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Cobalt-Catalyzed Annulation of Amides with Isocyanides via C(sp^2)−H Activation

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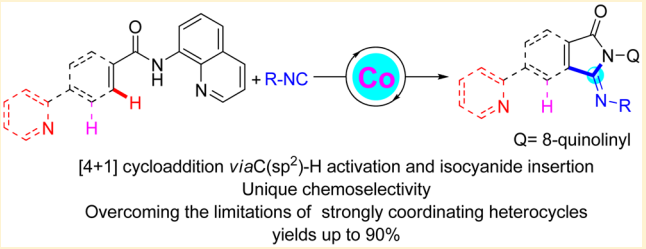
Supporting Information

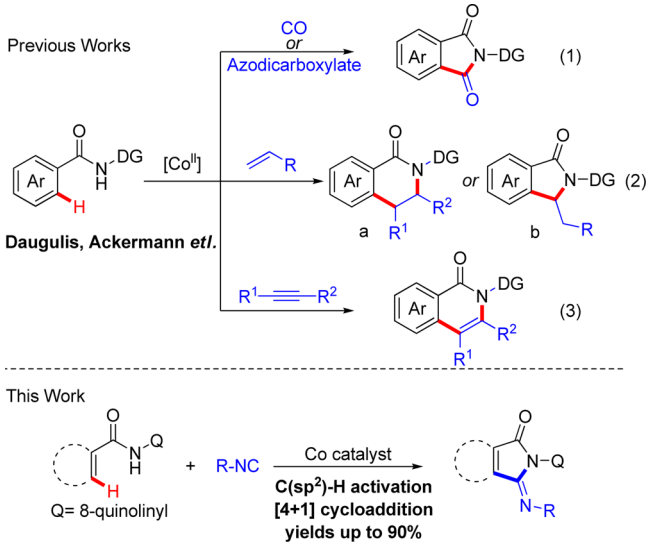
ABSTRACT: A cobalt-catalyzed [4 + 1] cycloaddition of easily accessible amides with isocyanides for the efficient synthesis of 3-iminoisoindolinone derivatives in high yield under mild conditions via intramolecular C(sp^2)−H activation and isocyanide insertion is reported. The annulation was found to be applicable to a broad range of substrates, including arylamides, heteroarylamides, and acrylamide derivatives. Strongly coordinating *N*-heterocyclic directing groups such as pyridine, pyrimidine, and even pyrazole were fully tolerated in this cobalt-catalyzed C−H activation reaction.



In recent years, tremendous breakthroughs have been achieved in transition-metal-catalyzed C−H activation or functionalization, and this method provides an attractive alternative to traditional cross-coupling reactions for selective C−C and C−X bond formations.[1] Thus, C−H activation or functionalization processes can significantly simplify the synthesis of natural products, pharmaceuticals, agrochemicals, polymers, and feedstock commodity chemicals.[2]

Within this reaction class, cobalt-catalyzed C−H bond activation has gathered increasing attention in terms of its low cost and low toxicity of cobalt complexes and their interesting modes of action.[3] Notable success has been achieved with the development of cobalt-catalyzed C−H activations by Daugulis,[4] Ackermann,[5] Yoshika,[6] and Matsunaga,[7] et al., with either in situ generated or single-component cobalt-complexes under mild reaction conditions (Scheme 1). Because Daugulis initially devised directing groups based on 8-aminoquinoline (Q) for the palladium-catalyzed functionalization of C−H bonds,[8] the directing group has been extensively exploited for palladium-, ruthenium-, iron-, nickel-, or copper-catalyzed C−H activations, among others.[9] On the basis of these findings, Daugulis' group and Zhang's group developed a method for directed cobalt-catalyzed carbonylation of benzamdies to access the isoindoline-1,3-dione derivatives using CO or azodicarboxylates as the carbonyl source, respectively (Scheme 1, eq 1).[4c,10] Subsequently, Daugulis and Ackermann developed the alkene annulation by benzamides with the Q-directing group under different catalytic conditions to furnish dihydroisoquinolinones and isoindolinones (Scheme 1, eq 2).[4b,11] Meanwhile, Daugulis and co-workers further found the cobalt-catalyzed oxidative alkyne annulation with the bidentate Q-auxiliary (Scheme 1, eq 3).[4a] The Sundararaju group also reported a cobalt catalyzed C−H bond annulation of sulfonamide with terminal and internal alkynes.[12] More recently, transition-metal-catalyzed C−H functionalization that fully overcomes the limitations of strongly coordinating heterocycles has been developed.[13] Isocyanides are considered an important source of C1 in organic synthesis due to their unique, versatile, and useful properties.[14] To the best of our knowledge, the cobalt-catalyzed annulation of arylamides with isocyanides via C(sp^2)−H activation has not been developed. As part of our research interests in isocyanide chemistry,[15] we herein report a cobalt-catalyzed annulation reactions of arylamides with isocyanides via C(sp^2)−H activation to afford 3-iminoisoindolinone

Scheme 1. Cobalt-Catalyzed C−H Activation/ Functionalization Reactions



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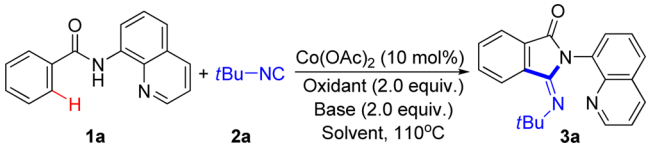
derivatives. Strongly coordinating *N*-heterocyclic directing groups such as pyridine, pyrimidine, and even pyrazole were fully tolerated in this cobalt-catalyzed C−H activation reaction.

Initially, we tried the reaction of *N*-(quinolin-8-yl)benzamide **1a** with isonitrile **2a** in 1,4-dioxane at 110 °C for 12 h in the presence of 10 mol % $Co(OAc)_2$ as catalyst and 2 equiv of KOAc and AgOAc as additions. However, the desired product 3-(*tert*-butylimino)-2-(quinolin-8-yl)isoindolin-1-one **3aa** was obtained only in 4% LC yield (Table 1, entry 1). Different

Table 1. Optimization of the Reaction Conditions[a]



	oxidant (2.0 equiv)	base (2.0 equiv)	solvent	yield (%[b])
1	AgOAc	KOAc	1,4-dioxane	4
2	AgOAc	KOAc	CH_3CN	2
3	AgOAc	KOAc	THF	2
4	AgOAc	KOAc	DME	3
5	AgOAc	KOAc	DMF	
6	AgOAc	KOAc	DMSO	
7	AgOAc	KOAc	PhCl	
8	AgOAc	KOAc	1,4-dioxane	4
9	$K_2S_2O_8$	KOAc	1,4-dioxane	4
10	$Na_2S_2O_8$	KOAc	1,4-dioxane	2
11	TBPB	KOAc	1,4-dioxane	39
12	DTBP	KOAc	1,4-dioxane	5
13	CHP	KOAc	1,4-dioxane	12
14	BPO	KOAc	1,4-dioxane	7
15	$K_2S_2O_8$	KOAc	1,4-dioxane	4
16	$K_2S_2O_8$	Na_2CO_3	1,4-dioxane	7
17	$K_2S_2O_8$	NaOAc	1,4-dioxane	4
18	$K_2S_2O_8$	K_2CO_3	1,4-dioxane	10
19	TBPB	Na_2CO_3	1,4-dioxane	70[c]
20	TBPB	Na_2CO_3 (3.0)	1,4-dioxane	79 (70)[c,d]

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), $Co(OAc)_2$ (10 mol %), oxidant (2.0 equiv), base (2.0 equiv), and solvent (3 mL) at 110 °C for 12 h under air atmosphere. [b]The yields were determined by LC analysis using diphenyl as the internal standard. [c]The reaction was catalyzed by 20 mol % Co(OAc)2 under Ar atmosphere and anhydrous conditions. [d]Isolated yield.

solvents such as CH_3CN, THF, DME, DMF, DMSO, and PhCl did not increase the yield of the desired product **3aa** (Table 1, entries 1−7). It was found that inorganic oxidants such as $K_2S_2O_8$ and $Na_2S_2O_8$ could not improve the yields significantly. A number of organic oxidants were examined as well, and most of them failed to give a satisfactory result (Table 1, entries 12−14). Gratifyingly, the employment of *tert*-butyl perbenzoate (TBPB) could effectively promote the reaction to give the desired product **3aa** in 39% LC yield (Table 1, entry 11). The yield of **3aa** could be further improved to 79% by increasing the catalyst loading to 20 mol % in the presence of Na_2CO_3 (3.0 equiv).

Under the optimized reaction conditions, various substituted arylamides **1** and isocyanides **2** were explored for this C−H activation reaction, and the results are summarized in Scheme 2. First, the scope of isocyanides was investigated under the optimal conditions. It was found that 2-isocyano-1,3-dimethylbenzene **2b**, 2-isocyano-1,3,5-trimethylbenzene **2c**, and 1,3-diethyl-2-isocyanobenzene **2d** could furnish the desired products **3ab**, **3ac**, and **3ad** in 77, 73, and 86% yields, respectively. When 1-adamantyl isocyanide was subjected to the reaction with **1a**, product **3ae** could be isolated in 35% yield.

Unfortunately, some other isocyanides such as 1-isocyanobutane and isocyanocyclohexane decomposed under the current conditions, and only a trace amount of product could be detected. Then, we explored the reactions of arylamides **1** with **2a**. Substrates bearing electron-donating groups such as -Me, -OMe, and -Et at the *para* position participated in the reaction smoothly to give the desired products **3bb**, **3cb**, and **3db** in good yields (76−90%). When the 4-aryl benzamide **1e** was examined, no desired product **3eb** was detected. The halogen groups (-F, -Cl, -Br, and -I) at the *para* position were also tolerated, and the corresponding C−H activation products (**3fb**−**3ib**) were obtained in 76−80% yields. Arylamides with *ortho* substitution also worked well to give **3jb**−**3lb** in 70−77% yields. Iodo group showed somewhat lower efficiency, and the desired product **3mb** was obtained in 62% yield. It was noteworthy that the reaction of a *meta*-substituted substrate (-Me) could produce two products (**3nb** and **3nb′**), and the two regioisomers could be easy separated from each other by silica gel column chromatography.

Besides arylamides, acrylamides were also found to be appropriate substrates for this reaction (Scheme 3). To our delight, the more sterically hindered naphthalene compounds were also applicable substrates (**3pb** and **3qb**/**3qb′**). The acrylamides with 2-methyl, 3-phenyl, and 2-phenyl substituents, which could be useful for further derivatization,[16] were found to be suitable for this reaction to afford acceptable yields (**3rb**, **3sb** ,and **3tb**, respectively). The reaction of *n*-(quinolin-8-yl)-cyclohex-1-enecarboxamide **1u** with **2b** proceeded smoothly, and the corresponding product **3ub** could be isolated in 74% yield.

Encouraged by the good tolerance of functional groups, we tried the substrates which contain strongly coordinating *N*-heterocyclic directing groups such as pyridine, pyrimidine, and pyrazole (Scheme 4). Surprisingly, the cobalt catalyst could efficiently promote the C−H activation in a stereoselective manner to furnish (*E*)-3-(2,6-dimethylphenylimino)-2-(quinolin-8-yl)isoindolin-1-ones as the sole products. To explore the synthetic utility of this methodology, we examined the reaction of **3aa** catalyzed by H_2SO_4 using MeCN and H_2O (MeCN:H_2O = 2:1) as mixed solvents. It was found that the 2-(quinolin-8-yl)isoindoline-1,3-dione **4** could be easily obtained in 60% yield (Scheme 5).

In summary, we developed a cobalt-catalyzed annulation of easily prepared arylamides with isonitriles for the efficient synthesis of 3-iminoisoindolinone derivatives via intramolecular C(sp^2)−H activation. The annulation was found to be applicable to a broad range of substrates, including arylamidess, heteroarylamidess, and acrylamide derivatives. Strongly coordinating *N*-heterocyclic directing groups such as pyridine, pyrimidine, and pyrazole were fully tolerated in this cobalt-catalyzed C−H activation reactions. This cobalt catalyst system is readily applicable for practical applications in terms of its low cost, low toxicity, and availability to furnish the annulation product in high yield under mild conditions.

EXPERIMENTAL SECTION

General Experimental Information. All the solvents for routine isolation of products and chromatography were reagent grade. Flash chromatography was performed using silica gel (300−400 mesh) with

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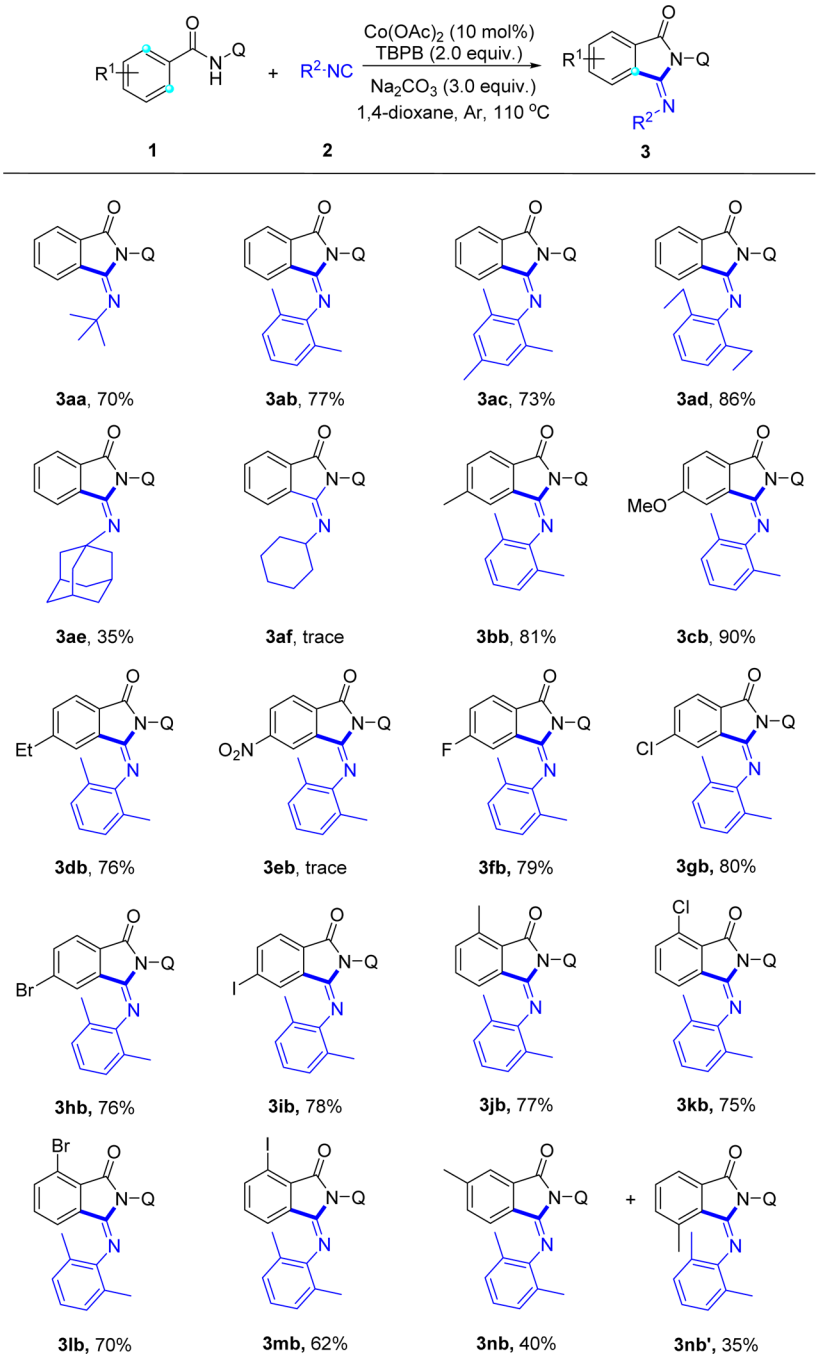
Scheme 2. Cobalt(II)-Catalyzed Annulation of Arylamides 1 and Isocyanide 2[a]



[a]Reaction conditions: **1** (0.5 mmol), **2** (0.6 mmol), $Co(OAc)_2$ (20 mol %), TBPB (2.0 equiv), $NaCO_3$ (2.0 equiv), and 1,4-dioxane (3 mL) at 110 °C for 12 h under Ar atmosphere and anhydrous conditions. [b]Isolated yield.

the indicated solvents. Melting points were recorded on an electrothermal digital melting point apparatus and were uncorrected. IR spectra were recorded on a spectrophotometer using KBr optics. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR) spectrometer using $CDCl_3$ or DMSO-*d6* as solvent and TMS as internal standard. The ^{1}H NMR data are reported as the chemical shift in parts per million, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant in hertz, and number of protons. High resolution mass spectra were obtained using a high resolution ESI-TOF mass spectrometer.

General Procedure for the Construction of 3. A mixture of acrylamides **1** (0.5 mmol), isonitriles **2** (0.6 mmol), $Co(OAc)_2$ (20 mol %), TBHP (2.0 equiv), Na_2CO_3 (2.0 equiv), and 1,4-dioxane (3 mL) were added into a flask and stirred at 110 °C under Ar atmosphere and anhydrous conditions. Then, the mixture was vigorously stirred under reflux conditions monitored by TLC analysis (about 12 h). After the solvents were removed in vacuo, the residue was directly purified by flash column chromatography using ethyl acetate and petroleum ether as eluents to afford pure product **3**.

General Procedure for the Construction of 4. A mixture of **3aa** (0.5 mmol), H_2SO_4 (0.6 mmol), and MeCN:H_2O (2:1, 3 mL) was added into a flask and stirred at 50 °C. Then, the mixture was vigorously stirred under reflux conditions monitored by TLC analysis (about 6 h). After removing the solvents in vacuo, the residue was

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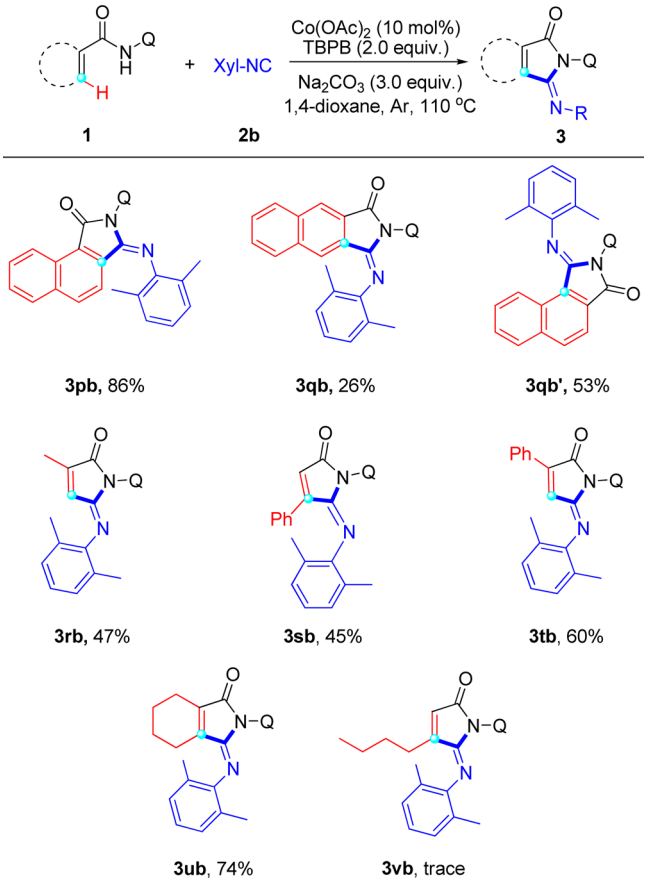
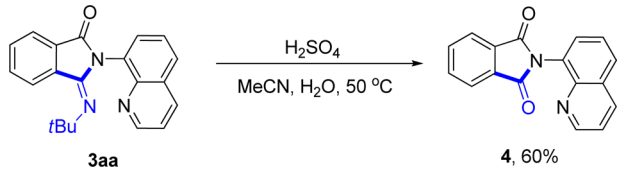
Scheme 3. Reactions of Amides 1 and Isocyanide 2b[a,b]



[a]Reaction conditions: **1** (0.5 mmol), **2a** (0.6 mmol), $Co(OAc)_2$ (20 mol %), TBPB (2.0 equiv), $NaCO_3$ (2.0 equiv), and 1,4-dioxane (3 mL) at 110 °C for 12 h under Ar atmosphere and anhydrous conditions. [b]Isolated yield.

Scheme 5. Transformation of Product 3aa



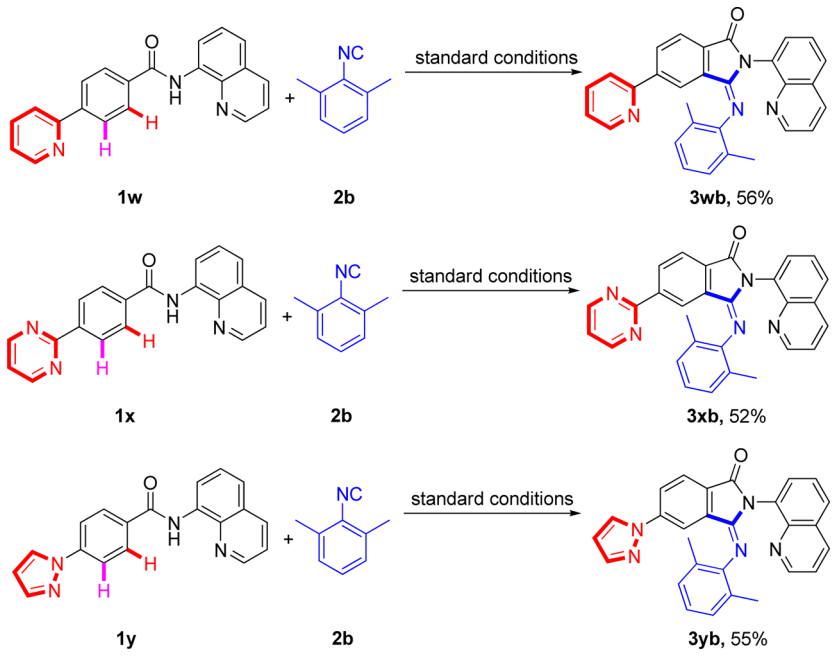
directly purified by flash column chromatography using ethyl acetate and petroleum ether as eluents to afford pure product **4**.

(E)-3-(tert-Butylimino)-2-(quinolin-8-yl)isoindolin-1-one (***3aa***).[17] Yellow solid (115 mg, 70%), mp 149.6–152.0 °C. IR 2967, 2161, 2914, 1976, 1724, 1657, 1397, 1360, 1127, 825, 702 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.82 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.18–8.07 (m, 2H), 8.06–8.00 (m, 1H), 7.84 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.73–7.58 (m, 4H), 7.33 (dd, *J* = 8.3, 4.1 Hz, 1H), 1.34 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 149.7, 147.1, 144.4, 135.6, 133.7, 132.7, 131.8, 130.7, 130.6, 128.5, 127.9, 126.7, 125.4, 123.4, 120.7, 53.3, 30.1 ppm. HRMS (ESI) *m*/*z* calcd for $C_{21}H_{19}N_3O$, $[M + H]^+$ 330.1606; found 330.1607.

(E)-3-(2,6-Dimethylphenylimino)-2-(quinolin-8-yl)isoindolin-1-one (***3ab***).[17] Yellow solid (145 mg, 77%), mp 158.0–160.2 °C. IR 1736, 1672, 1473, 1397, 1183, 1124, 920, 884, 818, 698 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.88 (d, *J* = 4.2 Hz, 1H), 8.22 (d, *J* = 8.3 Hz, 1H), 8.02–7.87 (m, 3H), 7.71 (t, *J* = 7.8 Hz, 1H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 7.1 Hz, 2H), 7.11–6.92 (m, 3H), 6.66 (d, *J* = 7.7 Hz, 1H), 2.07 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 151.9, 150.2, 145.7, 133.1, 131.9, 131.8, 130.5, 130.2, 129.0, 129.0, 127.8, 127.5, 126.6, 126.1, 125.9, 123.9, 123.4, 123.1, 121.3, 17.7, 17.6 ppm. HRMS (ESI) *m*/*z* calcd for $C_{25}H_{19}N_3O$, $[M + H]^+$ 378.1606; found 378.1601.

(E)-3-(Mesitylimino)-2-(quinolin-8-yl)isoindolin-1-one (***3ac***). Yellow solid (143 mg, 73%), mp 218.9–220.1 °C. IR 1731, 1668, 2916, 1475, 1400, 1188, 1116, 883, 825, 795, 703 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.87 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.22 (d, *J* = 8.2 Hz, 1H), 7.98 (dd, *J* = 17.9, 7.9 Hz, 2H), 7.88 (d, *J* = 7.2 Hz, 1H), 7.71 (t, *J* = 7.8 Hz, 1H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.47–7.37 (m, 2H), 6.85 (d, *J* = 6.4 Hz, 2H), 6.71 (d, *J* = 7.7 Hz, 1H), 2.29 (s, 3H), 2.02 (s, 3H), 1.95 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 152.1, 150.2, 143.1, 135.8, 133.1, 132.3, 131.9, 131.6, 131.5, 130.5, 130.2, 129.0,

Scheme 4. Chemoselective C–H Bond Activation



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129.0, 128.4, 128.2, 126.3, 125.9, 125.8, 124.0, 123.3, 121.3, 20.4, 17.6, 17.5 ppm. HRMS (ESI) m/z calcd for $C_{26}H_{22}N_3O$, $[M + H]^+$ 392.1763; found 392.1762.

*(E)-3-(2,6-Diethylphenylimino)-2-(quinolin-8-yl)isoindolin-1-one (**3ad**).* Yellow solid (174 mg, 86%), mp 250.5−251.0 °C. IR 1741, 1676, 1501, 1456, 1401, 1181, 1125, 1097, 922, 784, 699 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.88 (dd, J = 4.3, 1.7 Hz, 1H), 8.22 (dd, J = 8.4, 1.7 Hz, 1H), 7.98 (dd, J = 17.6, 7.9 Hz, 2H), 7.92−7.84 (m, 1H), 7.71 (t, J = 7.8 Hz, 1H), 7.61 (t, J = 7.5 Hz, 1H), 7.47−7.34 (m, 2H), 7.07 (d, J = 5.1 Hz, 3H), 6.63 (d, J = 7.7 Hz, 1H), 2.53−2.24 (m, 4H), 1.07 (t, J = 7.5 Hz, 3H), 0.83 (t, J = 7.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 151.8, 150.2, 144.8, 144.3, 135.8, 132.8, 132.4, 132.0, 131.7, 131.7, 130.5, 130.1, 129.0, 128.9, 125.9, 125.9, 125.6, 124.3, 123.4, 123.3, 121.3, 24.4, 24.0, 13.4, 13.2 ppm. HRMS (ESI) m/z calcd for $C_{27}H_{23}N_3O$, $[M + H]^+$ 406.1919; found 406.1917.

*(E)-3-(Adamantylimino)-2-(quinolin-8-yl)isoindolin-1-one (**3ae**).*[17] White solid (71 mg, 35%), mp 186.2−187.5 °C. IR 2903, 2849, 2160, 1726, 1654, 1524, 1500, 1396, 1235, 885, 790, 698 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.83 (dd, J = 4.2, 1.7 Hz, 1H), 8.21−8.13 (m, 2H), 8.02 (dd, J = 7.4, 1.2 Hz, 1H), 7.85 (dd, J = 8.1, 1.5 Hz, 1H), 7.73−7.59 (m, 4H), 7.36 (dd, J = 8.3, 4.2 Hz, 1H), 2.09−2.04 (m, 3H), 1.94−1.85 (m, 6H), 1.66 (t, J = 3.2 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 149.7, 146.3, 144.5, 135.5, 133.8, 132.8, 131.7, 130.7, 130.5, 129.9, 128.5, 127.8, 127.1, 125.3, 123.3, 120.7, 54.0, 42.0, 35.9, 35.9, 29.2 ppm. HRMS (ESI) m/z calcd for $C_{27}H_{25}N_3O$, $[M + H]^+$ 408.2076; found 408.2065.

*(E)-3-(2,6-Dimethylphenylimino)-5-methyl-2-(quinolin-8-yl)-isoindolin-1-one (**3bb**).* Yellow solid (159 mg, 81%), mp 185.5−187.0 °C. IR 1738, 1664, 1399, 1142, 1120, 810, 786, 717, 617 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.87 (d, J = 4.3 Hz, 1H), 8.21 (d, J = 8.2 Hz, 1H), 7.91 (dd, J = 27.5, 7.9 Hz, 3H), 7.71 (t, J = 7.8 Hz, 1H), 7.42 (d, J = 7.8 Hz, 2H), 7.09−6.89 (m, 3H), 6.40 (s, 1H), 2.25 (s, 3H), 2.07 (s, 3H), 1.99 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 152.1, 150.2, 145.8, 143.9, 135.7, 132.5, 131.7, 130.5, 129.4, 128.9, 127.7, 127.4, 126.6, 126.1, 125.8, 124.4, 123.2, 123.0, 121.2, 21.7, 17.7, 17.6 ppm. HRMS (ESI) m/z calcd for $C_{26}H_{21}N_3O$, $[M + H]^+$ 392.1763; found 392.1772.

*(E)-3-(2,6-Dimethylphenylimino)-5-methoxy-2-(quinolin-8-yl)-isoindolin-1-one (**3cb**).*[17] Yellow solid (183 mg, 90%), mp 212.3−215.2 °C. IR 1739, 1670, 1398, 1140, 1121, 812, 789, 713, 618 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.88 (d, J = 4.2 Hz, 1H), 8.21 (d, J = 8.2 Hz, 1H), 7.92 (dd, J = 20.6, 8.5 Hz, 3H), 7.70 (t, J = 7.8 Hz, 1H), 7.42 (dd, J = 8.5, 4.3 Hz, 1H), 7.13−6.90 (m, 4H), 6.10 (s, 1H), 3.55 (s, 3H), 2.08 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 152.1, 150.2, 145.8, 143.9, 135.7, 132.5, 131.7, 130.5, 129.4, 128.9, 127.7, 127.4, 126.6, 126.1, 125.8, 124.4, 123.2, 123.0, 121.2, 21.7, 17.7, 17.6 ppm. HRMS (ESI) m/z calcd for $C_{26}H_{21}N_3O_2$, $[M + H]^+$ 408.1712; found 408.1709.

*(E)-3-(2,6-Dimethylphenylimino)-5-ethyl-2-(quinolin-8-yl)-isoindolin-1-one (**3db**).* Yellow solid (154 mg, 76%), mp 217.3−218.9 °C. IR 1734, 1671, 1501, 1474, 1400, 1125, 1083, 806, 782, 714 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.93−8.83 (m, 1H), 8.22 (d, J = 8.2 Hz, 1H), 7.99−7.86 (m, 3H), 7.71 (t, J = 7.8 Hz, 1H), 7.49−7.39 (m, 2H), 7.09−6.91 (m, 3H), 6.43 (s, 1H), 2.53 (q, J = 7.6 Hz, 2H), 2.07 (s, 3H), 2.00 (s, 3H), 1.05 (t, J = 7.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 152.2, 150.1, 145.8, 135.9, 131.6, 131.5, 130.6, 130.6, 129.5, 128.9, 127.6, 127.4, 126.7, 126.2, 125.9, 123.2, 123.0, 121.2, 28.6, 17.6, 17.6, 14.4 ppm. HRMS (ESI) m/z calcd for $C_{27}H_{23}N_3O$, $[M + H]^+$ 406.1919; found 406.1914.

*(E)-3-(2,6-Dimethylphenylimino)-5-fluoro-2-(quinolin-8-yl)-isoindolin-1-one (**3fb**).* Yellow solid (156 mg, 79%), mp 182.4−184.1 °C. IR 2918, 2850, 2160, 1738, 1663, 1473, 1399, 1262, 1142, 1116, 888, 785, 718 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.88 (d, J = 4.2 Hz, 1H), 8.22 (d, J = 8.3 Hz, 1H), 8.05−7.84 (m, 3H), 7.71 (t, J = 7.8 Hz, 1H), 7.43 (dd, J = 8.3, 4.2 Hz, 1H), 7.31 (dt, J = 8.6, 4.3 Hz, 1H), 7.16−6.91 (m, 3H), 6.44−6.10 (m, 1H), 2.07 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 166.5, 164.0, 150.8, 150.3, 145.1, 144.2, 135.9, 132.1, 132.0, 131.3, 130.5, 129.2, 129.0, 127.9, 127.9, 127.6, 126.4, 125.9, 125.9, 125.6, 125.5, 123.5, 121.4, 119.2, 118.9, 111.7, 111.4, 17.6, 17.6 ppm. HRMS (ESI) m/z calcd for $C_{25}H_{18}FN_3O$, $[M + H]^+$ 396.1512; found 396.1519.

*(E)-5-Chloro-3-(2,6-dimethylphenylimino)-2-(quinolin-8-yl)-isoindolin-1-one (**3gb**).*[17] Yellow solid (164 mg, 80%), mp 166.6−168.1 °C. IR 2919, 2853, 1732, 1672, 1501, 1474, 1399, 1128, 1085, 779, 721 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.92−8.83 (m, 1H), 8.23 (d, J = 8.3 Hz, 1H), 8.00−7.85 (m, 3H), 7.72 (t, J = 7.8 Hz, 1H), 7.63−7.57 (m, 1H), 7.47−7.41 (m, 1H), 7.11−6.92 (m, 3H), 6.54 (s, 1H), 2.06 (s, 3H), 1.98 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 150.8, 150.2, 145.2, 139.3, 135.9, 132.0, 131.4, 131.2, 130.5, 130.1, 129.2, 128.9, 127.9, 127.6, 126.4, 125.9, 124.6, 124.2, 123.5, 121.4, 17.6, 17.6 ppm. HRMS (ESI) m/z calcd for $C_{25}H_{18}ClN_3O$, $[M + H]^+$ 412.1217; found 412.1225.

*(E)-5-Bromo-3-(2,6-dimethylphenylimino)-2-(quinolin-8-yl)-isoindolin-1-one (**3hb**).*[17] Yellow solid (173 mg, 76%), mp 189.0−190.5 °C. IR 2917, 2854, 1738, 1668, 1502, 1401, 1174, 1086, 930, 786, 713 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.95−8.82 (m, 1H), 8.23 (d, J = 8.3 Hz, 1H), 7.98 (dt, J = 10.9, 5.6 Hz, 2H), 7.88 (d, J = 7.3 Hz, 1H), 7.72 (t, J = 7.8 Hz, 1H), 7.44 (dd, J = 8.3, 4.2 Hz, 1H), 7.31 (td, J = 8.6, 2.3 Hz, 1H), 7.01 (dt, J = 26.8, 7.3 Hz, 3H), 6.28 (dd, J = 8.5, 2.3 Hz, 1H), 2.06 (s, 3H), 1.99 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 150.8, 150.3, 145.2, 144.2, 135.8, 134.9, 131.5, 131.2, 130.6, 130.4, 129.2, 128.9, 127.9, 127.6, 127.1, 126.4, 125.8, 124.7, 123.5, 121.4, 17.7, 17.6 ppm. HRMS (ESI) m/z calcd for $C_{25}H_{18}BrN_3O$, $[M + H]^+$ 456.0711; found 456.0714.

*(E)-3-(2,6-Dimethylphenylimino)-5-iodo-2-(quinolin-8-yl)-isoindolin-1-one (**3ib**).* Yellow solid (196 mg, 78%), mp 218.2−220.2 °C. IR 2917, 2851, 1740, 1668, 1593, 1501, 1402, 1174, 1125, 784, 712 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 9.00−8.84 (m, 1H), 8.32 (d, J = 8.2 Hz, 1H), 8.06−7.86 (m, 3H), 7.72 (t, J = 7.8 Hz, 2H), 7.49 (dd, J = 8.0, 4.0 Hz, 1H), 7.16−6.95 (m, 3H), 6.90 (s, 1H), 2.03 (d, J = 19.9 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 150.7, 149.6, 145.1, 140.9, 135.2, 133.1, 131.4, 131.1, 129.2, 129.0, 127.9, 127.7, 127.6, 126.5, 126.3, 125.8, 124.7, 123.6, 121.4, 100.1, 18.0, 17.7 ppm. HRMS (ESI) m/z calcd for $C_{25}H_{18}IN_3O$, $[M + H]^+$ 504.0573; found 504.0558.

*(E)-3-(2,6-Dimethylphenylimino)-7-methyl-2-(quinolin-8-yl)-isoindolin-1-one (**3jb**).*[17] Gray solid (151 mg, 77%), mp 236.1−237.1 °C. IR 2918, 2853, 1732, 1673, 1500, 1398, 1225, 1172, 1085, 936, 777, 717 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.96−8.84 (m, 1H), 8.22 (d, J = 8.2 Hz, 1H), 7.95 (d, J = 8.2 Hz, 1H), 7.88 (d, J = 7.3 Hz, 1H), 7.71 (t, J = 7.8 Hz, 1H), 7.42 (dd, J = 8.4, 4.2 Hz, 1H), 7.36 (d, J = 7.7 Hz, 1H), 7.29−7.23 (m, 1H), 7.02 (d, J = 6.6 Hz, 2H), 6.96 (d, J = 7.4 Hz, 1H), 6.52 (d, J = 7.6 Hz, 1H), 2.77 (s, 3H), 2.04 (d, J = 22.3 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 151.7, 150.2, 145.9, 144.4, 137.9, 135.8, 134.1, 132.6, 131.6, 130.7, 130.6, 129.0, 128.9, 128.6, 127.7, 127.4, 126.5, 126.1, 125.9, 122.9, 121.5, 121.2, 17.6, 17.6, 17.3 ppm. HRMS (ESI) m/z calcd for $C_{26}H_{21}N_3O$, $[M + H]^+$ 392.1763; found 392.1773.

*(E)-7-Chloro-3-(2,6-dimethylphenylimino)-2-(quinolin-8-yl)-isoindolin-1-one (**3kb**).* Yellow solid (154 mg, 75%), mp 257.4−259.6 °C. IR 2917, 2854, 1736, 1671, 1593, 1501, 1399, 1256, 1123, 1086, 922, 779 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.88 (d, J = 4.2 Hz, 1H), 8.23 (d, J = 8.2 Hz, 1H), 7.96 (d, J = 8.3 Hz, 1H), 7.88 (d, J = 7.3 Hz, 1H), 7.71 (t, J = 7.8 Hz, 1H), 7.54 (d, J = 8.1 Hz, 1H), 7.47−7.41 (m, 1H), 7.31 (t, J = 7.9 Hz, 1H), 6.99 (dt, J = 30.4, 7.1 Hz, 3H), 6.58 (d, J = 7.7 Hz, 1H), 2.02 (d, J = 18.8 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0, 150.2, 150.1, 145.4, 136.1, 133.9, 133.6, 132.1, 131.4, 131.0, 130.6, 129.2, 128.9, 127.8, 127.6, 126.4, 125.9, 123.2, 122.3, 121.3, 17.6, 17.6 ppm. HRMS (ESI) m/z calcd for $C_{25}H_{18}ClN_3O$, $[M + H]^+$ 412.1217; found 412.1224.

*(E)-7-Bromo-3-(2,6-dimethylphenylimino)-2-(quinolin-8-yl)-isoindolin-1-one (**3lb**).* Yellow solid (159 mg, 70%), mp 272.1−273.1 °C. IR 2917, 2851, 1741, 1667, 1501, 1398, 1254, 1136, 1085, 919, 835, 777, 708 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.76 (d, J = 4.1 Hz, 1H), 8.10 (d, J = 8.3 Hz, 1H), 7.81 (dd, J = 30.2, 7.8 Hz, 2H), 7.62 (dd, J = 12.3, 7.9 Hz, 2H), 7.31 (dd, J = 8.3, 4.2 Hz, 1H), 7.17−7.08 (m, 1H), 6.88 (dt, J = 31.0, 7.1 Hz, 3H), 6.53 (d, J = 7.7 Hz, 1H), 1.91 (d, J = 18.5 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.3, 150.3, 150.0, 145.5, 144.2, 136.8, 135.8, 133.9, 132.2, 131.2, 130.4,

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129.2, 129.2, 128.9, 127.8, 127.6, 126.4, 125.9, 125.8, 123.2, 122.9, 121.3, 118.7, 17.6, 17.6 ppm. HRMS (ESI) m/z calcd for $C_{25}H_{18}BrN_3O$, $[M + H]^+$ 456.0711; found 456.0708.

*(E)-3-(2,6-Dimethylphenylimino)-7-iodo-2-(quinolin-8-yl)-isoindolin-1-one (**3mb**).* Yellow solid (156 mg, 62%), mp 169.1−171.2 °C. IR 2918, 2850, 1734, 1671, 1469, 1398, 1183, 1123, 921, 772, 699 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.93−8.84 (m, 1H), 8.27−8.18 (m, 1H), 7.98 (dd, J = 18.2, 7.9 Hz, 2H), 7.89 (d, J = 7.2 Hz, 1H), 7.71 (t, J = 7.8 Hz, 1H), 7.62 (t, J = 7.5 Hz, 1H), 7.46−7.37 (m, 2H), 7.04 (t, J = 7.1 Hz, 2H), 6.96 (t, J = 7.4 Hz, 1H), 6.66 (d, J = 7.7 Hz, 1H), 2.07 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 151.9, 150.2, 145.7, 144.3, 135.9, 133.1, 131.9, 131.8, 131.5, 130.5, 130.2, 129.0, 129.0, 127.8, 127.5, 126.6, 126.1, 125.9, 123.9, 123.4, 123.1, 121.3, 17.7, 17.6 ppm. HRMS (ESI) m/z calcd for $C_{25}H_{18}IN_3O$, $[M + H]^+$ 504.0573; found 504.0579.

*(E)-3-(2,6-Dimethylphenylimino)-6-methyl-2-(quinolin-8-yl)-isoindolin-1-one (**3nb**).*[17] Yellow solid (78 mg, 40%), mp 171.5−173.1 °C. IR 2919, 2852, 1733, 1664, 1591, 1472, 1358, 1247, 1077, 894, 775, 727 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.78 (dd, J = 4.3, 1.7 Hz, 1H), 8.03 (dd, J = 8.3, 1.7 Hz, 1H), 7.85 (dd, J = 6.1, 2.4 Hz, 1H), 7.61−7.52 (m, 3H), 7.43 (dd, J = 7.3, 1.4 Hz, 1H), 7.35 (dd, J = 8.3, 4.3 Hz, 1H), 7.20 (t, J = 7.8 Hz, 1H), 6.57 (d, J = 7.5 Hz, 1H), 6.32 (t, J = 7.5 Hz, 1H), 6.13 (d, J = 7.5 Hz, 1H), 2.86 (s, 3H), 2.11 (s, 3H), 1.51 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 149.5, 146.6, 144.6, 137.1, 135.8, 135.0, 132.4, 131.3, 130.9, 130.8, 129.8, 128.3, 128.2, 128.0, 127.8, 126.7, 126.3, 126.1, 126.0, 125.3, 124.4, 121.8, 121.0, 120.9, 19.3, 18.3, 17.6 ppm. HRMS (ESI) m/z calcd for $C_{26}H_{21}N_3O$, $[M + H]^+$ 392.1763; found 392.1769.

*(E)-3-(2,6-Dimethylphenylimino)-4-methyl-2-(quinolin-8-yl)-isoindolin-1-one (**3nb′**).*[17] Yellow solid (68 mg, 35%), mp 196.8−198.3 °C. IR 2917, 2852, 1733, 1670, 1474, 1395, 1187, 1132, 893, 787, 767 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.87 (dd, J = 4.2, 1.7 Hz, 1H), 8.23 (d, J = 8.3 Hz, 1H), 7.96 (d, J = 8.3 Hz, 1H), 7.88 (d, J = 7.3 Hz, 1H), 7.81 (s, 1H), 7.71 (t, J = 7.8 Hz, 1H), 7.43 (dd, J = 8.4, 4.2 Hz, 1H), 7.20 (d, J = 7.9 Hz, 1H), 7.08−6.90 (m, 3H), 6.51 (d, J = 7.8 Hz, 1H), 2.46 (s, 3H), 2.01 (d, J = 32.4 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.7, 152.1, 150.1, 145.8, 142.7, 135.8, 133.8, 132.1, 131.6, 130.5, 128.9, 127.7, 127.4, 126.7, 126.2, 125.9, 123.8, 122.9, 121.3, 21.3, 17.6, 17.6 ppm. HRMS (ESI) m/z calcd for $C_{26}H_{21}N_3O$, $[M + H]^+$ 392.1763; found 392.1771.

*(E)-3-(2,6-Dimethylphenylimino)-2-(quinolin-8-yl)-2,3-dihydro-1H-benzo[e]isoindol-1-one (**3pb**).* Yellow solid (184 mg, 86%), mp 203.2−205.9 °C. IR 2916, 2850, 1731, 1670, 1500, 1398, 1285, 1126, 1085, 830, 800, 748 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 9.10 (d, J = 8.4 Hz, 1H), 8.79 (d, J = 4.0 Hz, 1H), 8.17 (d, J = 8.2 Hz, 1H), 7.88 (dd, J = 13.1, 7.8 Hz, 2H), 7.77 (t, J = 8.6 Hz, 2H), 7.63 (dt, J = 18.0, 7.7 Hz, 2H), 7.53 (t, J = 7.6 Hz, 1H), 7.36 (dd, J = 8.2, 3.9 Hz, 1H), 7.02−6.85 (m, 3H), 6.61 (d, J = 8.5 Hz, 1H), 1.96 (d, J = 27.7 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.6, 152.1, 150.1, 145.7, 136.1, 134.9, 133.9, 131.5, 130.9, 129.8, 129.4, 129.0, 128.5, 128.2, 127.8, 127.7, 127.7, 127.4, 126.9, 126.7, 126.2, 126.0, 124.9, 123.1, 121.3, 119.4, 17.7, 17.7 ppm. HRMS (ESI) m/z calcd for $C_{29}H_{21}N_3O$, $[M + H]^+$ 428.1763; found 428.1770.

*(E)-3-(2,6-Dimethylphenylimino)-2-(quinolin-8-yl)-2,3-dihydro-1H-benzo[f]isoindol-1-one (**3qb**).*[17] Yellow solid (56 mg, 26%), mp 210.6−212.1 °C. IR 2923, 2853, 1735, 1656, 1356, 1084, 834, 792, 762 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 9.68−9.57 (m, 1H), 8.76 (dd, J = 4.2, 1.7 Hz, 1H), 8.19 (d, J = 8.3 Hz, 1H), 8.04 (dq, J = 6.8, 2.2, 1.7 Hz, 3H), 7.75−7.66 (m, 2H), 7.57 (dd, J = 8.3, 1.4 Hz, 1H), 7.49 (dd, J = 7.3, 1.4 Hz, 1H), 7.34 (dd, J = 8.3, 4.2 Hz, 1H), 7.21 (dd, J = 8.3, 7.3 Hz, 1H), 6.65 (d, J = 7.4 Hz, 1H), 6.41 (t, J = 7.5 Hz, 1H), 6.20 (d, J = 7.4 Hz, 1H), 2.21 (s, 3H), 1.54 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 150.1, 147.9, 144.6, 144.0, 136.3, 135.3, 132.6, 131.8, 131.4, 129.7, 129.5, 128.4, 128.4, 128.2, 128.2, 128.0, 127.7, 126.6, 126.3, 126.1, 125.1, 124.7, 122.1, 121.0, 118.7, 18.4, 17.5 ppm. HRMS (ESI) m/z calcd for $C_{29}H_{21}N_3O$, $[M + H]^+$ 428.1763; found 428.1770.

*(E)-1-(2,6-Dimethylphenylimino)-2-(quinolin-8-yl)-1H-benzo[e]-isoindol-3(2H)-one (**3qb′**).*[17] Yellow solid (113 mg, 53%), mp 97.9−98.5 °C. IR 2919, 2851, 1736, 1665, 1474, 1397, 1165, 896, 784, 754 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.88 (d, J = 4.0 Hz, 1H), 8.51 (s, 1H), 8.24 (d, J = 8.0 Hz, 1H), 8.07−7.91 (m, 3H), 7.74 (t, J = 7.7 Hz, 1H), 7.59 (dq, J = 24.9, 7.6 Hz, 3H), 7.44 (dd, J = 8.3, 4.0 Hz, 1H), 7.20−6.93 (m, 4H), 2.10 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 151.8, 150.3, 146.0, 144.2, 135.8, 135.0, 134.0, 131.7, 130.4, 129.6, 129.3, 129.1, 129.0, 128.3, 128.0, 127.9, 127.9, 127.6, 126.8, 126.3, 126.0, 125.9, 125.1, 124.3, 123.1, 121.3, 17.6, 17.6 ppm. HRMS (ESI) m/z calcd for $C_{29}H_{21}N_3O$, $[M + H]^+$ 428.1763; found 428.1767.

*(E)-5-(2,6-Dimethylphenylimino)-3-methyl-1-(quinolin-8-yl)-1H-pyrrol-2(5H)-one (**3rb**).* Yellow solid (102 mg, 60%), mp 144.3−146.7 °C. IR 2920, 2852, 1736, 1661, 1591, 1475, 1404, 1238, 1132, 1084, 894, 760 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.92 (d, J = 4.2 Hz, 1H), 8.23 (d, J = 8.2 Hz, 1H), 7.94 (d, J = 8.2 Hz, 1H), 7.82 (d, J = 7.2 Hz, 1H), 7.68 (t, J = 7.8 Hz, 1H), 7.45 (dd, J = 8.3, 4.2 Hz, 1H), 6.97 (d, J = 7.4 Hz, 2H), 6.94−6.83 (m, 1H), 6.39 (s, 1H), 2.14 (s, 3H), 2.03 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 156.1, 150.0, 145.6, 142.2, 130.6, 129.0, 128.8, 127.2, 126.0, 123.1, 121.9, 121.2, 29.2, 17.9, 11.0 ppm. HRMS (ESI) m/z calcd for $C_{22}H_{19}N_3O$, $[M + H]^+$ 342.1606; found 342.1607.

*(E)-5-(2,6-Dimethylphenylimino)-4-phenyl-1-(quinolin-8-yl)-1H-pyrrol-2(5H)-one (**3sb**).* Yellow solid (91 mg, 45%), mp 230.8−231.7 °C. IR 2918, 1733, 1659, 1470, 1389, 1236, 1126, 1045, 878, 816, 769, 692 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.89−8.77 (m, 1H), 8.30−7.90 (m, 3H), 7.63−7.31 (m, 6H), 7.19 (s, 1H), 6.90 (s, 1H), 6.59 (d, J = 7.5 Hz, 1H), 6.36 (t, J = 7.5 Hz, 1H), 6.14 (d, J = 7.4 Hz, 1H), 2.14 (s, 3H), 1.47 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.0, 144.4, 135.4, 131.4, 130.4, 129.6, 129.1, 128.2, 127.9, 126.3, 126.2, 126.1, 125.1, 122.3, 121.1, 18.2, 17.5 ppm. HRMS (ESI) m/z calcd for $C_{27}H_{21}N_3O$, $[M + H]^+$ 404.1763; found 404.1760.

*(E)-5-(2,6-Dimethylphenylimino)-3-phenyl-1-(quinolin-8-yl)-1H-pyrrol-2(5H)-one (**3tb**).* Yellow solid (121 mg, 60%), mp 95.5−97.1 °C. IR 2918, 2853, 1725, 1662, 1591, 1473, 1403, 1239, 1150, 1086, 908, 786, 728, 691 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.92 (dd, J = 4.2, 1.7 Hz, 1H), 8.20 (dd, J = 8.3, 1.8 Hz, 1H), 8.09−8.00 (m, 2H), 7.93 (ddd, J = 12.9, 7.8, 1.4 Hz, 2H), 7.71 (dd, J = 8.2, 7.3 Hz, 1H), 7.45−7.39 (m, 4H), 7.05 (d, J = 7.4 Hz, 2H), 6.96 (dd, J = 8.1, 6.8 Hz, 1H), 6.84 (s, 1H), 2.12 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 155.8, 150.3, 145.8, 144.4, 140.6, 135.8, 131.2, 130.5, 130.0, 129.5, 129.0, 128.3, 128.0, 127.4, 125.8, 123.3, 121.3, 118.5, 18.0 ppm. HRMS (ESI) m/z calcd for $C_{27}H_{21}N_3O$, $[M + H]^+$ 404.1763; found 404.1762.

*(E)-3-(2,6-Dimethylphenylimino)-2-(quinolin-8-yl)-2,3,4,5,6,7-hexahydro-1H-isoindol-1-one (**3ub**).* Yellow solid (141 mg, 74%), mp 165.4−166.8 °C. IR 3022, 2870, 1724, 1665, 1596, 1470, 1405, 1238, 1151, 1089, 910, 787, 723, 690 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.97−8.88 (m, 1H), 8.18 (d, J = 8.3 Hz, 1H), 7.89 (d, J = 8.2 Hz, 1H), 7.77 (d, J = 7.2 Hz, 1H), 7.65 (t, J = 7.7 Hz, 1H), 7.41 (dd, J = 8.3, 4.2 Hz, 1H), 6.88 (dt, J = 35.8, 7.0 Hz, 3H), 2.54−2.42 (m, 2H), 2.04 (d, J = 13.9 Hz, 6H), 1.75−1.54 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 154.5, 150.1, 145.7, 144.8, 139.6, 138.3, 135.7, 131.8, 130.6, 128.9, 128.6, 127.3, 127.0, 126.3, 125.8, 122.7, 121.1, 22.4, 21.7, 20.6, 20.2, 17.9, 17.8 ppm. HRMS (ESI) m/z calcd for $C_{25}H_{23}N_3O$, $[M + H]^+$ 382.1919; found 382.1917.

*(E)-3-(2,6-Dimethylphenylimino)-5-(pyridin-2-yl)-2-(quinolin-8-yl)isoindolin-1-one (**3wb**).* Yellow solid (127 mg, 56%), mp 183.5−184.9 °C. IR 2921, 2853, 1732, 1670, 1567, 1501, 1398, 1377, 1124, 1084, 883, 780, 713, 621 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.98 (s, 1H), 8.65 (d, J = 4.7 Hz, 1H), 8.46 (d, J = 7.9 Hz, 1H), 8.22 (d, J = 8.2 Hz, 1H), 8.10 (d, J = 7.9 Hz, 1H), 7.93 (dd, J = 16.8, 7.7 Hz, 2H), 7.69 (dt, J = 17.9, 7.8 Hz, 2H), 7.57−7.35 (m, 2H), 7.20 (d, J = 8.6 Hz, 2H), 7.06 (t, J = 6.4 Hz, 3H), 2.05 (d, J = 31.3 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 154.9, 152.1, 150.3, 149.4, 145.9, 144.2, 143.9, 136.6, 136.1, 132.0, 131.3, 130.8, 130.7, 129.2, 129.0, 127.8, 127.6, 127.5, 126.9, 126.4, 126.0, 123.8, 123.2, 122.6, 122.1, 121.4, 120.2, 17.7, 17.6 ppm. HRMS (ESI) m/z calcd for $C_{30}H_{22}N_4O$, $[M + H]^+$ 455.1872; found 455.1885.

*(E)-3-(2,6-Dimethylphenylimino)-5-(pyrimidin-2-yl)-2-(quinolin-8-yl)isoindolin-1-one (**3xb**).* Yellow solid (118 mg, 52%), mp 133.5−135.2 °C. IR 2922, 2852, 1733, 1673, 1557, 1475, 1399, 1238, 1124,

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1087, 885, 785, 713, 634 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.96 (s, 1H), 8.82−8.65 (m, 3H), 8.23 (d, J = 8.2 Hz, 1H), 8.12 (d, J = 7.9 Hz, 1H), 8.04−7.65 (m, 4H), 7.48−7.41 (m, 1H), 7.09 (ddd, J = 35.5, 16.8, 6.8 Hz, 4H), 2.06 (d, J = 35.2 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 162.7, 156.8, 151.8, 150.3, 145.5, 144.3, 142.5, 136.0, 133.4, 131.9, 131.6, 131.4, 130.6, 129.1, 127.8, 127.5, 127.4, 126.5, 125.9, 124.1, 123.4, 123.2, 121.4, 119.3, 17.8, 17.7 ppm. HRMS (ESI) m/z calcd for $C_{29}H_{21}N_5O$, $[M + H]^+$ 456.1824; found 456.1830.

(E)-3-(2,6-Dimethylphenylimino)-5-(1H-pyrazol-1-yl)-2-(quinolin-8-yl)isoindolin-1-one (**3yb**). Yellow solid (122 mg, 55%), mp 211.2−212−6 °C. IR 2920, 2851, 1739, 1667, 1601, 1524, 1501, 1377, 1279, 1047, 892, 779, 711, 643 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.97−8.88 (m, 1H), 8.22 (ddd, J = 22.3, 8.1, 1.8 Hz, 2H), 8.07 (d, J = 8.3 Hz, 1H), 7.98 (d, J = 8.3 Hz, 1H), 7.91 (d, J = 7.3 Hz, 1H), 7.75−7.69 (m, 2H), 7.48−7.40 (m, 2H), 7.07 (dt, J = 14.9, 7.1 Hz, 3H), 6.70−6.61 (m, 1H), 6.43 (s, 1H), 2.09 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 151.6, 150.3, 145.8, 144.2, 143.4, 141.6, 135.9, 131.4, 131.2, 130.5, 130.4, 129.2, 129.0, 128.4, 127.9, 127.6, 127.5, 126.9, 126.4, 126.1, 125.9, 124.9, 123.4, 122.2, 121.4, 112.9, 108.3, 29.2, 17.7, 17.6 ppm. HRMS (ESI) m/z calcd for $C_{28}H_{21}N_5O$, $[M + H]^+$ 444.1824; found 444.1816.

2-(Quinolin-8-yl)isoindoline-1,3-dione (**4**).[17] Ochre solid (82 mg, 60%), mp 226.0−228.0 °C. IR 2958, 2922, 1775, 1710, 1595, 1501, 1400, 1235, 1114, 883, 790, 718, 624 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 8.85 (dd, J = 4.2, 1.7 Hz, 1H), 8.22 (dd, J = 8.3, 1.7 Hz, 1H), 8.02−7.94 (m, 3H), 7.80 (dd, J = 5.4, 3.1 Hz, 2H), 7.75 (dd, J = 7.3, 1.5 Hz, 1H), 7.67 (dd, J = 8.2, 7.3 Hz, 1H), 7.43 (dd, J = 8.3, 4.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 150.5, 143.8, 135.7, 133.7, 132.0, 129.8, 129.3, 129.1, 128.8, 125.7, 123.4, 121.4 ppm. HRMS (ESI) m/z calcd for $C_{17}H_{10}N_2O_2$, $[M + H]^+$ 275.0821; found 275.0815.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02797.

Copies of ^1H and ^{13}C NMR spectra of the products (PDF)

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Notes

The authors declare no competing financial interest.

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