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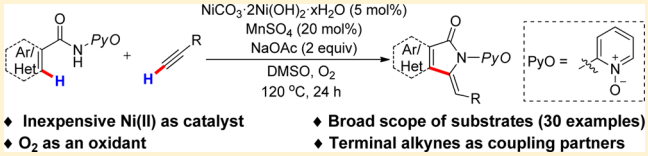
Ni(II)-Catalyzed C(sp^2)−H Alkynylation/Annulation with Terminal Alkynes under an Oxygen Atmosphere: A One-Pot Approach to 3-Methyleneisoindolin-1-one

Xin-Xiang Zheng, Cong Du, Xue-Mei Zhao, Xinju Zhu, Jian-Feng Suo, Xin-Qi Hao, Jun-Long Niu,* and Mao-Ping Song*

The College of Chemistry and Molecular Engineering, Zhengzhou University, Zhengzhou 450001, People's Republic of China

Supporting Information

ABSTRACT: A nickel(II)-catalyzed alkynylation/annulation cascade via double C−H cleavage has been successfully achieved. This methodology adopted a removable N,O-bidentate directing group with a broad range of amide substrates and terminal alkynes being well tolerated. The catalytic system allowed for atom-economical and environmentally benign one-pot construction of the corresponding 3-methyleneisoindolin-1-one derivatives using O_2 as the external oxidant.



INTRODUCTION

The 3-methyleneisoindolin-1-one framework is an important intermediate for the preparation of alkaloids such as lennoxamine and widely exists in bioactive natural products and pharmaceuticals.[1,2] Representative compounds containing the 3-methyleneisoindolin-1-one unit possess various biological activities, including local anesthetic activity (**A**), sedative activity (**B**), and vasorelaxant activity (**AKS 186**) (Scheme 1). Therefore, a variety of strategies for their synthesis have emerged.[2,3] In general, phthalimides have been utilized as the starting materials to provide the target products via Wittig reactions or addition reactions with organometallic reagents followed by dehydration.[3b,f] In addition, methods with respect to the condensation of phosphorylated derivatives with aldehydes[3e,g] and the addition/cyclization of 2-alkynylbenzonitriles via methanolysis have also been developed.[3c,d] However, these strategies always encounter some limitations such as the employment of organometallic reagents, poor regioselectivities, or additional steps to synthesize phosphorylated derivatives or 2-alkynylbenzonitriles. In this context, a strategy via metal-catalyzed reactions to obtain 3-methyleneisoindolin-1-one has drawn much attention.[4] In 2009, Ma and co-workers reported copper-catalyzed coupling/cyclization of terminal alkynes with 2-bromobenzamides.[4b] In 2014, Cu-catalyzed decarboxylative cross-coupling reactions of 2-halobenzamides with aryl alkynyl acids was described by the Patel group.[4f] Nevertheless, the prefunctionalization of starting materials confined its further application in organic synthesis. Thus, it is highly necessary to develop an efficient, one-pot protocol to construct the 3-methyleneisoindolin-1-one moiety.

During the past few decades, transition-metal-catalyzed C(sp^2)−H bond activation has been developed rapidly in constructing valuable molecules which avoids the C−H prefunctionalization step.[5] Accordingly, methods for synthesizing 3-methyleneisoindolin-1-ones via C−H activation are more favorable and have attracted considerable attention.[6] Among them, the coupling reactions of aromatic rings with olefins to furnish 3-methyleneisoindolin-1-ones have been extensively developed by Booker-Milburn,[6a] Glorius,[6b] Li,[6c] Xi,[6e] Jeganmohan[6f] and Liu.[6h] Nevertheless, the catalysts utilized among the previous literature reports were limited to precious metals such as Pd, Ru, and Rh. On the other hand, the copper-promoted alkynylation/annulation of C(sp^2)−H bonds with terminal alkynes or alkynyl carboxylic acids has also been disclosed by Huang[7a] and You,[7b] respectively, which demonstrated the significant potential of the first-row metal for the synthesis of 3-methyleneisoindolin-1-ones (Scheme 2a). More recently, our group[7e] discovered the direct coupling of simple arenes with terminal alkynes by employing an inexpensive cobalt salt as the catalyst (Scheme 2b). In addition, similar work on alkynylation/annulation of C(sp^2)−H and C(sp^3)−H bonds catalyzed by copper or cobalt salts has been reported by Zhang and co-workers (Scheme 2a,b).[7i,8] However, the first-row-metal-catalyzed alkynylation/annulation of simple arenes with terminal alkynes is still rare and remains to be further explored.[7,8]

As one of the low-cost and earth-abundant metals, nickel has emerged as a promising alternative for C−H functionalization such as alkylation,[9] arylation,[10] thiolation,[11] amination,[12] and alkenylation.[13] Meanwhile, the alkynylation of C−H bonds catalyzed by nickel salts has also been realized.[14] In 2015, Li[14a] and Shi[14b] have reported the Ni-catalyzed alkynylation of arenes with bromoalkynes, respectively. Subsequently, ethynyltriisopropylsilane utilized as the coupling partner of arenes was disclosed by Shi.[14c] However, to our knowledge, Ni-catalyzed

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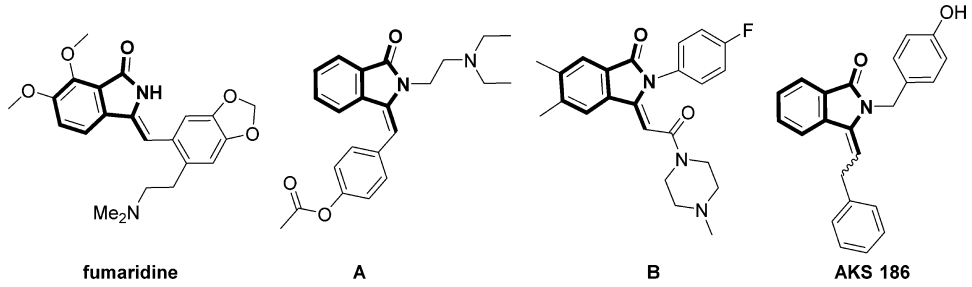
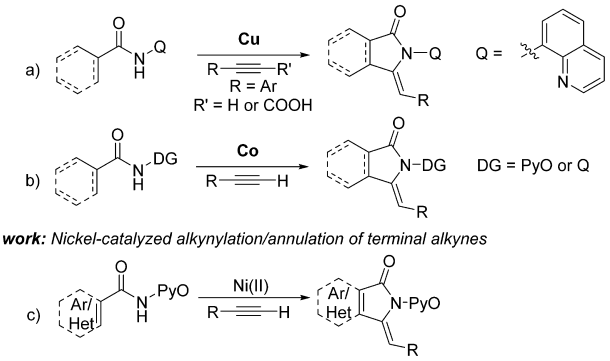
Scheme 1. Bioactive Molecules Containing the Skeleton of 3-Methyleneisoindolin-1-one



Scheme 2. First-Row-Metal-Catalyzed C(sp^2)−H Alkynylation/Annulation with Terminal Alkynes

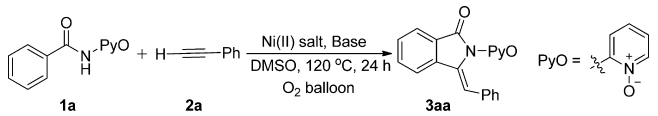


C(sp^2)−H alkynylation/annulation with simple terminal alkynes has not been investigated. Encouraged by the previous work, we set out to explore a low-cost and environmentally benign system to produce the 3-methyleneisoindolin-1-one. Herein, we report nickel-catalyzed C(sp^2)−H alkynylation/annulation cascades with terminal alkynes via double C−H bond cleavage under an oxygen atmosphere with the assistance of a removable N,O-bidentate directing group (Scheme 2c).

RESULTS AND DISCUSSION

We commenced our study using 2-benzamidopyridine 1-oxide (**1a**) and phenylacetylene (**2a**) as the starting materials under an oxygen atmosphere (Table 1). To our delight, the desired product was obtained in 38% yield in the presence of $NiCl_2 \cdot 6H_2O$ (15 mol %), NaOAc (2 equiv), and DMSO (0.5 mL), at 120 °C for 24 h (entry 1). In order to search out an appropriate set of conditions, we first screened a series of Ni(II) salts. $NiCO_3 \cdot 2Ni(OH)_2 \cdot xH_2O$ (5 mol %) was chosen as the superior catalyst to give the corresponding product with a yield of 69% (entry 6). Among the bases investigated (entries 6−9), KOAc and NaOAc showed similar reaction activities (entries 6 and 7). The employment of other bases such as carbonate salts, phosphate salts, and even organic salts almost hampered the reaction (entries 9−11). Accordingly, NaOAc was chosen as the optimal base. According to a previous report, Mn(II) salts could be utilized as cocatalysts in the Co-catalyzed C(sp^2)−H alkenylation.[7j] Thus, we attempted to add $MnSO_4$ (20 mol %) to the catalytic system. To our delight, the yield of **3aa** increased to 75% (*Z*:*E* = 95:5) (entry 12). In addition, the yield

Table 1. Optimization of the Reaction Conditions[a]



entry[a]	catalyst	amount (mol %)	base	yield (%)[b]
1	$NiCl_2 \cdot 6H_2O$	15	NaOAc	38
2	$NiC_2O_4 \cdot 2H_2O$	15	NaOAc	53
3	$NiSO_4 \cdot 6H_2O$	15	NaOAc	41
4	$Ni(NO_3)_2 \cdot 6H_2O$	15	NaOAc	61
6	$NiCO_3 \cdot 2Ni(OH)_2 \cdot xH_2O$	5	NaOAc	69
7	$NiCO_3 \cdot 2Ni(OH)_2 \cdot xH_2O$	5	KOAc	68
8	$NiCO_3 \cdot 2Ni(OH)_2 \cdot xH_2O$	5	CsOAc	52
9	$NiCO_3 \cdot 2Ni(OH)_2 \cdot xH_2O$	5	Na_2CO_3	N.R.
10	$NiCO_3 \cdot 2Ni(OH)_2 \cdot xH_2O$	5	$K_2HPO_4 \cdot 3H_2O$	trace
11	$NiCO_3 \cdot 2Ni(OH)_2 \cdot xH_2O$	5	Et_3N	trace
12[c]	**$NiCO_3 \cdot 2Ni(OH)_2 \cdot xH_2O$**	**5**	**NaOAc**	**75**
13[c,d]	$NiCO_3 \cdot 2Ni(OH)_2 \cdot xH_2O$	5	NaOAc	63
14[c,e]	$NiCO_3 \cdot 2Ni(OH)_2 \cdot xH_2O$	5	NaOAc	49
15[c]	$NiCO_3 \cdot 2Ni(OH)_2 \cdot 4H_2O$	5	NaOAc	74
16[c]			NaOAc	N.R.
17[c]	$NiCO_3 \cdot 2Ni(OH)_2 \cdot xH_2O$	5		N.R.

[a]Reaction conditions unless specified otherwise: substrate **1a** (0.15 mmol), phenylacetylene **2a** (0.27 mmol, 1.8 equiv), Ni(II) (15 mol %), base (0.30 mmol, 2.0 equiv), solvent (0.5 mL), O_2 atmosphere, 120 °C, 24 h. [b]Isolated yields. N.R. = no reaction. [c]$MnSO_4$ (20 mol %) was added. [d]110 °C, 36 h. [e]130 °C.

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Scheme 3. Effect of Directing Groups for the Alkynylation/Annulation Reaction under Standard Reaction Conditions

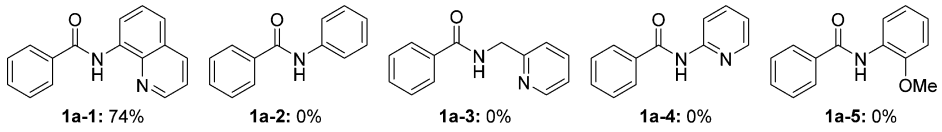
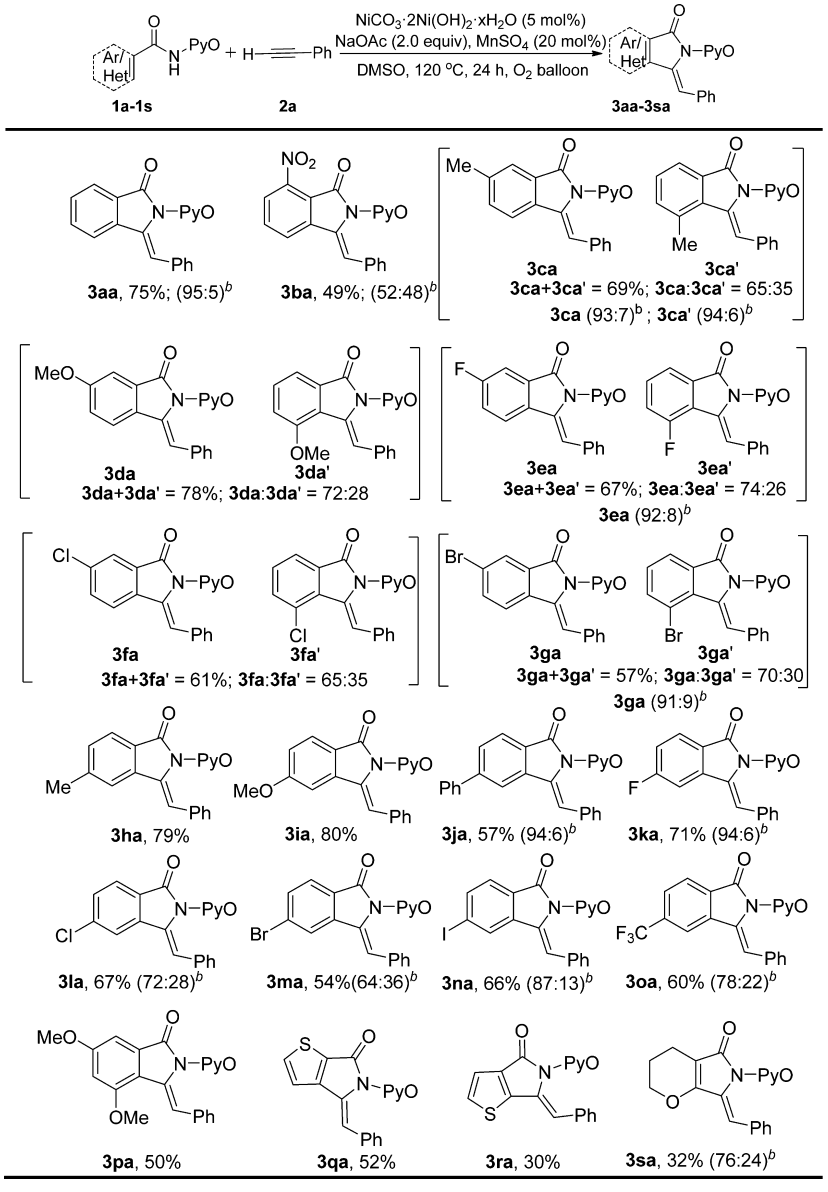


Table 2. Scope of Amides[a,b]



[a]Reaction conditions: substrate **1a–s** (0.15 mmol), phenylacetylene (**2a**; 0.27 mmol, 1.8 equiv), $NiCO_3{\cdot}2Ni(OH)_2{\cdot}xH_2O$ (5 mol %), NaOAc (0.30 mmol, 2.0 equiv), DMSO (0.5 mL), $MnSO_4$ (20 mol %), O_2 balloon, 120 °C, 24 h. The *Z*:*E* ratio, if not mentioned, was close to 100/0. [b]The *Z*:*E* ratio was determined by ^1H NMR analysis.

of product did not improve when the reaction temperature was adjusted (entries 13 and 14). A variety of solvents were also attempted but failed to give any product. When $NiCO_3{\cdot}2Ni(OH)_2{\cdot}4H_2O$ was used as the catalyst, the reaction could also proceed smoothly with a yield of 74% (*Z*:*E* = 95:5) (entry 15). No reaction occurred without bases or nickel salts, indicating the necessity of both Ni(II) salts and bases for the reaction (entries 16–17).

Next, we examined the applicability of the catalytic system for different directing groups, as shown in Scheme 3. Interestingly, *N*-(quinolin-8-yl)benzamide (**1a-1**) could promote the alkynylation/annulation reaction smoothly as well, delivering the corresponding isoindolinone in 74% yield, with high selectivity (*Z*:*E* = 93:7). Nevertheless, other common directing groups, including the monodentate group *N*-phenylbenzamide (**1a-2**) and the bidentate coordinating groups *N*-(pyridin-2-ylmethyl)benzamide (**1a-3**), *N*-(pyridin-2-yl)-benzamide (**1a-4**), and *N*-(2-methoxyphenyl)benzamide (**1a-5**), were incapable of promoting the reaction.

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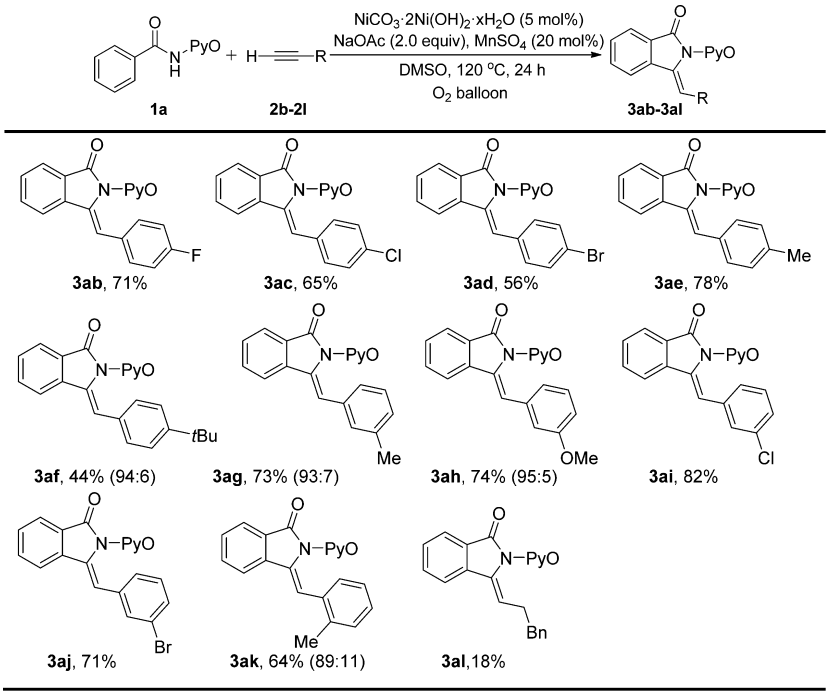
Table 3. Scope of Terminal Alkynes[a,b]



[a]Reaction conditions unless specified otherwise: substrate **1a** (0.15 mmol), terminal alkyne (0.27 mmol, 1.8 equiv), $NiCO_3{\cdot}2Ni(OH)_2{\cdot}xH_2O$ (5 mol %), NaOAc (2.0 equiv), DMSO (0.5 mL), $MnSO_4$ (20 mol %), O_2 balloon, 120 °C, 24 h. The *Z*:*E* ratio, if not mentioned, was close to 100/0. [b]The *Z*:*E* ratio was determined by ^1H NMR analysis.

With the optimized reaction conditions in hand, we set out to examine the scope of substituted 2-aminopyridine 1-oxide amides (**1**). As summarized in Table 2, the reaction of the amide substrates bearing electron-withdrawing and electron-donating substituents with **2a** proceeded smoothly under the optimized conditions, affording the corresponding isoindolinones in 30−80% yields. A strong electron-withdrawing nitro group at the ortho position of arenes (**3b**) did not inhibit the transformation and provided the desired product (**3ba**) in 49% yield. In addition, for the meta-substituted amide substrates, the alkynylation/annulation reaction mainly occurred at the less hindered ortho position (**3ca**−**ga**). Synthetically valuable groups, such as F, Cl, Br, and I, were also tolerated as well in this transformation, delivering the corresponding products (**3ea**−**ga**, **3ka**−**na**) in moderate to good yields. An amide substrate bearing a trifluoromethyl group (**3o**) could also afford the corresponding product **3oa** in 60% yield. Moreover, the disubstituted amide substrate **1p** could be converted into the alkynylation/annulation product in 50% yield (**3pa**). Notably, the protocol was also compatible with heterocyclic and olefin substrates, liberating **3qa**−**sa** in acceptable yields (30−52%).

Subsequently, we investigated a series of terminal alkynes. As summarized in Table 3, we were pleased to find that the aryl acetylenes **2b**−**k** bearing both electron-rich and electron-poor groups could be successfully converted into corresponding isoindolinone compounds **3ab**−**ak** under the optimized conditions. First, a series of terminal alkynes containing para-substituted arenes were investigated (**2b**−**f**). The yields of the para-substituted halogenated products **3ab**−**ad** decreased as the electron-withdrawing ability of substituted halogen decreased. The steric hindrance of the para position had an apparent effect on the reaction. For instance, a substrate with less steric hindrance such as methyl offered a yield surpassing that of the *tert*-butyl group (**3ae**,**af**). In comparison with phenylacetylenes bearing substituents on the para site (**3ac**, 65%; **3ad**, 56%), meta-substituted species gave higher yields (**3ai**, 82%; **3aj**, 71%). Additionally, ortho-substituted substrates could also be tolerated under the catalytic system, furnishing the product **3ak** in a moderate yield (64%). Interestingly, the methodology was also appropriate for but-3-yn-1-ylbenzene (**2l**), albeit in a low yield (18%). In comparison with our previous work,[7e] the current strategy provided the desired products in lower yields with similar stereoselectivities. However, the olefinic carboxamide substrate **1s** and the aliphatic alkyne **2l**, which could not react in the prior method, delivered the corresponding products **3sa** and **3al** successfully, although in low yields.

To probe the mechanism of the reaction, we performed a series of control experiments. As shown in Scheme 4, an intermolecular kinetic isotope experiment of **1a** and deuterated amide **1a-d$_5$** with phenylacetylene was carried out simultaneously in DMSO for 12 h, and an intermolecular kinetic isotope effect (KIE) of 2.4 was obtained (Scheme 4a), illustrating that the cleavage of *o*-C(sp^2)−H bonds of amides may play an important role in the catalytic system. Meanwhile, only negligible H content was observed when **1a-d$_5$** was treated with $NiCO_3{\cdot}2Ni(OH)_2{\cdot}xH_2O$ and NaOAc in the absence of the phenylacetylene for 12 h. When **1a-d$_5$** was replaced with **1a** and D_2O (5 equiv) was added to the catalyst system, no obvious deuterium incorporation was detected (Scheme 4b). These results suggested that the C−H cleavage step was largely irreversible. Subsequently, compounds **4** and **5** were synthesized according to the literature.[7e] The compound **4** could be transformed into **3aa** smoothly in 84% yield, whereas compound **5** failed to accomplish this transformation under the standard reaction conditions, which revealed that compound **4** was the possible intermediate (Scheme 4c). When 2,2,6,6-tetramethylpiperidine (TEMPO, 1 equiv) was added as a radical quencher to the alkynylation/annulation

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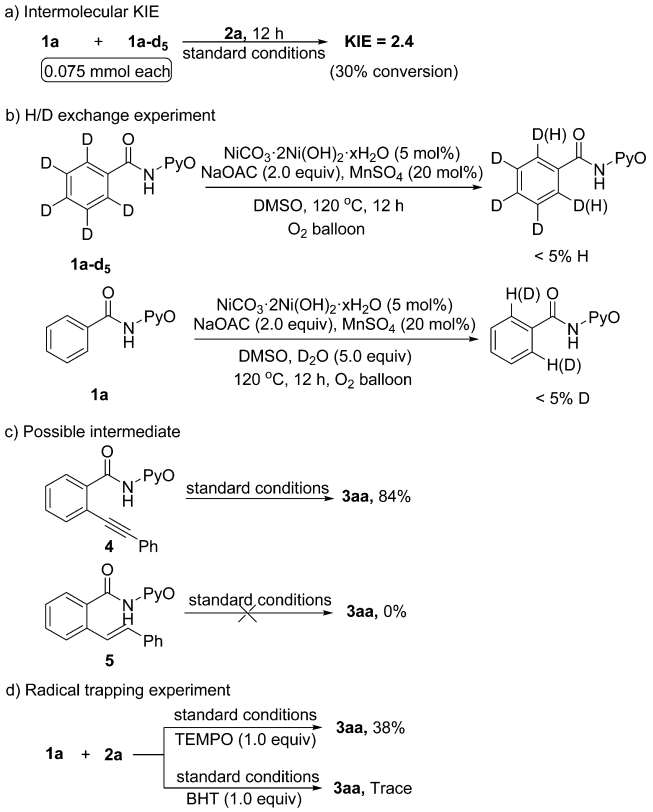
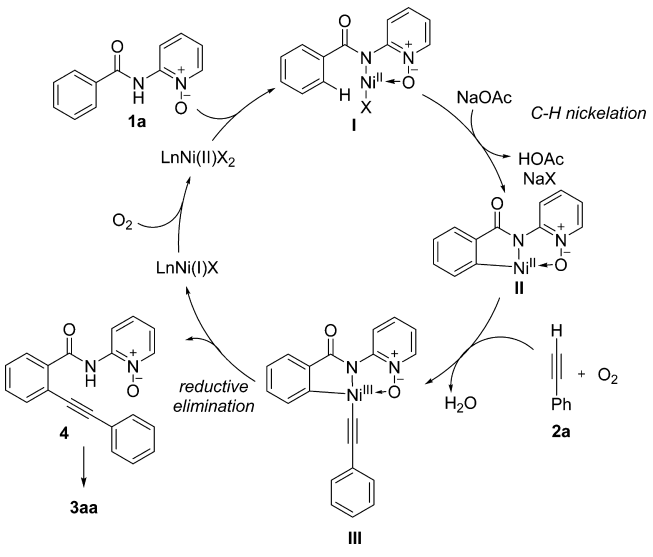
Scheme 4. Mechanistic Experiments



reaction mixture of **1a** with **2a**, the yield of **3aa** decreased to 38%. When BHT was used, only a trace of **3aa** was obtained, implying that a single-electron-transfer pathway may be involved in the reaction process (Scheme 4d).

Very recently, the nickel-catalyzed direct amination of arenes has been reported by Zhang, in which the Ni(I)/Ni(III) catalytic cycle was proved.[12] On the basis of the above control experiments and relevant literature reports,[9b,c,11c,12] we speculated that the reaction might also proceed through a Ni(I)/Ni(III) catalytic process, and a plausible reaction mechanism is proposed in Scheme 5. The catalytic cycle

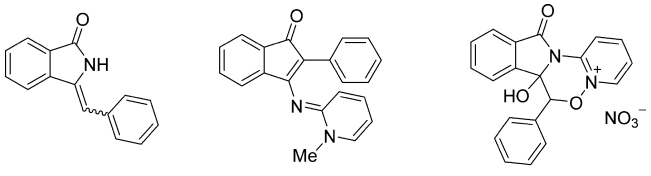
Scheme 5. Proposed Reaction Mechanism



initiates with the coordination of the Ni(II) species with 2-benzamidopyridine 1-oxide (**1a**), which is followed by C−H activation to generate intermediate **II**. Then the intermediate **II** coordinates with phenylacetylene via oxidative addition, releasing the essential intermediate **III**.[15] Subsequently, the migration and reductive elimination of intermediate **III** liberate the Ni(I) species and the *o*-alkynyl amide **4**, which is transformed to **3aa** via intramolecular annulation. The Ni(I) species is oxidized to an Ni(II) species in the presence of O_2 to fulfill the catalytic cycle. However, an alternative route from **III** to **3aa** reported by You and co-workers could not be excluded.[7b]

As disclosed in a previous work,[7e] the PyO group of **3aa** could be easily removed to give compound **6**. In addition, **3aa** could be transformed into compound **7** via a rearrangement reaction or oxidized to the oxadiazine salt **8** on treatment with CAN (Scheme 6).

Scheme 6. Compounds Converted from 3aa



CONCLUSIONS

In summary, we have reported a nickel(II)-catalyzed C(sp^2)−H alkynylation/annulation via 2-fold C−H activation assisted by a removable N,O-bidentate directing group. The catalytic system could tolerate a broad scope of amides and terminal alkynes, delivering a series of substituted 3-methyleneisoindolin-1-ones successfully in one pot. Moreover, O_2 was used as the oxidant, thus providing a step-economical and environmentally friendly approach to construct the desired functional molecules.

EXPERIMENTAL SECTION

General Information. The materials involved were obtained from commercial suppliers and used as received. The molecular weight of $NiCO_3·2Ni(OH)_2·xH_2O$ is 304.11 without considering xH_2O content, and the content of Ni is 45−47%. ^1H NMR spectra were recorded at 400 or 600 MHz and ^{13}C NMR spectra at 101 or 151 MHz, and TMS was taken as an internal standard. The HRMS measurements of the target product were acquired by a Q-TOF mass spectrometer. Melting points were obtained on a WC-1 instrument and are uncorrected. Data are represented as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, etc.). All of the amide substrates were synthesized according to the literature method,[7e] and the *Z*:*E* ratios of all products were determined by ^1H NMR analysis.

Procedure for Examples Described in Scheme 2 and Tables 2 and 3. In a 10 mL overdried two-necked Schlenk tube were placed substrates **1** (0.15 mmol), terminal alkynes **2** (0.27 mmol, 1.8 equiv), $NiCO_3·2Ni(OH)_2·xH_2O$ (2.3 mg, 5 mol %), NaOAc (24.6 mg, 0.3 mmol, 2.0 equiv), $MnSO_4$ (4.5 mg, 20 mol %), and DMSO (0.5 mL) under an oxygen atmosphere. Then the reaction mixture was stirred at 120 °C for 24 h with inclusion of an O_2 balloon. After the reaction was complete, the mixture was cooled to room temperature and then diluted with ethyl acetate (20 mL) and washed with saturated NaCl solution (2 × 10 mL). The collected organic layer was dried over Na_2SO_4 and concentrated under vacuum. Then the desired products were obtained by TLC.

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Reaction in the Presence of TEMPO. A 10 mL overdried two-necked Schlenk tube was placed in an oil bath and charged with a magnetic stirrer, 2-benzamidopyridine 1-oxide (**1a**; 32.1 mg, 0.15 mmol), phenylacetylene (**2a**; 30 uL, 0.27 mmol, 1.8 equiv), TMPEO (2,2,6,6-tetramethylpiperidine; 23.4 mg, 0.15 mmol, 1.0 equiv), $NiCO_3{\cdot}2Ni(OH)_2{\cdot}xH_2O$ (2.3 mg, 5 mol %), NaOAc (24.6 mg, 0.3 mmol, 2.0 equiv), $MnSO_4$ (4.5 mg, 20 mol %), and DMSO (0.5 mL) under an oxygen atmosphere. Then the reaction tube was heated to 120 °C for 24 h with inclusion of an O_2 balloon. After the reaction was complete, the mixture was cooled to room temperature, diluted with ethyl acetate (20 mL), and washed with a saturated NaCl solution (2 × 10 mL); the organic layer was dried over Na_2SO_4 and concentrated under vacuum. Pure product **3aa** was obtained as a white solid (17.8 mg, 38%) by TLC (dichloromethane/acetone 6/1).

Reaction in the Presence of BHT. A 10 mL overdried two-necked Schlenk tube was placed in an oil bath and charged with a magnetic stirrer, 2-benzamidopyridine 1-oxide (**1a**; 32.1 mg, 0.15 mmol), phenylacetylene (**2a**; 30 uL, 0.27 mmol, 1.8 equiv), BHT (2,6-di-*tert*-butyl-4-methylphenol; 33.0 mg, 0.15 mmol, 1.0 equiv), $NiCO_3{\cdot}2Ni(OH)_2{\cdot}xH_2O$ (2.3 mg, 5 mol %), NaOAc (24.6 mg, 0.3 mmol, 2.0 equiv), $MnSO_4$ (4.5 mg, 20 mol %), and DMSO (0.5 mL) under an oxygen atmosphere. Then the reaction tube was heated to 120 °C for 24 h with inclusion of an O_2 balloon. After the reaction was complete, the mixture was cooled to room temperature and diluted with ethyl acetate (20 mL) and washed with a saturated NaCl solution (2 × 10 mL); the organic layer was dried over Na_2SO_4 and concentrated under vacuum. **3aa** was observed in a trace amount.

Reaction of 3aa from Possible Intermediate 4. A 10 mL overdried two-necked Schlenk tube was placed in an oil bath and charged with a magnetic stirrer, 2-(2-(phenylethynyl)benzamido)-pyridine 1-oxide (**4**; 47.1 mg, 0.15 mmol), $NiCO_3{\cdot}2Ni(OH)_2{\cdot}xH_2O$ (2.3 mg, 5 mol %), NaOAc (24.6 mg, 0.3 mmol, 2.0 equiv), $MnSO_4$ (4.5 mg, 20 mol %), and DMSO (0.5 mL) under an oxygen atmosphere. Then the reaction tube was heated to 120 °C for 24 h with inclusion of an O_2 balloon. After the reaction was complete, the mixture was cooled to room temperature, diluted with ethyl acetate (20 mL), and washed with a saturated NaCl solution (2 × 10 mL); the organic layer was dried over Na_2SO_4 and concentrated under vacuum. The product was obtained as a white solid (39.5 mg, 84%) by TLC (CH_2Cl_2/acetone 6/1).

Reaction of 3aa from Possible Intermediate 5. A 10 mL overdried two-necked Schlenk tube was placed in an oil bath and charged with a magnetic stirrer, (*E*)-2-(2-styrylbenzamido)pyridine 1-oxide (**5**; 47.4 mg, 0.15 mmol), $NiCO_3{\cdot}2Ni(OH)_2{\cdot}xH_2O$ (2.3 mg, 5 mol %), NaOAc (24.6 mg, 0.3 mmol, 2.0 equiv), $MnSO_4$ (4.5 mg, 20 mol %), and DMSO (0.5 mL) under an oxygen atmosphere. Then the reaction tube was heated to 120 °C for 24 h with inclusion of an O_2 balloon. After the reaction was complete, the mixture was cooled to room temperature, diluted with ethyl acetate (20 mL), and washed with a saturated NaCl solution (2 × 10 mL); the organic layer was dried over Na_2SO_4 and under vacuum. The product **3aa** was not observed.

Experiments for Intermolecular Kinetic Isotope Effects. A 10 mL overdried two-necked Schlenk tube was placed in an oil bath and charged with a magnetic stirrer, 2-benzamidopyridine 1-oxide (**1a**; 16.1 mg, 0.075 mmol), **1a-d$_5$** (16.4 mg, 0.075 mmol), phenylacetylene (**2a**; 30 uL, 0.27 mmol, 1.8 equiv), $NiCO_3{\cdot}2Ni(OH)_2{\cdot}xH_2O$ (2.3 mg, 5 mol %), NaOAc (24.6 mg, 0.3 mmol, 2.0 equiv), $MnSO_4$ (4.5 mg, 20 mol %), and DMSO (0.5 mL) under an oxygen atmosphere. Then the reaction tube was heated to 120 °C for 12 h with inclusion of an O_2 balloon. After the reaction was complete, the mixture was cooled to room temperature, diluted with ethyl acetate (20 mL), and washed with a saturated NaCl solution (2 × 10 mL); the organic layer was dried over Na_2SO_4 and concentrated under vacuum. The product was obtained as a white solid (14.1 mg, 30%) using TLC (CH_2Cl_2/acetone 6/1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.95 (d, J = 7.6 Hz, 1H), 7.92 (dd, J = 6.1, 1.7 Hz, 1.4H), 7.86 (d, J = 7.8 Hz,1H), 7.70 (td, J = 7.8, 0.9 Hz, 1H), 7.55 (t, J = 7.5 Hz, 1H), 7.14−7.12 (m, 1.4H), 7.08−7.06 (m, 2.9H), 7.02−7.01 (m, 4.3H), 6.97−6.92 (m, 2.9H), 6.89 (s, 1.4H). The KIE value was calculated as k_H/k_D = 2.4.

H/D Exchange Experiment. A 10 mL overdried two-necked Schlenk tube was placed in an oil bath and charged with a magnetic stirrer, 2-benzamidopyridine 1-oxide (**1a-d$_5$**; 32.9 mg, 0.15 mmol), $NiCO_3{\cdot}2Ni(OH)_2{\cdot}xH_2O$ (2.3 mg, 5 mol %), NaOAc (24.6 mg, 0.3 mmol, 2.0 equiv), $MnSO_4$ (4.5 mg, 20 mol %), and DMSO (0.5 mL) under an oxygen atmosphere. Then the reaction tube was heated to 120 °C for 12 h with inclusion of an O_2 balloon. After the reaction was complete, the mixture was cooled to room temperature, diluted with ethyl acetate (20 mL), and washed with a saturated NaCl solution (2 × 10 mL); the organic layer was dried over Na_2SO_4 and concentrated under vacuum. Then the resulting crude product was purified by TLC (CH_2Cl_2/acetone 6/1). Only negligible H content was observed by ^{1}H NMR.

A 10 mL overdried two-necked Schlenk tube was placed in an oil bath and charged with a magnetic stirrer, 2-benzamidopyridine 1-oxide (**1a**; 32.1 mg, 0.15 mmol), $NiCO_3{\cdot}2Ni(OH)_2{\cdot}xH_2O$ (2.3 mg, 5 mol %), NaOAc (24.6 mg, 0.3 mmol, 2.0 equiv), D_2O (13 uL 5.0 equiv), $MnSO_4$ (4.5 mg, 20 mol %), and DMSO (0.5 mL) under an oxygen atmosphere. Then the reaction tube was heated to 120 °C for 12 h with inclusion of an O_2 balloon. After the reaction was complete, the mixture was cooled to room temperature, diluted with ethyl acetate (20 mL), and washed with a saturated NaCl solution (2 × 10 mL); the organic layer was dried over Na_2SO_4 and concentrated under vacuum. Then the resulting crude product was purified by TLC (CH_2Cl_2/acetone 6/1). No obvious deuterium incorporation was detected by ^{1}H NMR.

Characterizations of Products. *2-(1-Benzylidene-3-oxoisoindolin-2-yl)pyridine 1-oxide (**3aa**).*[7e] Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (3/1) as an eluent: R_f = 0.35; white solid (35 mg, 75%); mp 131−132 °C (dichloromethane). Z:E = 95:5. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (t, J = 6.9 Hz, 2H), 7.85 (d, J = 7.8 Hz, 1H), 7.69 (td, J = 7.7, 0.9 Hz, 1H), 7.55 (dd, J = 11.0, 3.9 Hz, 1H), 7.11 (dd, J = 7.0, 3.0 Hz, 1H), 7.07−7.00 (m, 5H), 6.97−6.90 (m, 2H), 6.89 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.8, 142.4, 139.9, 138.6, 133.4, 133.1, 132. 9, 129.4, 128.3, 127.5, 127.3, 127.1, 124.8, 124.4, 124.3, 120.0, 108.1. HRMS (positive ESI): calcd for $C_{20}H_{15}N_2O_2$ $[M + H]^+$ 315.1128, found 315.1130.

*(Z)-3-Benzylidene-2-(quinolin-8-yl)isoindolin-1-one (**3aa-1**).*[7b] Purified by analytical TLC on silica gel with hexane/EtOAc (2/1) as an eluent: R_f = 0.23; yellow solid (38.6 mg, 74%); mp 212−214 °C (dichloromethane). Z:E = 93:7; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.85 (dd, J = 4.1, 0.2 Hz, 1H), 8.00−7.96 (m, 2H), 7.88 (d, J = 7.7 Hz, 1H), 7.70−7.67 (m, 1H), 7.58−7.55 (m, 2H), 7.48−7.46 (m, 1H), 7.31−7.26 (m, 2H), 6.80 (s, 1H), 6.70−6.66 (m, 1H), 6.56−6.52 (m, 4H).^{13}C NMR (151 MHz, $CDCl_3$): δ 168.1, 151.3, 150.4, 144.4, 138.7, 136.3, 136.1, 135.8, 134.2, 133.6, 132.3, 131.8, 131.4, 130.1, 129.5, 129.4, 129.1, 128.9, 128.5, 128.4, 128.3, 128.2, 127.6, 126.4, 126.3, 126.0, 125.6, 124.0, 123.8, 123.3, 121.9, 121.2, 119.7, 112.1, 107.3. HRMS (positive ESI): calcd for $C_{24}H_{17}N_2O$ $[M + H]^+$ 349.1335, found 349.1341.

*2-(1-Benzylidene-4-nitro-3-oxoisoindolin-2-yl)pyridine 1-Oxide (**3ba**).* Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.31; yellow solid (26.4 mg, 49%); mp 112−115 °C (dichloromethane). Z:E = 52:48. ^{1}H NMR (600 MHz, DMSO): δ 8.56 (d, J = 7.7 Hz, $1H_{[z]}$), 8.53 (dd, J = 6.5, 0.9 Hz, 1H (E)), 8.13 (d, J = 7.8 Hz, $1H_{[z]}$), 8.07−8.04 (m, $2H_{[z]}$+1H (E)), 7.91 (dd, J = 7.9, 2.0 Hz, 1H (E)), 7.83 (t, J = 8.0 Hz, 1H (E)), 7.68 (d, J = 8.0 Hz, 1H (E)), 7.64−7.62 (m, $1H_{[z]}$), 7.56 (tt, J = 10.5, 5.3 Hz, $1H_{[z]}$), 7.50−7.44 (m, 6H (E)), 7.40 (s, $1H_{[z]}$), 7.22−7.19 (m, $1H_{[z]}$), 7.11 (td, J = 7.8, 1.3 Hz, $1H_{[z]}$), 7.08−7.04 (m, $4H_{[z]}$+1H (E)), 6.38 (s, 1H (E)). ^{13}C NMR (151 MHz, DMSO): δ 162.1, 160.8, 146.3, 146.0,141.2, 140.8, 140.8, 139.8, 137.2, 135.0, 135.0, 134.0, 133.0, 132.8, 131.1, 129.8, 129.4, 129.1, 128.5, 128.5, 127.9, 126.8, 126.7, 126.4, 125.4, 125.3, 124.3, 124.2, 119.9, 117.8, 115.1, 112.2. HRMS (positive ESI): calcd for $C_{20}H_{14}N_3O_4$ $[M + H]^+$ 360.0979, Found 360.0985.

*2-(1-Benzylidene-5-methyl-3-oxoisoindolin-2-yl)pyridine 1-Oxide (**3ca**)*[7e] *and 2-(3-Benzylidene-4-methyl-1-oxoisoindolin-2-yl)-pyridine 1-Oxide (**3ca′**).* Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (3/1) as an eluent: R_f = 0.44; white solid (34

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mg, 69%); mp 216−217 °C (dichloromethane). **3ca**:**3ca′** = 65:35, *Z*:*E* (**3ca**) = 93:7, *Z*:*E* (**3ca′**) = 94:6. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (dd, *J* = 6.3, 1.4 Hz, 1H (**3ca**)), 7.92−7.90 (m, 1H (**3ca′**)), 7.74 (d, *J* = 8.5 Hz, 1H (**3ca**)), 7.58−7.56 (m, 1H (**3ca′**)), 7.50−7.46 (m, 1H (**3ca**)), 7.39−7.38 (m, 1H (**3ca**) + 1H (**3ca′**)), 7.24 (d, *J* = 2.4 Hz, 1H (**3ca′**)), 7.19 (d, *J* = 8.0 Hz, 1H (**3ca′**)), 7.10−7.04 (m, 3H (**3ca**) + 3H (**3ca′**)), 7.02−6.99 (m, 3H (**3ca**) + 3H (**3ca′**)), 6.95−6.88 (m, 2H (**3ca**) + 2H (**3ca′**)), 6.75 (s, 1H (**3ca**)), 4.04 (s, 3H (**3ca′**)), 3.91 (s, 3H (**3ca**)). ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.8, 161.1,155.7, 142.5, 139.9,134.5, 133.6, 132.8,132.0 131.5, 130.2, 129.0, 128.3, 128.2, 127.5, 127.4, 127.3, 126.9, 126.7, 124.8, 124.6, 124.4, 122.0, 121.3, 116.5, 114.9, 113.9, 106.9, 106.3, 55.9, 55.7. HRMS (positive ESI): calcd for $C_{21}H_{17}N_2O_2$ $[M + H]^+$ 329.1285, found 329.1288.

*2-(1-Benzylidene-5-methoxy-3-oxoisoindolin-2-yl)pyridine 1-Oxide (**3da**)*[7e] *and 2-(3-Benzylidene-4-methoxy-1-oxoisoindolin-2-yl)pyridine 1-Oxide (**3da′**).* Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.28; white solid (40 mg, 77%); mp 185−186 °C (dichloromethane). **3da**:**3da′** = 72:28, *Z*:*E* (**3da**) > 99%, *Z*:*E* (**3da′**) > 99%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01−7.86 (m, 1H (**3da**) + 1H (**3da′**)), 7.84 (d, *J* = 7.2 Hz, 1H (**3da′**)), 7.78−7.67 (m, 2H (**3da**)), 7.54−7.47 (m, 1H (**3da**) + 1H$_{[3da']}$), 7.44 (t, *J* = 7.4 Hz, 1H$_{[3da']}$), 7.14−7.03 (m, 3H (**3da**) + 4H$_{[3da']}$), 7.03−6.98 (m, 3H (**3da**) + 3H (**3da′**)), 6.95−6.87 (m, 2H (**3da**) + 2H (**3da′**)), 6.82 (s, 1H (**3da**)), 2.73 (s, 3H (**3da′**)), 2.50 (s, 3H (**3da**)). ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.0, 142.5, 139.9, 139.8, 136.2, 136.2, 135.5, 134.5, 134.2, 134.0, 133.6, 133.5, 133.0, 128.9, 128.5, 128.4, 128.3, 127.7, 127.6, 127.5, 127.4, 127.2, 127.0, 126.9, 124.8, 124.5, 124.3, 122.4, 119.8, 112.9, 107.4, 21.6, 21.6. HRMS (positive ESI): calcd for $C_{21}H_{17}N_2O_3$ $[M + H]^+$ 345.1234, found 345.1238.

*2-(1-Benzylidene-5-fluoro-3-oxoisoindolin-2-yl)pyridine 1-Oxide (**3ea**) and 2-(3-Benzylidene-4-fluoro-1-oxoisoindolin-2-yl)pyridine 1-Oxide (**3ea′**).* Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (3/1) as an eluent: R_f = 0.47; white solid (34.1 mg, 68%); mp 160−163 °C (dichloromethane). **3ea**:**3ea′** = 74:26, *Z*:*E* (**3ea**) = 92:8. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96−7.87 (m, 1H (**3ea**) + 1H (**3ea′**)), 7.83 (dd, *J* = 8.5, 4.2 Hz, 1H (**3ea′**)), 7.77 (d, *J* = 7.5 Hz, 1H (**3ea**)), 7.60 (dt, *J* = 7.3, 3.7 Hz, 1H (**3ea′**)), 7.51 (td, *J* = 7.8, 4.5 Hz, 1H (**3ea**)), 7.44−7.35 (m, 1H (**3ea**) + 2H (**3ea′**)), 7.19 (d, *J* = 2.1 Hz, 1H (**3ea**)), 7.12 (dd, *J* = 6.9, 2.9 Hz, 1H (**3ea**) + 1H (**3ea′**)), 7.09−6.98 (m, 5H (**3ea**) + 5H (**3ea′**)), 6.98−6.89 (m, 2H (**3ea**) + 2H (**3ea′**)), 6.84 (d, *J* = 3.7 Hz, 1H (**3ea′**)). ^{13}C NMR (151 MHz, $CDCl_3$): δ 165.8, 162.6, 157.8 (d, $^1J_{C-F}$ = 254.8 Hz), 142.1, 139.9, 134.4, 133.5, 133.1, 132.1, 130.6, 130.6, 130.4, 130.1, 130.1, 129.7, 129.7, 128.3, 128.1, 127.5, 127.5, 127.3, 127.2, 125.0, 125.0, 124.6, 122.0, 122.0, 121.1, 120.9, 120.5, 120.4, 120.4, 120.3, 114.4, 114.3, 110.8, 110.6, 109.3, 108.4.^{19}F NMR (564 MHz, $CDCl_3$): δ −97.3, −104.5, −110.2, −116.9. HRMS (positive ESI): calcd for Chemical Formula: Chemical Formula: $C_{20}H_{14}FN_2O_2$ $[M + H]^+$ 333.1034, found 333.1038.

*2-(1-Benzylidene-5-chloro-3-oxoisoindolin-2-yl)pyridine 1-Oxide (**3fa**)*[7e] *and 2-(3-Benzylidene-4-chloro-1-oxoisoindolin-2-yl)pyridine 1-Oxide (**3fa′**).* Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.30; white solid (31.8 mg, 61%); mp 198−199 °C (dichloromethane). **3fa**/**3fa′** = 65:35, *Z*:*E* (**3fa**) > 99%, *Z*:*E* (**3fa′**) > 99%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (dd, *J* = 12.4, 8.7 Hz, 2H (**3fa**) + 2H (**3fa′**)), 7.79 (dd, *J* = 18.6, 10.3 Hz, 1H (**3fa**) + 1H (**3fa′**)), 7.71−7.61 (m, 1H (**3fa**) + 1H (**3fa′**)), 7.47 (t, *J* = 7.7 Hz, 1H (**3fa′**)), 7.17−7.07 (m, 1H (**3fa**) + 3H (**3fa′**)), 7.07−6.98 (m, 5H (**3fa**) + 3H (**3fa′**)), 6.93 (dd, *J* = 14.4, 4.7 Hz, 2H (**3fa**) + 2H (**3fa′**)), 6.87 (s, 1H (**3fa**)). ^{13}C NMR (151 MHz, $CDCl_3$): δ 165.5, 139.9, 136.8 135.5, 135.3, 133.6, 133.4, 133.3, 133.0, 132.1, 131.8, 130.5, 129.7, 129.0, 128.9, 128.2, 128.2, 127.5, 127.5, 127.3, 127.2, 125.0, 124.9, 124.6, 124.6, 124.2, 123.2, 121.4, 114.6, 109.1. HRMS (positive ESI): calcd for $C_{20}H_{14}ClN_2O_2$ $[M + H]^+$ 349.0738, found 349.0740.

*2-(1-Benzylidene-5-bromo-3-oxoisoindolin-2-yl)pyridine 1-Oxide (**3ga**)*[7e] *and 2-(3-Benzylidene-4-bromo-1-oxoisoindolin-2-yl)-pyridine 1-Oxide (**3ga′**).* Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.44; white solid (31.7 mg, 57%); mp 199−200 °C (dichloromethane). **3ga**/**3ga′** = 70:30, *Z*:*E* (**3ga**) = 91:9, *Z*:*E* (**3ga′**) > 99%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, *J* = 1.6 Hz, 1H (**3ga**)), 8.02 (s, 1H (**3ga′**)), 7.96−7.94 (m, 1H (**3ga**) + 1H (**3ga′**)), 7.90 (d, *J* = 7.9 Hz, 1H (**3ga′**)), 7.80 (dd, *J* = 8.3, 1.7 Hz, 1H (**3ga**)), 7.73 (d, *J* = 8.3 Hz, 1H (**3ga**)), 7.62−7.50 (m, 1H (**3ga′**)),7.42−7.37 (m, 3H (**3ga′**)), 7.15−7.08 (m, 1H (**3ga**) + 2H (**3ga′**)), 7.06−7.01 (m, 5H (**3ga**) + 2H (**3ga′**)), 6.97−6.91 (m, 2H (**3ga**) + 2H (**3ga′**)), 6.89 (s, 1H (**3ga**)). ^{13}C NMR (151 MHz, $CDCl_3$): δ 165.4, 142.0, 139.9, 138.9, 137.2, 136.1, 132.9, 132.1, 129.9, 129.4, 129.1, 128.2, 127.5, 127.3, 127.2, 127.2, 125.0, 124.8, 123.3, 121.6, 113.9, 109.2. HRMS (positive ESI): calcd for $C_{20}H_{14}BrN_2O_2$ $[M + H]^+$ 393.0233, found 393.0235.

*(Z)-2-(3-Benzylidene-5-methyl-1-oxoisoindolin-2-yl)pyridine 1-Oxide (**3ha**).*[7e] Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.30; white solid (38.9 mg, 79%); mp 231−232 °C (dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (dd, *J* = 5.1, 2.8 Hz, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.65 (s, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.13−710 (m, 1H), 7.07−7.04 (m, 2H), 7.02−7.00 (m, 3H), 6.95−6.90 (m, 2H), 6.85 (s, 1H), 2.54 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.9, 144.0, 142.5, 139.9, 139.0, 133.5, 133.0, 130.5, 128.3, 127.5, 127.3, 127.0, 125.1, 124.7, 124.4, 124.1, 120.3, 107.7, 22.2. HRMS (positive ESI): calcd for $C_{21}H_{17}N_2O_2$ $[M + H]^+$ 329.1285, found 329.1285.

*(Z)-2-(3-Benzylidene-5-methoxy-1-oxoisoindolin-2-yl)pyridine 1-Oxide (**3ia**).*[7e] Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.25; white solid (41.3 mg, 80%); mp 172−173 °C (dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89−7.87 (m, 1H), 7.84 (d, *J* = 8.5 Hz, 1H), 7.28 (d, *J* = 2.1 Hz, 1H), 7.14−7.11 (m, 1H), 7.08−7.04 (m, 3H), 7.01−7.00 (m, 3H),6.95−6.90 (m, 2H), 6.83 (s, 1H), 3.95 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.6, 164.1, 142. 5, 140.9, 139.8, 133.3, 132.8, 128.3, 127.4, 127.3, 127.0, 125.8, 124.7, 124.5, 120.3, 116.9, 107.9, 103.9, 55.9. HRMS (positive ESI): calcd for $C_{21}H_{17}N_2O_3$ $[M + H]^+$ 345.1234, found 345.1235.

*2-(3-Benzylidene-1-oxo-5-phenylisoindolin-2-yl)pyridine 1-Oxide (**3ja**).*[7e] Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.28; white solid (33.1 mg, 57%); mp 140−141 °C (dichloromethane). *Z*:*E* = 94:6. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43−8.42 (m, 1H (*E*)), 8.03−7.99 (m, 2H (*Z*) + 1H (*E*)), 7.93−7.91 (m, 1H (*Z*)), 7.77−7.74 (m, 1H (*Z*)), 7.70−7.65 (m, 2H (*Z*) + 3H (*E*)), 7.53−7.49 (m, 2H (*Z*) + 2H (*E*)), 7.46−7.40 (m, 1H (*Z*) + 10H (*E*)), 7.17−7.14 (m, 1H (*Z*)), 7.09−7.07 (m, 2H (*Z*)), 7.03−7.01 (m, 3H (*Z*)), 6.96−6.94 (m, 3H (*Z*)), 6.18 (s, 1H (*E*)). ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.7, 146.5, 142.4, 140.3, 139.9, 139.2, 133.3, 132.9, 129.6, 129.1, 128.70, 128.4, 128.3, 127.5, 127.5, 127.3, 127.1, 126.3, 124.8, 124.7, 124.4, 118.7, 108.2. HRMS (positive ESI): calcd for $C_{26}H_{19}N_2O_2$ $[M + H]^+$ 391.1441, found 391.1443.

*2-(3-Benzylidene-5-fluoro-1-oxoisoindolin-2-yl)pyridine 1-Oxide (**3ka**).*[7e] Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.38; white solid (35.5 mg, 71%); mp 187−188 °C (dichloromethane). *Z*:*E* = 94:6. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95−7.89 (m, 2H), 7.50 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.26−7.22 (m, 1H), 7.16−7.13 (m, 1H), 7.07−7.02 (m, 5H), 6.96 (dd, *J* = 5.9, 2.9 Hz, 2H), 6.85 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.2 (d, $^1J_{C-F}$ = 251.5 Hz), 165.8, 142.1, 141.1, 141.0, 139.9, 132.9, 132.0, 132.0, 129.3, 128.8, 128.3, 127.5, 127.3, 127.2, 126.7, 126.6, 124.9, 124.5, 123.6, 117.4, 117.3, 109.3, 107.2, 107.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ −104.5. HRMS (positive ESI): calcd for $C_{20}H_{14}FN_2O_2$ $[M + H]^+$ 333.1034, found 333.1038.

*2-(3-Benzylidene-5-chloro-1-oxoisoindolin-2-yl)pyridine 1-Oxide (**3la**).* Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.33; white solid (33.5 mg, 67%); mp 104−107 °C (dichloromethane). *Z*:*E* = 72:28. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (s, 1H (*E*)), 7.92−7.84 (m, 2H (*Z*) + 3H (*E*)), 7.61−7.59 (m, 1H (*E*)), 7.52 (dd, *J* = 8.1, 1.6 Hz, 1H (*Z*)), 7.47−7.39 (m, 2H (*Z*) + 4H (*E*)), 7.19−7.09 (m, 1H (*Z*)), 7.09−6.99 (m, 4H (*Z*) + 3H (*E*)), 6.96 (d, *J* = 4.4 Hz, 2H (*Z*)), 6.87 (s, 1H (*Z*)), 6.19 (s, 1H (*E*)). ^{13}C NMR (151 MHz, $CDCl_3$): δ 165.9, 140.0, 139.9, 139.7, 132.9, 131.8, 130.0, 130.0, 129.4, 128.8, 128.5, 128.3, 127.5, 127.3, 127.2, 125.8, 125.6, 125.4, 124.9, 124.5, 123.7, 120.4, 113.4, 109.4. HRMS (positive ESI): calcd for $C_{20}H_{14}ClN_2O_2$ $[M + H]^+$ 349.0738, found 349.0740.

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*2-(3-Benzylidene-5-bromo-1-oxoisoindolin-2-yl)pyridine 1-Oxide (**3ma**).* Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.36; white solid (31.8 mg, 54%); mp 73−76 °C (dichloromethane). *Z*:*E* = 64:36. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (dd, *J* = 5.0, 2.9 Hz, 1H (*E*)), 8.02 (d, *J* = 1.3 Hz, 1H (*Z*)), 7.91 (dd, *J* = 5.1, 2.8 Hz, 1H (*Z*)), 7.80 (dd, *J* = 8.1, 3.8 Hz, 1H (*Z*) + 1H (*E*)), 7.68 (dt, *J* = 3.8, 2.1 Hz, 2H (*E*)), 7.63−7.54 (m, 2H (*Z*)), 7.46−7.35 (m, 2H (*Z*) + 4H (*E*)), 7.13 (dd, *J* = 6.3, 3.7 Hz, 1H (*Z*)), 7.08−6.99 (m, 3H (*Z*) + 3H (*E*)), 7.00−6.92 (m, 1H (*Z*) + 1H (*E*)), 6.85 (d, *J* = 14.3 Hz, 1H (*Z*)), 6.19 (s, 1H (*E*)). ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.0, 140.9, 140.2, 139.9, 132.8, 132.6, 131.7, 129.4, 128.8, 128.5, 128.4, 128.3, 128.0, 127.5, 127.3, 127.2, 126.7, 126.2, 126.1, 125.7, 125.5, 125.4, 125.0, 124.5, 123.4, 113.4, 109.5. HRMS (positive ESI): calcd for $C_{20}H_{14}BrN_2O_2$ $[M + H]^+$ 393.0233, found 393.0236.

*2-(3-Benzylidene-5-iodo-1-oxoisoindolin-2-yl)pyridine 1-Oxide (**3na**).*[7e] Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.43; white solid (43.4 mg, 66%); mp 206−207 °C (dichloromethane). *Z*:*E* = 87:13. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42−8.41 (m, 1H (*E*)), 8.24 (d, *J* = 0.9 Hz,1H (*Z*)), 7.92−7.88 (m, 2H (*Z*)), 7.84−7.80 (m, 2H (*E*)), 7.66 (dd, *J* = 8.0, 4.0 Hz, 1H$_{[Z]}$+1H (*E*)), 7.60−7.58 (m, 1H (*E*)), 7.43−7.40 (m, 7H (*E*)), 7.14−7.11 (m, 1H (*Z*)), 7.05−7.03 (m, 5H (*Z*)), 6.96−6.93 (m, 2H (*Z*)), 6.86 (s, 1H (*Z*)), 6.18 (s, 1H (*E*)). ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.2, 140.0, 139.9, 138.4, 132.9, 131.5, 129.4, 129.4, 128.8, 128.2, 127.5, 127.3, 127.2, 126.8, 125.6, 125.0, 124.5, 109.4, 100.2. HRMS (positive ESI): calcd for $C_{20}H_{14}IN_2O_2$ $[M + H]^+$ 441.0094, found 441.0097.

*2-(3-Benzylidene-1-oxo-5-(trifluoromethyl)isoindolin-2-yl)-pyridine 1-Oxide (**3oa**).*[7e] Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.39; white solid (34.4 mg, 60%); mp 200−201 °C (dichloromethane). *Z*:*E* = 78:22. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (d, *J* = 3.2 Hz, 1H (*E*)), 8.13 (s, 1H (*Z*)), 8.06 (t, *J* = 6.7 Hz, 1H (*Z*) + 1H (*E*)), 8.01−7.90 (m, 1H (*Z*) + 1H (*E*)), 7.80 (d, *J* = 7.9 Hz, 1H (*Z*)), 7.73 (d, *J* = 8.0 Hz, 1H (*E*)), 7.66−7.61 (m, 2H (*E*)), 7.45−7.38 (m, 2H (*Z*) + 1H (*E*)), 7.17−7.14 (m, 1H (*Z*)), 7.08−7.01 (m, 4H (*Z*) + 3H (*E*)), 7.00−6.95 (m, 2H (*Z*) + 2H (*E*)), 6.27 (s, 1H (*E*)). ^{13}C NMR (151 MHz, $CDCl_3$): δ 165.5, 139.9, 138.8, 132.7, 131.9, 130.1, 129.3, 128.8, 128.7, 128.2, 127.6, 127.5, 127.2, 126.1, 126.1, 125.1, 125.0, 124.8, 124.8, 123.6 (q, $^1J_{C-F}$ = 272.0 Hz), 117.5, 117.5, 113.9, 110.1. ^{19}F NMR (564 MHz, $CDCl_3$): δ −62.6, −63.0. HRMS (positive ESI): calcd for $C_{21}H_{14}F_3N_2O_2$ $[M + H]^+$ 383.1002, found 383.1005.

*(Z)-2-(3-Benzylidene-4,6-dimethoxy-1-oxoisoindolin-2-yl)pyridine 1-Oxide (**3pa**).*[7e] Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.22; white solid (28 mg, 50%); mp 217−218 °C (dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (dd, *J* = 6.4, 1.3 Hz, 1H), 7.31 (s, 1H), 7.07−7.03 (m, 4H), 7.02−6.96 (m, 3H), 6.93−6.83 (m, 2H), 6.74 (d, *J* = 2.0 Hz, 1H), 3.99 (s, 3H), 3.90 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.8, 162.0, 156.5, 142.7, 139.8, 134.6, 131.9, 130.6, 128.2, 127.4, 127.3, 126.6, 124.6, 124.3, 119.4, 112.2, 104.31, 98.4, 56.0, 55.8. HRMS (positive ESI): calcd for $C_{22}H_{19}N_2O_4$ $[M + H]^+$ 375.1339, found 375.1343.

*(Z)-2-(4-Benzylidene-6-oxo-4,6-dihydro-5H-thieno[2,3-c]pyrrol-5-yl)pyridine 1-Oxide (**3qa**).* Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.21; white solid (24.7 mg, 52%); mp 86−89 °C (dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (d, *J* = 6.6 Hz, 1H), 7.79 (d, *J* = 5.1 Hz, 1H), 7.41−7.39 (m, 2H), 7.29−7.22 (m, 4H), 7.18−7.14 (m, 2H), 7.10−7.06 (m, 1H), 6.76 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 157.8, 145.8, 145.2, 144.6, 140.1, 134.9, 134.8, 129.2, 128.8, 128.3, 128.1, 127.9, 125.6, 125.1, 124.7, 105.1. HRMS (positive ESI): calcd for $C_{18}H_{13}N_2O_2S$ $[M + H]^+$ 321.0692, found 321.0694.

*(Z)-2-(6-Benzylidene-4-oxo-4,6-dihydro-5H-thieno[2,3-c]pyrrol-5-yl)pyridine 1-Oxide (**3ra**).* Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.17; white solid (14.1 mg, 30%); mp 233−236 °C (dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (t, *J* = 9.3 Hz, 1H), 7.69 (d, *J* = 5.3 Hz, 1H), 7.41−7.39 (m, 2H), 7.33 (d, *J* = 5.3 Hz, 1H), 7.27−7.21(m, 3H), 7.18−7.06 (m, 3H), 6.81 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 158.2, 148.6, 145.4, 143.5, 140.1, 134.6, 129.5, 129.3, 128.3, 128.0, 127.8, 125.7, 125.6, 125.1, 124.8, 103.8. HRMS (positive ESI): calcd for $C_{18}H_{13}N_2O_2S$ $[M + H]^+$ 321.0692, found 321.0694.

*2-(7-Benzylidene-5-oxo-3,4,5,7-tetrahydropyrano[2,3-c]pyrrol-6(2H)-yl)pyridine 1-Oxide (**3sa**).* Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.19; white solid (15.4 mg, 32%); mp 173−176 °C (dichloromethane). *Z*:*E* = 76:24. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36−8.34 (m, 1H (*E*)), 7.87 (dd, *J* = 6.2, 1.5 Hz, 1H (*Z*)), 7.51−7.45 (m, 1H (*Z*)), 7.37−7.32 (m, 2H$_{[E]}$), 7.31−7.24 (m, 2H$_{[E]}$), 7.12 (dd, *J* = 7.7, 2.2 Hz, 1H (*Z*)), 7.02−6.97 (m, 5H (*Z*) + 1H (*E*)), 6.96−6.90 (m, 1H (*Z*) + 3H (*E*)), 6.52 (s, 1H (*Z*)), 5.90 (s, 1H (*E*)), 4.43−4.34 (m, 2H (*Z*)), 4.31−4.20 (m, 2H (*E*)), 2.52−2.36 (m, 2H (*Z*) + 2H (*E*)), 2.10−1.97 (m, 2H (*Z*) + 2H (*E*)). ^{13}C NMR (151 MHz, $CDCl_3$): δ 168.8, 162.6, 142.3, 140.7, 139.7, 132.9, 130.4, 130.2, 128.9, 128.3, 127.9, 127.8, 127.4, 127.2, 125.5, 125.4, 124.6, 124.2, 113.8, 109.0, 107.1, 103.9, 69.2, 68.9, 21.4, 20.9, 16.9, 16.6. HRMS (positive ESI): calcd for $C_{19}H_{17}N_2O_3$ $[M + H]^+$ 321.1234, found 321.1236.

*(Z)-2-(1-(4-Fluorobenzylidene)-3-oxoisoindolin-2-yl)pyridine 1-Oxide (**3ab**).*[7e] Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (6:1) as an eluent: R_f = 0.33; white solid (35.1 mg, 71%); mp 219−220 °C (dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96−7.91 (m, 2H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.70 (td, *J* = 7.8, 1.0 Hz, 1H), 7.58−7.54 (m, 1H), 7.17−7.15 (m, 1H), 7.07−7.00 (m, 4H), 6.82 (s, 1H), 6.74−6.70 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.8, 161.7 (d, $^1J_{C-F}$ = 246.9 Hz), 142.3, 139.9, 138.4, 133.2, 130.1, 130.1, 129.5, 129.3, 129.3, 128.3, 127.5, 127.5, 127.3, 124.9, 124.5, 124.4, 120.0, 114.5, 114.3, 106.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ −114.0. HRMS (positive ESI): calcd for $C_{20}H_{14}FN_2O_2$ $[M + H]^+$ 333.1034, found 333.1033.

*(Z)-2-(1-(4-Chlorobenzylidene)-3-oxoisoindolin-2-yl)pyridine 1-Oxide (**3ac**).*[7e] Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.43; white solid (34.1 mg, 65%); mp 249−250 °C (dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95−7.90 (m, 2H), 7.84 (d, *J* = 7.84 Hz, 1H), 7.70 (td, *J* = 7.7, 1.0 Hz, 1H), 7.58−7.52 (m, 1H), 7.17 (dt, *J* = 7.6, 3.5 Hz, 1H), 7.04−7.01 (m, 2H), 7.00−6.97 (m, 4H),6.80 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.7, 142.3, 139.9, 138.3, 133.4, 133.2, 133.0, 131.8, 129.7, 129.5, 127.5, 127.4, 127.3, 124.9, 124.6, 124.4, 120.0, 106.7. HRMS (positive ESI): calcd for $C_{20}H_{14}ClN_2O_2$ $[M + H]^+$ 349.0738, found 349.0739.

*(Z)-2-(1-(4-Bromobenzylidene)-3-oxoisoindolin-2-yl)pyridine 1-Oxide (**3ad**).*[7e] Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.47; white solid (32.8 mg, 56%); mp 227−228 °C (dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95−7.90 (m, 2H), 7.84 (d, *J* = 7.8 Hz, 1H), 7.72−7.68 (m, 1H), 7.58−7.54 (m, 1H), 7.18−7.13 (m, 3H), 7.07−7.00 (m, 2H), 6.94 (d, *J* = 8.1 Hz, 2H), 6.78 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.7, 142.3, 140.0, 138.3, 133.4, 133.2, 132.3, 130.5, 130.0, 129.6, 127.5, 127.3, 124.9, 124.6, 124.4, 121.2, 120.0, 106.6. HRMS (positive ESI): calcd for $C_{20}H_{14}BrN_2O_2$ $[M + H]^+$ 393.0233, found 393.0236.

*(Z)-2-(1-(4-Methylbenzylidene)-3-oxoisoindolin-2-yl)pyridine 1-Oxide (**3ae**).*[7e] Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.33; white solid (38.4 mg, 78%); mp 212−213 °C (dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (dd, *J* = 4.6, 2.8 Hz, 2H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.68 (td, *J* = 7.7, 1.0 Hz, 1H), 7.55−7.52 (m, 1H), 7.12 (dd, *J* = 7.4, 2.5 Hz, 1H), 6.99−6.92 (m, 4H), 6.87 (s, 1H), 6.82 (d, *J* = 7.9 Hz, 2H), 2.20 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.8, 142.5, 139.9, 138.7, 136.9, 133.0, 132.6, 130.4, 129.2, 128.2, 128.2, 127.4, 127.3, 124.5, 124.4, 124.3, 119.9, 108.4, 21.1. HRMS (positive ESI): calcd for $C_{21}H_{17}N_2O_2$ $[M + H]^+$ 329.1285, found 329.1289.

*2-(1-(4-(tert-Butyl)benzylidene)-3-oxoisoindolin-2-yl)pyridine 1-Oxide (**3af**).*[7e] Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.42; white solid (24.6 mg, 44%); mp 168−169 °C (dichloromethane). *Z*:*E* = 94:6. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, *J* = 7.6 Hz, 1H), 7.90 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.86 (d, *J* = 7.8, 1H), 7.71−7.67 (m, 1H), 7.56−7.52 (m, 1H), 7.10−7.08 (m, 1H), 7.04−6.98 (m, 4H), 6.92−6.89 (m, 3H), 1.21 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.8, 150.0, 142.5, 139.8, 138.6, 133.0, 132.9, 130.4, 129.2, 128.0, 127.5, 127.3, 124.5, 124.3, 124.3,

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120.0, 108.3, 34.4, 31.2. HRMS (positive ESI): calcd for $C_{24}H_{23}N_2O_2$ $[M + H]^+$ 371.1754, found 371.1752.

*2-(1-(3-Methylbenzylidene)-3-oxoisoindolin-2-yl)pyridine 1-Oxide (**3ag**).*[7e] Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.45; white solid (36 mg, 73%); mp 103−104 °C (dichloromethane). *Z*:*E* = 93:7. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42−8.40 (m, 1H (*E*)) 7.97−7.93 (m, 2H (*Z*) + 1H (*E*)), 7.85 (d, *J* = 7.8 Hz, 1H (*Z*)), 7.69 (td, *J* = 7.7, 1.0 Hz, 1H (*Z*)), 7.60−7.52 (m, 1H (*Z*) + 2H (*E*)), 7.48−7.46 (m, 2H (*E*)) 7.43−7.38 (m, 3H (*E*)) 7.17−7.12 (m, 1H (*Z*) + 1H (*E*)), 6.98−6.82 (m, 7H (*Z*) + 2H (*E*)), 6.12 (s, 1H (*E*)), 2.36 (s, 3H (*E*))2.15 (s, 3H (*Z*)). ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.9, 142.5, 139.8, 138.7, 137.0, 133.3, 133.0, 132.7, 129.3, 129.1, 127.9, 127.5, 127.4, 127.1, 125.5, 124.7, 124.3, 120.0, 108.4, 21.1. HRMS (positive ESI): calcd for $C_{21}H_{17}N_2O_2$ $[M + H]^+$ 329.1285, found 329.1282.

*2-(1-(3-Methoxybenzylidene)-3-oxoisoindolin-2-yl)pyridine 1-Oxide (**3ah**).*[7e] Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.39; white solid (38 mg, 74%); mp 146−147 °C (dichloromethane). *Z*:*E* = 95:5. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42−8.40 (m, 1H (*E*)), 7.96 (dd, *J* = 16.9, 7.0 Hz, 2H (*Z*)), 7.84 (d, *J* = 7.8 Hz, 1H (*Z*)), 7.69 (t, *J* = 7.6 Hz, 1H (*Z*)), 7.55 (t, *J* = 7.5 Hz, 1H (*Z*) + 1H (*E*)), 7.49−7.46 (m, 3H (*E*)), 7.44−7.37 (m, 4H (*E*)), 7.08 (dt, *J* = 12.1, 6.1 Hz, 1H (*Z*)), 7.03 (d, *J* = 7.84 Hz, 2H (*E*)), 7.00−6.90 (m, 3H (*Z*) + 1H (*E*)), 6.85 (s, 1H (*Z*)), 6.65 (t, *J* = 5.4 Hz, 2H (*Z*)), 6.57 (dd, *J* = 8.2, 2.0 Hz, 1H (*Z*)), 6.12 (s, 1H (*E*)), 3.79 (s, 3H (*E*)) 3.71 (s, 3H (*Z*)). ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.8, 158.9, 142.5, 139.8, 138.5, 134.8, 133.2, 133.1, 129.4, 128.6, 127.5, 127.1, 124.8, 124.5, 124.3, 120.8, 120.0, 113.4, 113.3, 107.9, 55.1. HRMS (positive ESI): calcd for $C_{21}H_{17}N_2O_3$ $[M + H]^+$ 345.1234, found 345.1231.

*(Z)-2-(1-(3-Chlorobenzylidene)-3-oxoisoindolin-2-yl)pyridine 1-Oxide (**3ai**).*[7e] Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.43; white solid (42.8 mg, 82%); mp 149−150 °C (dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96−7.94 (m, 2H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.70 (td, *J* = 7.7, 1.0 Hz, 1H), 7.58−7.55 (m, 1H), 7.22 (dd, *J* = 7.6, 2.4 Hz, 1H), 7.06−6.96 (m, 6H), 6.79 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.8, 142.2, 140.0, 138.3, 135.1, 133.6, 133.3, 133.2, 129.6, 128.7, 128.5, 127.5, 127.2, 127.2, 126.7, 125.1, 124.7, 124.4, 120.1, 106.3. HRMS (positive ESI): calcd for $C_{20}H_{14}ClN_2O_2$ $[M + H]^+$ 349.0738, found 349.0733.

*(Z)-2-(1-(3-Bromobenzylidene)-3-oxoisoindolin-2-yl)pyridine 1-Oxide (**3aj**).*[7e] Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.45; pale yellow oil (41.5 mg, 71%).^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96−7.94 (m, 2H), 7.84 (d, *J* = 8.6 Hz, 1H), 7.72−7.68 (m, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.23 (dd, *J* = 7.7, 2.2 Hz, 1H), 7.16−7.15 (m, 2H), 7.09−7.00 (m, 3H), 6.96−6.92 (m, 1H), 6.78 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.8, 142.1, 140.0, 138.3, 135.4, 133.6, 133.2, 131.4, 130.1, 129.6, 129.0, 127.5, 127.2, 127.2, 125.1, 124.8, 124.4, 121.4, 120.1, 106.2. HRMS (positive ESI): calcd for $C_{20}H_{14}BrN_2O_2$ $[M + H]^+$ 393.0233, found 393.0235.

*2-(1-(2-Methylbenzylidene)-3-oxoisoindolin-2-yl)pyridine 1-Oxide (**3ak**).*[7e] Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.38; white solid (31.5 mg, 64%); mp 188−189 °C (dichloromethane). *Z*:*E* = 89:11. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43−8.41 (m, 1H (*E*)), 7.94 (t, *J* = 8.1 Hz, 1H (*Z*) + 1H (*E*)), 7.89 (d, *J* = 7.8 Hz, 1H (*Z*)), 7.85−7.83 (m, 1H (*Z*)), 7.71 (td, *J* = 7.7, 1.0 Hz, 1H (*Z*)), 7.60 (dt, *J* = 7.8, 4.2 Hz, 1H (*E*)), 7.56 (dd, *J* = 11.0, 4.0 Hz, 1H (*Z*)), 7.46 (t, *J* = 7.2 Hz, 1H (*E*)), 7.38 (ddd, *J* = 13.4, 7.4, 1.5 Hz, 4H (*E*)), 7.32−7.28 (m, 2H (*E*)), 7.24−7.19 (m, 1H (*E*)), 7.10 (ddd, *J* = 18.8, 10.1, 5.2 Hz, 1 (*Z*) + 1H (*E*)), 6.97 (t, *J* = 8.2 Hz, 1H (*Z*)), 6.94−6.87 (m, 4H (*Z*)), 6.80 (s, 1H (*Z*)), 6.72 (t, *J* = 7.4 Hz, 1H (*Z*)), 6.08 (s, 1H (*E*)), 2.32 (s, 3H (*Z*)), 2.28 (s, 3H (*E*)). ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.9, 142.1, 139.6, 138.4, 136.8, 133.0, 133.0, 132.4, 129.3, 129.1, 128.7, 127.6, 127.5, 127.0, 124.8, 124.7, 124.3, 124.2, 120.1, 107.6, 20.3. HRMS (positive ESI): calcd for $C_{21}H_{17}N_2O_2$ $[M + H]^+$ 329.1285, found 329.1284.

*(Z)-2-(1-Oxo-3-(3-phenylpropylidene)isoindolin-2-yl)pyridine 1-Oxide (**3al**).* Purified by analytical TLC on silica gel with CH_2Cl_2/acetone (4/1) as an eluent: R_f = 0.49; white solid (9.3 mg, 18%); mp 103−106 °C (dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, *J* = 5.7 Hz, 1H), 8.35 (d, *J* = 7.9 Hz, 1H), 7.67 (t, *J* = 7.1 Hz, 1H), 7.50−7.36 (m, 5H), 7.24−7.16 (m, 3H), 7.03 (d, *J* = 7.0 Hz, 2H), 6.49 (s, 1H), 2.96−2.83 (m, 2H), 2.75−2.67 (m, 1H), 2.49−2.41 (m, 1H).^{13}C NMR (151 MHz, $CDCl_3$): δ 140.7, 133.3, 128.6, 128.4, 128.3, 128.1, 126.6, 126.4, 126.1, 125.8, 105.5, 34.3, 33.9. HRMS (positive ESI): calcd for $C_{22}H_{19}N_2O_2$ $[M + H]^+$ 343.1441, found 343.1445.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00129.

^{1}H NMR and ^{13}C NMR spectra for new compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail for J.-L.N.: niujunlong@zzu.edu.cn.

*E-mail for M.-P.S.: mpsong@zzu.edu.cn.

Notes

The authors declare no competing financial interest.

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