,1′-biphenyl]-4-carboxylate (**23i**):* R_f = 0.09 (hexane/EtOAc 5/1); white solid; yield 109 mg, 91%; mp 120−121 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.54 (s, 3H), 3.80 (s, 3H), 7.30−7.54 (m, 6H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.90 (d, *J* = 8.4 Hz, 2H), 8.11 (d, *J* = 8.0 Hz, 1H), 8.61 (dd, *J* = 4.0, 2.0 Hz, 1H), 8.76 (dd, *J* = 7.2, 1.2 Hz, 1H), 9.69 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 19.9, 52.1, 116.9, 121.6, 122.1, 127.4, 127.6, 128.0, 128.8, 129.0, 129.5, 129.6, 130.3, 134.1, 136.1, 136.5, 136.8, 138.2, 138.6, 145.2, 148.1, 166.9, 168.1; IR (neat) 3340 w, 3057 w, 2951 w, 2339 w, 2251 w, 1938 w, 1718 w, 1672 m, 1610 w, 1593 w, 1520 s, 1482 s; MS *m*/*z* (relative intensity, %) 396 (M^+, 100), 209 (92), 171(6), 144 (12); HRMS calcd for $C_{25}H_{20}N_2O_3$: 396.1474, found 396.1472.

*4′-Acetyl-3-methyl-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**23j**):* R_f = 0.09 (hexane/EtOAc 5/1); white solid; yield 74 mg, 65%; mp 151 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.42 (s, 3H), 2.54 (s, 3H), 7.29- 7.37 (m, 3H), 7.41−7.52 (m, 3H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.81 (d, *J* = 8.0 Hz, 2H), 8.07 (d, *J* = 8.0 Hz, 1H), 8.60 (d, *J* = 3.6 Hz, 1H), 8.76 (d, *J* = 6.8 Hz, 1H), 9.69 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 19.9, 26.6, 116.7, 121.6, 122.1, 127.3, 127.5, 127.9, 128.4, 129.0, 129.5, 130.3, 134.2, 135.8, 136.1, 136.3, 136.8, 138.3, 138.5, 145.4, 148.1, 168.0, 197.8; IR (neat) 3341 w, 3056 w, 2362 w, 2249 w, 1677 s, 1604 w, 1520 s, 1482 s; MS *m*/*z* (relative intensity, %) 380 (M^+, 64), 195 (100), 171 (4), 144 (6); HRMS calcd for $C_{25}H_{20}N_2O_2$ 380.1525, found 380.1527.

*3-Methyl-N-(quinolin-8-yl)-4′-(trifluoromethyl)-[1,1′-biphenyl]-2-carboxamide (**23k**):* R_f = 0.26 (hexane/EtOAc 5/1); yellow oil; yield 117 mg, 87%; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.55 (s, 3H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.34−7.40 (m, 2H), 7.43−7.55 (m, 5H), 7.64 (d, *J* = 8.4 Hz, 2H), 8.11 (d, *J* = 8.4 Hz, 1H), 8.60 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.74 (dd, *J* = 6.8, 2.0 Hz, 1H), 9.68 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 20.0, 117.0, 121.7, 122.2, 124.2 (q, *J* = 272.1 Hz), 125.3, 127.4, 127.6, 128.0, 129.2, 129.4 (q, *J* = 32.6 Hz), 129.6, 130.4, 133.4, 134.1, 136.3, 136.6, 136.9, 138.3, 144.2, 148.1, 168.0; IR (neat) 3340 w, 3056 w, 1674 m, 1619 w, 1594 w, 1521 s, 1483 m; MS *m*/*z* (relative intensity, %) 406 (M^+, 38), 263 (100), 171 (2), 144 (3); HRMS calcd for $C_{24}H_{17}F_3N_2O$ 406.1293, found 406.1292.

*3,3′-Dimethyl-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**24**):* R_f = 0.21 (hexane/EtOAc 5/1); white solid; yield 74 mg, 59%; mp 98−99 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.17 (s, 3H), 2.53 (s, 3H), 6.87 (d, *J* = 7.2 Hz, 1H), 7.07 (t, *J* = 7.2 Hz, 1H), 7.23−7.51 (m, 8H), 8.04 (dd, *J* = 8.4, 2.0 Hz, 1H), 8.59 (dd, *J* = 4.0, 1.2 Hz, 1H), 8.77 (dd, *J* = 7.2, 1.6 Hz, 1H), 9.64 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 19.9, 21.4, 116.5, 121.5, 121.7, 125.8, 127.3, 127.6, 127.8, 128.1, 128.1, 129.3, 129.5, 129.5, 134.5, 135.9, 136.2, 136.9, 137.8, 138.4, 139.9, 140.4, 148.0, 168.5; IR (neat) 3345 w, 3051 w, 1673 m, 1579 w, 1520 s, 1482 s; MS *m*/*z* (relative intensity, %) 352 (M^+, 33), 209 (100), 171(1), 144 (9); HRMS calcd for $C_{24}H_{20}N_2O$ 352.1576, found 352.1579.

*2-(1H-Indol-7-yl)-6-methyl-N-(quinolin-8-yl)benzamide (**25**):* R_f = 0.14 (hexane/EtOAc 3/1); brown solid; yield 76 mg, 67%; mp 207−208 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.54 (s, 3H), 6.45 (t, *J* = 2.0 Hz, 1H), 7.05 (t, *J* = 2.8 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.26−7.29 (m, 2H), 7.33−7.47 (m, 5H), 7.80 (d, *J* = 0.8 Hz, 1H), 8.00 (dd, *J* = 8.0, 1.6 Hz, 2H), 8.51 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.75 (dd, *J* = 7.2, 1.2 Hz, 1H), 9.64 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 20.1, 103.0, 110.8, 116.7, 121.1, 121.4, 121.6, 123.2, 124.5, 127.3, 127.9, 128.1, 128.4, 128.9, 129.2, 132.4, 134.6, 135.2, 135.8, 136.1, 137.2, 138.5, 141.0, 148.0, 169.0; IR (neat) 3332 w, 3056 w, 2925 w, 2246 w, 1658 m, 1578 w, 1522 s, 1483 s; MS *m*/*z* (relative intensity, %) 377 (M^+, 35), 234 (100), 171 (1), 144 (39); HRMS calcd for $C_{25}H_{19}N_3O$ 377.1528, found 377.1523.

*2-Methyl-N-(quinolin-8-yl)-6-(thiophen-2-yl)benzamide (**26**):* R_f = 0.20 (hexane/EtOAc 5/1); white solid; yield 102 mg, 98%; mp 111−113 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.49 (s, 3H), 6.84 (dd, 5.2, 3.6 Hz, 1H), 7.12 (d, *J* = 5.2 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.34−7.42 (m, 3H), 7.48−7.56 (m, 2H), 8.08 (d, *J* = 8.4 Hz, 1H), 8.63 (d, *J* = 4.0 Hz, 1H), 8.88 (d, *J* = 7.2 Hz, 1H), 9.82 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 19.7, 116.8, 121.7, 122.0, 126.0, 126.6, 127.4, 127.7, 127.8, 128.0, 129.3, 129.9, 132.1, 134.6, 136.0, 136.3, 136.8, 138.6, 141.6, 148.3, 168.4; IR (neat) 2984 w, 2360 w, 1738 s, 1648 w, 1530 w, 1446 w; MS *m*/*z* (relative intensity, %) 344 (M^+, 36), 201 (100), 171 (11), 144 (4); HRMS calcd for $C_{21}H_{16}N_2OS$ 344.0983, found 344.0980.

*4′-Methoxy-N-(quinolin-8-yl)-4-(trifluoromethyl)-[1,1′-biphenyl]-2-carboxamide (**27b**):* R_f = 0.17 (hexane/EtOAc 5/1); white solid; mp 152 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 3.66 (s, 3H), 6.84 (dd, *J* = 6.8, 1.6 Hz, 2H), 7.37 (dd, *J* = 8.4, 4.0 Hz, 1H), 7.45−7.60 (m, 5H), 7.79 (dd, *J* = 8.4, 1.2 Hz, 1H), 8.10 (dd, *J* = 8.8, 1.2 Hz, 1H), 8.18 (s, 1H), 8.52 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.81 (dd, *J* = 7.2. 1.6 Hz, 1H), 9.82 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 55.3, 114.3, 116.8, 121.6, 122.1, 124.0(q, *J* = 272.2 Hz), 126.7, 127.2, 127.4, 127.9, 129.1 (q, *J* = 29.7 Hz), 129.7 (q, *J* = 33.6 Hz), 130.3, 131.0, 131.3, 134.3, 136.4, 138.4, 143.4, 147.9, 160.1, 166.7; IR (neat) 3313 w, 2960 w, 2838 w, 1667 m, 1610 m, 1579 w, 1523 s, 1486 m; MS *m*/*z* (relative intensity, %) 422 (M^+, 41), 279 (100), 171 (7), 144 (13); HRMS calcd for $C_{24}H_{17}F_3N_2O_2$: 422.1242, found 422.1240.

*4-(Dimethylamino)-4′-methyl-N-(quinolin-8-yl)-[1,1′-biphenyl]-2-carboxamide (**28a**):* R_f = 0.14 (hexane/EtOAc 5/1); yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.16 (s, 3H), 3.05 (s, 6H), 7.03 (d, *J* = 8.0 Hz, 2H), 7.32−7.38 (m, 4H), 7.45 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.52 (t, *J* = 8.4 Hz, 1H), 8.07 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.49 (dd, *J* = 4.0, 2.0 Hz, 1H), 8.83 (dd, *J* = 7.6, 1.2 Hz, 1H), 9.80 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 21.1, 40.9, 114.8, 116.4, 121.4, 121.5, 127.4, 127.8, 128.6, 129.0, 129.1, 131.7, 134.9, 136.0, 136.5, 136.7, 137.3, 138.6, 147.7, 168.8; IR (neat) 3327 w, 2928 w, 2250 w, 1665 m, 1605 m, 1522 s, 1499 m, 1483 s, 1424 m, 1384 m, 1360 m, 1326 m, 1263 w, 1224 w, 1167 w, 1110 w, 1064 w, 971 w, 911 m, 826 m, 809 m, 792 m, 742 m; MS *m*/*z* (relative intensity, %) 381 (M^+, 62), 238 (100), 171 (2), 144 (1); HRMS calcd for $C_{25}H_{23}N_3O$ 381.1841, found 381.1838.

*4′-Methyl-N-(quinolin-8-yl)-4-(trifluoromethyl)-[1,1′-biphenyl]-2-carboxamide (**28b**):* . R_f = 0.30 (hexane/EtOAc 5/1); white solid; mp 125−128 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.21 (s, 3H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.36 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.48−7.61 (m, 3H), 7.80 (d, *J* = 8.0 Hz, 1H), 8.09 (dd, *J* = 8.4, 1,2 Hz, 1H), 8.20 (s, 1H), 8.51 (dd, *J* = 4.4, 1.2 Hz, 1H), 8.81 (d, *J* = 7.2 Hz, 1H), 9.83 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 21.2, 116.7, 121.6, 122.0, 124.0 (q, *J* = 272.2 Hz), 126.6, 126.6, 127.2, 127.4, 127.8, 128.9, 129.5, 129.8 (q, *J* = 32.6 Hz), 131.4, 134.3, 135.8, 136.2, 136.6, 138.5, 143.8, 147.9, 166.6; IR (neat) 3314 w, 3049 w, 2250 w, 1668 m, 1615 w, 1526 s, 1485 m, 1425 w, 1386 w, 1327 s, 1288 w, 1258 m, 1228 w, 1171 m, 1128 s, 1084 m, 1049 w, 1007 w, 911 w, 848 w, 819 m, 792 m, 733 m, 706 w; MS *m*/*z* (relative intensity, %) 406 (M^+, 48), 263 (100), 171 (9), 144 (21); HRMS calcd for $C_{24}H_{17}F_3N_2O$ 406.1293, found 406.1291.

*4-(Dimethylamino)-N-(quinolin-8-yl)-4′-(trifluoromethyl)-[1,1′-biphenyl]-2-carboxamide (**29a**):* R_f = 0.14 (hexane/EtOAc 5/1); white solid; mp 178−179 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 3.08 (s, 6H), 7.25 (d, *J* = 2.4 Hz, 1H), 6.92 (d, *J* = 7.6 Hz, 1H), 7.32−7.38 (m, 2H), 7.45−7.49 (m, 3H), 7.51−7.59 (m, 3H), 8.08 (dd, *J* = 8.4, 1.2 Hz, 1H), 8.45 (dd, *J* = 4.4, 1.2 Hz, 1H), 8.80 (d, *J* = 7.6 Hz, 1H), 9.74 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 29.8, 41.0, 113.5, 115.0, 116.5, 121.6, 121.7, 121.9, 124.3 (q, *J* = 272.2 Hz), 125.3, 127.4, 127.9, 128.9 (q, *J* = 35.5 Hz), 129.1 (q, *J* = 14.4 Hz), 129.4, 129.6, 131.7, 134.4, 136.3, 136.9, 138.4, 143.9, 147.9, 168.1; IR (neat) 3330 w, 2923 w, 2853 w, 2248 w, 1668 m, 1604 m, 1522 s, 1484 m, 1425 m, 1384 w, 1363 w, 1323 s, 1261 w, 1226 w, 1163 m, 1119 m, 1068 m, 1018 w, 971 w, 910 w, 849 w, 824 m, 792 w, 734 m, 688 w; MS *m*/*z* (relative intensity, %) 435 (M^+, 88), 292 (100), 171 (55), 144 (4); HRMS calcd for $C_{25}H_{20}F_3N_3O$ 435.1558, found 435.1560.

*N-(Quinolin-8-yl)-4,4′-bis(trifluoromethyl)-[1,1′-biphenyl]-2-carboxamide (**29b**):* R_f = 0.43 (hexane/EtOAc 5/1); white solid; ^{1}H NMR ($CDCl_3$, 400 MHz) 7.38 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.50−7.66 (m, 7H), 7.86 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.11 (dd, *J* = 8.4, 1.2 Hz, 1H), 8.24 (d, *J* = 0.8 Hz, 1H), 8.49 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.76 (dd, *J* = 7.2, 2.0 Hz, 1H), 9.79 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100. MHz) 116.7, 121.8, 122.4, 123.9 (q, *J* = 368.5 Hz), 125.1, 125.7, 125.8, 126.8, 127.3, 127.6, 127.9, 129.5, 130.6 (q, *J* = 31.7 Hz), 131.3, 134.0, 136.3,

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136.8, 138.4, 142.3, 142.4, 148.1, 165.8; HRMS calcd for $C_{27}H_{13}F_6N_2O$ 460.1010, found 460.1005.

*4′-Acetyl-N-(quinolin-8-yl)-4-(trifluoromethyl)-[1,1′-biphenyl]-2-carboxamide (**30b**):* R_f = 0.06 (hexane/EtOAc 5/1); yellow solid; mp 155−158 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.46 (s, 3H), 7.36 (dd, *J* = 8.4, 4.0 Hz, 1H), 7.50−7.56 (m, 2H), 7.62−7.64 (m, 3H), 7.85 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 2H), 8.10 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.20 (s, 1H), 8.51 (dd, *J* = 4.0, 2.0 hz, 1H), 8.76 (dd, *J* = 6.8, 2.0 Hz, 1H), 9.82 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) 26.7, 116.8, 121.1 (q, *J* = 272.2 Hz), 122.0 (d, *J* = 61.3 Hz), 126.6, 127.4, 127.5, 127.9, 128.8, 129.3, 130.8 (q, *J* = 33.6 Hz), 131.2, 134.0, 136.4, 136.8, 138.4, 142.6, 143.5, 148.0, 166.0, 197.7; IR (neat) 3322 w, 3052 w, 2251 w, 1679 s, 1605 w, 1577 w, 1525 s, 1485 m; MS *m*/*z* (relative intensity, %) 434 (M^+, 100), 171 (41), 144 (41); HRMS calcd for $C_{25}H_{17}F_3N_2O_2$: 434.1242, found 434.1244.

■ ASSOCIATED CONTENT

Supporting Information

Text, tables, and figures giving experimental procedures and characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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