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Metal-Free Iodine(III)-Promoted Synthesis of Isoquinolones

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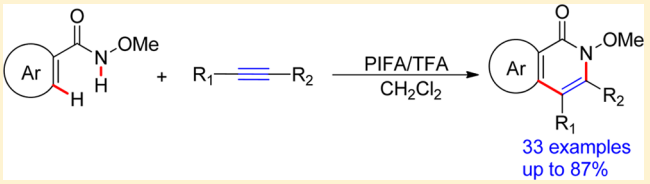
Supporting Information

ABSTRACT: A metal-free oxidative cycloaddition reaction of substituted benzamides and alkynes has been developed for the synthesis of isoquinolones by using bis(trifluoracetoxy)-iodobenzene (PIFA) and trifluoroacetic acid (TFA). Under mild conditions, a wide variety of isoquinolones were conveniently prepared via oxidative annulation of simple *N*-methoxybenzamide and diarylacetylene or aryl/alkyl acetylene derivatives in yields up to 87%.



INTRODUCTION

Isoquinolone is an important molecular skeleton in natural alkaloids, and compounds containing this skeleton have shown unique biological activities.[1] Great efforts have therefore been devoted to establishing some efficient methods to achieve the synthesis of isoquinolone in recent years.[2] A clear majority of those approaches employed transition metal catalysts, such as palladium, rhodium, ruthenium, and nickel catalysts (Scheme 1). Palladium catalyst has been widely applied in the reaction of prefunctionalized substrates,[3] including highly reactive intermediate acyl azide.[4] Similar high energy species benzotriazinone has recently been transformed into isoquinolone by nickel catalyst.[5] With the same non-noble metal catalyst, substrates with a halogen substituent or pyridine directing group worked well to produce the isoquinolone.[6] Prefunctionalization usually makes the substrates nonavailable and expensive to prepare; hence, the cycloaddition strategy with simple benzamide and alkyne reactants has recently emerged. Use of rhodium catalyst within this strategy was reported in 2010 by Fagnou's and Rovis's groups, respectively, and was an improvement.[7] Ruthenium-catalyzed C−H and N−H activation pathways have also been applied to synthesize isoquinolone in satisfactory yields.[8] The aforementioned palladium-catalyzed reaction was successfully extended to this annulation of simple benzamide and alkyne by Huang's group.[9] Besides the transition-metal-catalyzed cycloaddition methods, the electrophilic cyclization of *o*-(1-alkynyl)benzamides with nonmetal reagents can also yield the isoquinolone.[10] However, the approaches mentioned above mostly depended on transition metal catalysts or started from complex substrates; thus, there remains a great challenge to develop a convenient and easily accessible metal-free method to obtain this kind of product.

Hypervalent iodine reagents have been extensively used in organic synthesis owing to their unusual oxidation, low toxicity, commercial availability, and environmental friendliness.[11] Consequently, organic trivalent iodine-mediated C−C,[12] C−N,[13] C−O,[14] and N−N[15] bond formation reactions have become a convenient method to synthesize various functional molecules and heterocyclic compounds. Very recently, Antonchick and co-workers reported a regioselective annulation of *N*-alkoxybenzamide derivatives with alkynes to synthesize isoquinolone derivatives using hypervalent iodine catalyst which was generated in situ from peroxyacetic acid and iodobenzene in trifluoroethanol.[16] Herein, we present another metal-free intermolecular oxidative annulation for the synthesis of isoquinolone from simple *N*-methoxybenzamide derivatives and disubstituted acetylene. Besides the diarylacetylene, aryl/alkyl acetylene was also found to be suitable for this transformation. With DCM as solvent, a wide variety of isoquinolone compounds were easily prepared using this PIFA-mediated method in the presence of TFA.

RESULTS AND DISCUSSION

The readily available *N*-methoxybenzamide **1a** and diphenylacetylene **2a** were initially selected as the model substrates to screen the reaction conditions. As shown in Table 1, PIFA was found to be more efficient than (bisacetoxy)iodobenzene (PIDA) and iodosylbenzene in DCM (entries 1−3). The effect of solvents was further investigated with PIFA as an oxidant. When the weak polar aprotic solvents $CHCl_3$ and DCE were used, the yield of **3aa** was 19% and 33%, respectively (entries 4 and 5). In the polar protic solvent MeOH, and polar aprotic solvents 1,4-dioxane, ethyl acetate, and DMF, **3aa** was not obtained (entries 7−10). The reaction was also observed to be strongly suppressed in MeCN, and no reaction occurred in THF (entries 11 and 12). Trifluoroethanol gave a result similar to that for DCM, due to its weaker nucleophilicity compared to MeOH. Although reactions in DCM, DCE, and CF_3CH_2OH gave nearly equal yield, DCM was finally selected as the solvent for subsequent studies in view of economic cost.

Effect of additive on the reaction was further explored, and the results are summarized in Table 1 (entries 13−22). Lewis acids such as $BF_3{\cdot}Et_2O$, TMSOTf, $Cu(OTf)_2$, CuCl, Cu-

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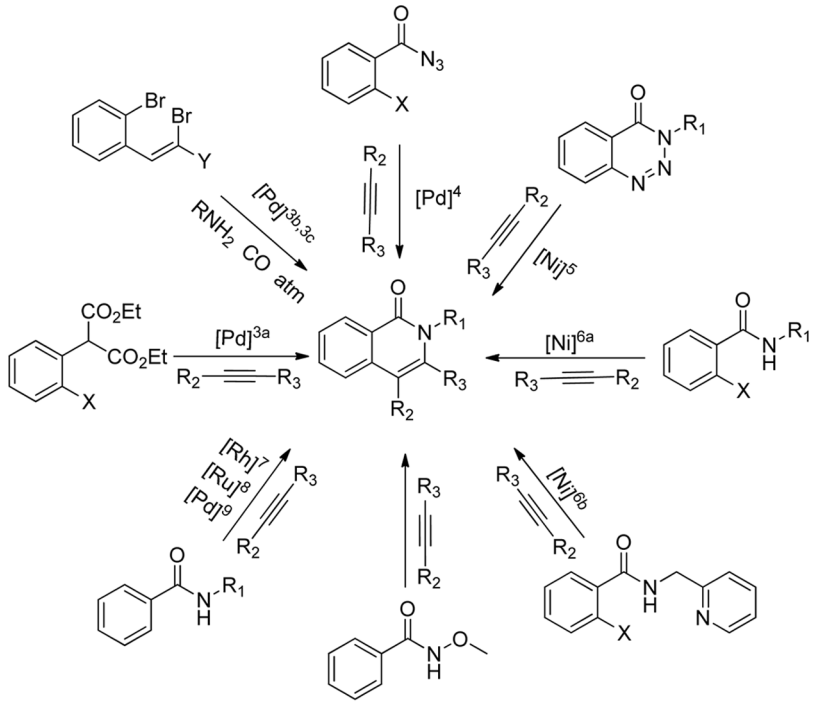
Scheme 1. Transition-Metal-Catalyzed Synthesis of Isoquinolone



$(OAc)_2$, and AgOTf all show promotion of the reaction (entries 13−18). Protonic acids such as acetic acid, TfOH, TsOH, and TFA were also tested, and the addition of TFA was observed to significantly increase the yield of **3aa** up to 56% (entries 19−22) and show higher efficiency in comparison to other additives.

With PIFA as oxidant and TFA as additive, we continued to investigate the effect of temperature, equivalent ratio of the reactants, and concentration in sequence (see Tables S1 and S2 in Supporting Information for details). When the reaction temperature was lowered to −20 °C, the yield of **3aa** was increased to 59% (entry 23). Furthermore, the equivalent ratio and concentration of reactants both showed great influence on the yields of **3aa** (entries 24−26). To our delight, under the optimized conditions, the yield of **3aa** was finally improved to 84% (entry 26).

The substrate scope of this method was studied. Various substituents such as alkyl, halogen, and aryl were introduced to the phenyl ring of *N*-methoxybenzamide first, and the product structures and results are depicted in Scheme 2. Electronic effect and steric effect both have great influence on the yield of product. Substrates with weak electron-donating groups such as **1b** and **1c** were found to decrease the yields of products (**3ba** and **3ca**) in varying degrees compared with **3aa**. Interestingly, replacing the weak electron-donating groups with a methoxy group resulted in a kind of spirodienone instead of isoquinolone (Scheme 3). That can be attributed to the occurrence of demethylation, similar to that reported for iodine(III)-mediated Kita's oxidation reaction of phenol derivatives.[17] When halogen atoms were introduced to the phenyl ring (**1d**, **1e**, and **1f**), the yields increased in accordance with the decreasing order of the electron-withdrawing ability of the substituents (**3da**−**3fa**). Substrates with a nitro substituent, a strong electron-withdrawing group, were found to be inert under the same condition. A higher yield for **3ba** than for **3ga** may be due to the steric effect of the methyl group in the phenyl ring of **1b** and **1g**. When 3-methylbenzamide **1j** was used as the precursor, a regioisomer mixture was obtained because of the very close polarity, and the ratio of 7-methylisoquinolone (Scheme 2, **3ja**) to 5-methylisoquinolone (Scheme 2, **3j′a**) was evaluated to be 2:1 by ^{1}H NMR (see Supporting Information for details). In addition, substrates containing biphenylene, naphthalene, and thiophene also worked well and gave the desired product in moderate yields.

The substituent effect of alkyne was further explored. As shown in Scheme 4, five other symmetrical and three unsymmetrical alkynes were prepared and applied in the annulation reaction. Substituents on the phenyl ring of diphenylacetylene showed great influence on the yield of compound **3**. Electron-donating groups both enhanced the reactivity of alkynes **2** and stabilized the intermediate of the reaction. For example, the presence of weak electron-withdrawing chloro decreased the yield of **3ad** obviously in comparison to compound **3aa**. When a nitro group was introduced to the diphenylacetylene, the resulting alkyne was found to be inert under the same condition. In the meantime, a weak electron-donating group such as methyl resulted in a slight increase of the yield (**3ab**). Notably, diphenylacetylene containing a strong electron-donating methoxy group and electron-rich 1,2-di(thiophen-2-yl)ethyne underwent complete transformation without additive TFA (**3ac**, **3ag**). Because of poor solubility of **2e** in dichloromethane, product **3ae** was prepared in 51% yield with 40% recovery of **2e**. With respect to unsymmetrical alkynes, the structure of the product becomes relatively complicated. Unsymmetrical alkynes having a tiny discrepancy in the electron density of the end-substituents resulted in a product mixture. For instance, a 75% yield in a ratio of 1:2 (**3ai**:**3ai′**) was obtained for the alkyne substrate **2i**.

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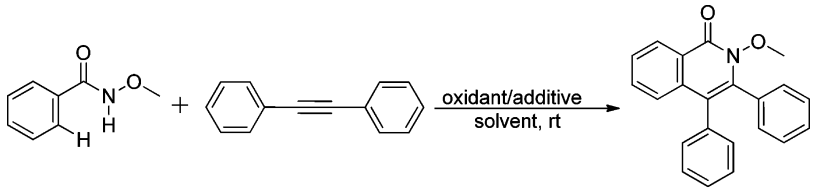
Table 1. Optimization of Oxidative Annulation of Benzamide and Alkyne[a]



1a **2a** **3aa**

entry	oxidant	additive	solvent	t (h)	yield (%)[b]
1	iodosylbenzene	–	DCM	24	n.d
2	PIDA	–	DCM	24	n.d
3	PIFA	–	DCM	0.2	34
4	PIFA	–	$CHCl_3$	0.2	19
5	PIFA	–	DCE	0.2	33
6	PIFA	–	CF_3CH_2OH	0.2	32
7	PIFA	–	MeOH	3	n.d
8	PIFA	–	dioxane	3	n.d
9	PIFA	–	EtOAc	3	n.d
10	PIFA	–	DMF	3	n.d
11	PIFA	–	MeCN	2	9
12	PIFA	–	THF	2	n.d
13	PIFA	$BF_3{\cdot}Et_2O$	DCM	0.1	45
14	PIFA	TMSOTf	DCM	0.1	42
15	PIFA	$Cu(OTf)_2$	DCM	3	39
16	PIFA	CuCl	DCM	6	37
17	PIFA	$Cu(OAc)_2$	DCM	3	35
18	PIFA	AgOTf	DCM	2	47
19	PIFA	CH_3COOH	DCM	2	34
20	PIFA	CF_3SO_3H	DCM	0.1	28
21	PIFA	TsOH	DCM	3	21
22	PIFA	TFA	DCM	0.5	56
23[c]	PIFA	TFA	DCM	1	59
24[d]	PIFA	TFA	DCM	1	69
25[e]	PIFA	TFA	DCM	0.5	78
26[f]	PIFA	TFA	DCM	0.5	84

[a]The reaction was performed under argon atmosphere with **1a** (0.17 mmol), **2a** (0.17 mmol), oxidant (0.17 mmol), and additive (0.17 mmol). Unless otherwise stated, reactions were carried out at room temperature with 0.1 M reactant concentration. [b]Isolated yield. [c]The reaction was performed at −20 °C. [d]The reaction was performed at −20 °C with **1a** (0.25 mmol), **2a** (0.17 mmol), PIFA (0.34 mmol), and TFA (0.17 mmol). The concentration of **2a** was 0.1 M. [e]The reaction was performed at −20 °C with **1a** (0.25 mmol), **2a** (0.17 mmol), PIFA (0.34 mmol), and TFA (0.85 mmol). The concentration of **2a** was 0.1 M. [f]Kept the same reaction condition as in footnote *e* except the concentration was diluted two-fold.

In the case of unsymmetrical acetylenes such as *p*-anisylphenylacetylene and phenyl(2-thienyl)acetylene, which have a larger electron density difference between the two end-substituents, excellent regioselectivity was observed (**3ag** and **3ah**). This indicates that only one product is obtained if the difference of electron density between two end-substituents of the acetylene is large enough.

To our delight, an unsymmetrical alkyne with an aryl end-substituent and an alkyl end-substituent can also be transformed into isoquinolone (Scheme 5). Using (3-methoxy-1-propynyl)benzene **2j** as substrate gave compound **3aj** and another isoquinolone **3ak** in 12% and 19% yield, respectively. This product mixture might be attributed to the decomposition of (3-methoxy-1-propynyl)benzene to yield another substrate phenylpropiolaldehyde in situ because we failed to transform **3aj** into **3ak** under the same oxidative annulation condition. With phenylpropiolaldehyde **2k** as reactant, the reaction gave compound **3ak** in 21% yield. The structure of **3ak** was further confirmed by single crystal diffraction analysis. Compared to the yield of diarylacetylene substrate, it seems that the alkyl group cannot sufficiently stabilize the reaction intermediate and causes alot of side products. Although the yield is relatively low at this moment, the regioselectivity of the reaction with aryl/alkyl acetylenes is excellent, in that only one isomer can be observed.

The methoxy group of isoquinolone products was efficiently removed according to a literature method.[9b,16] When compound **3aa** was treated with 3 equiv of sodium hydride in DMF at 120 °C for 2 h, isoquinolin-1(2*H*)-one **4a** was obtained in 87% yield (Scheme 6).

On the basis of the properties of PIFA[18] and the characteristics of iodine(III)-mediated intramolecular cyclization of benzamide derivatives, a plausible mechanism for the formation of isoquinolone is shown in Scheme 7. First, PIFA oxidized benzamide **1** to give intermediate **A**. Intermediate **A** might experience two reaction processes, path a and path b. In path a, nucleophilic attack by **2** on intermediate **A** generates **E** while the release of iodobenzene and trifluoroacetic acid to form nitrenium **B** occurs before nucleophilic attack by **2** in path b. A possible alternate path c begins with activation of the C≡

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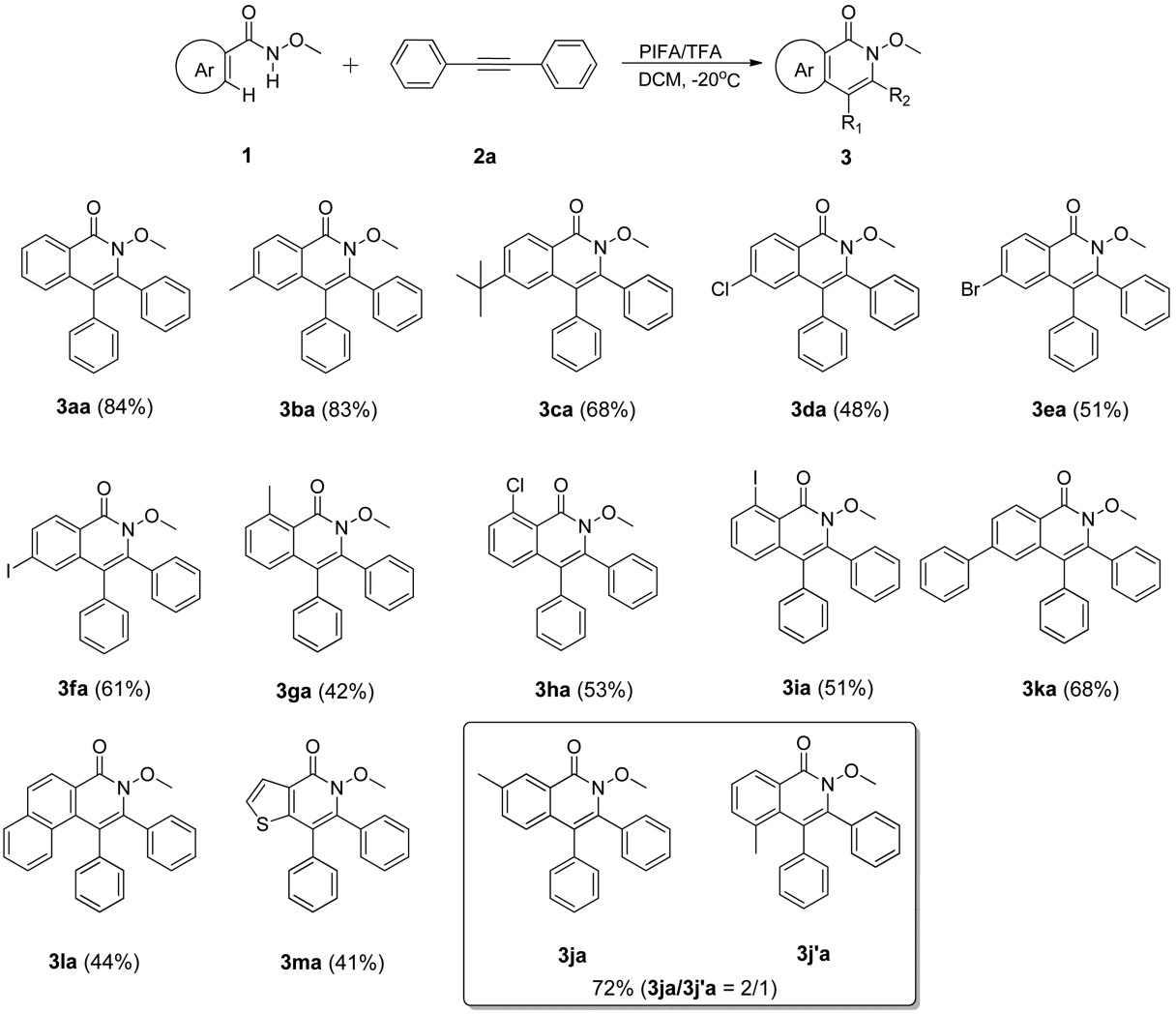
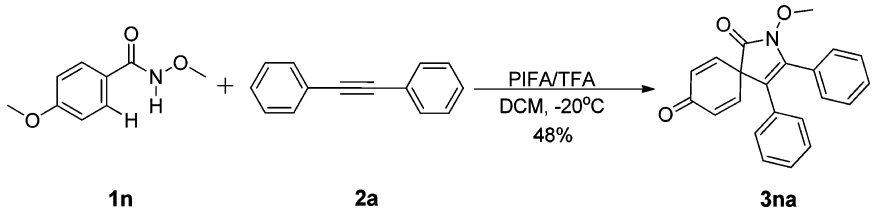
Scheme 2. PIFA-Mediated Oxidative Annulation with Various Benzamide Derivatives[a]



[a]The reaction was performed at −20 °C under argon atmosphere with **1a** (0.25 mmol), **2a** (0.17 mmol), PIFA (0.34 mmol), and TFA (0.85 mmol). The concentration of **2a** was 0.05 M.

Scheme 3. PIFA-Mediated Oxidative Spirocyclization



C bond by PIFA to give electrophilic intermediate **C**, which then reacts with nucleophilic amide **1** to yield intermediate **D**,[19] releasing iodobenzene and $CF_3COO_3^-$ from **D** to finally reach the same intermediate **E** as in the other paths. The final cyclization was achieved through an intramolecular electrophilic reaction of intermediate **F**. We obtained positive support for path b. Treating nitrenium **B**, obtained by reacting *N*-chloro-*N*-methoxybenzamide and Ag_2CO_3 in TFA,[20] with diphenylacetylene led to isoquinolone **3aa** in 40% yield. Unfortunately, because of the relatively low yield for path b, the other pathways cannot be ruled out at this moment.

CONCLUSION

In summary, PIFA-mediated intermolecular oxidative annulation of *N*-methoxybenzamide and disubstituted acetylene has been achieved. In the presence of TFA, a wide variety of isoquinolones were conveniently synthesized from simple *N*-methoxybenzamide and diarylacetylene or aryl/alkyl acetylene derivatives using this metal-free method. Electronic and steric effects are discussed, and some fused or heterocyclic compounds were also obtained efficiently. Compared to the transition-metal-catalyzed method, the relative moderate oxidation ability of the hypervalent iodine reagent might benefit the reaction of unsymmetrical alkynes to give excellent

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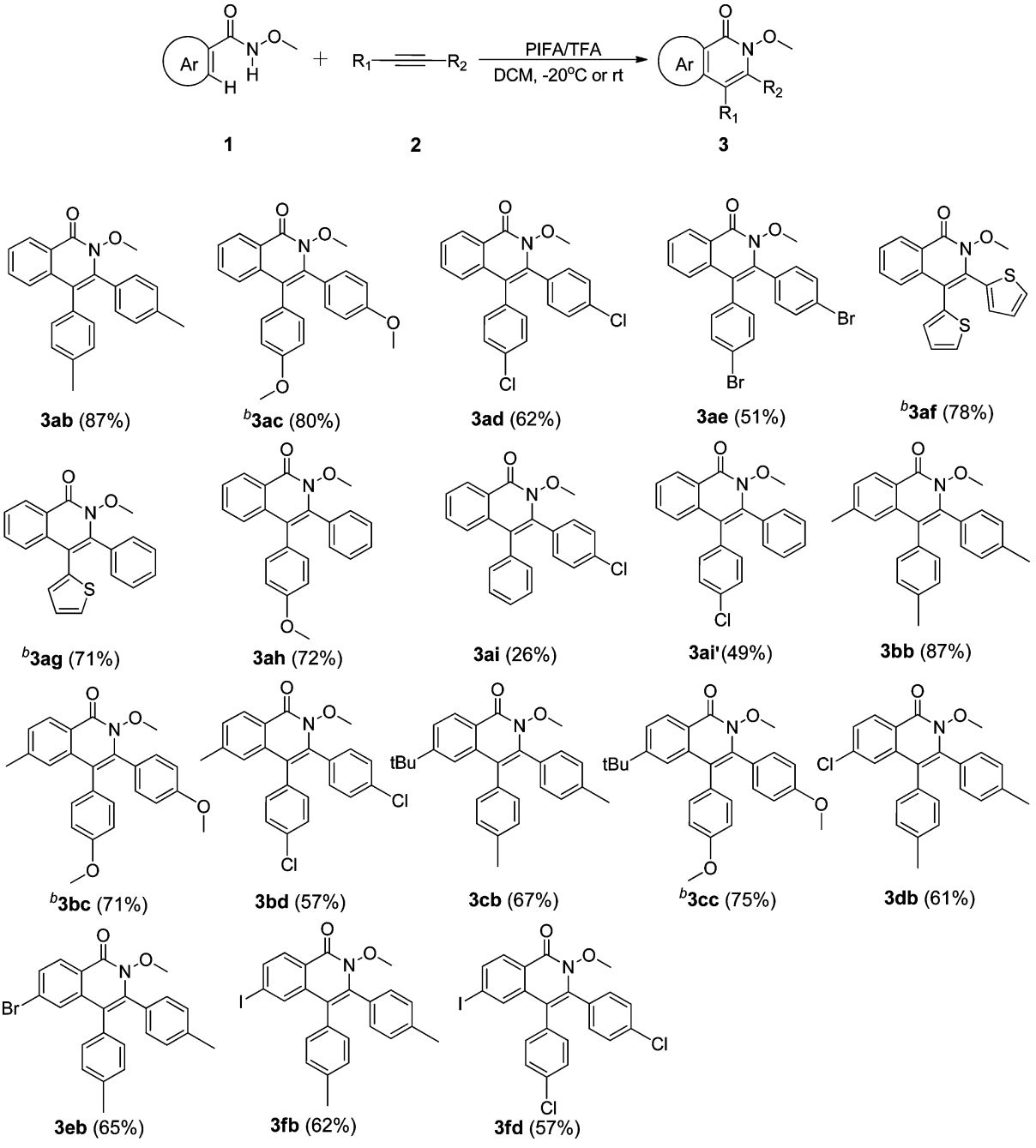
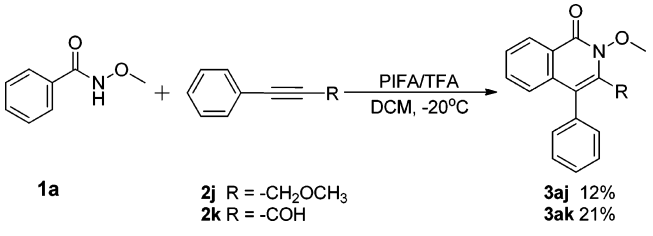
Scheme 4. PIFA-Mediated Oxidative Annulation with Symmetrical and Unsymmetrical Alkynes[a]

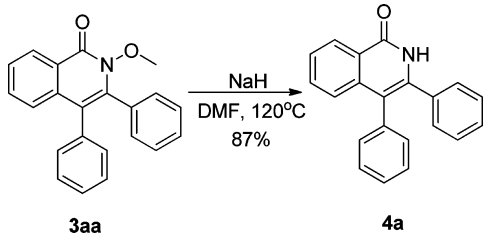


[a]The reactions were performed at −20 °C under argon atmosphere with **1** (0.25 mmol), **2** (0.17 mmol), PIFA (0.34 mmol), and TFA (0.85 mmol). The concentration of **2** was 0.05 M. [b]Without TFA, reactants were added at −20 °C and then warmed from −20 °C to rt.

Scheme 5. PIFA-Mediated Oxidative Annulation with Aryl/Alkyl Alkynes



Scheme 6. Removal of the Methoxy Group from Isoquinolone 3aa



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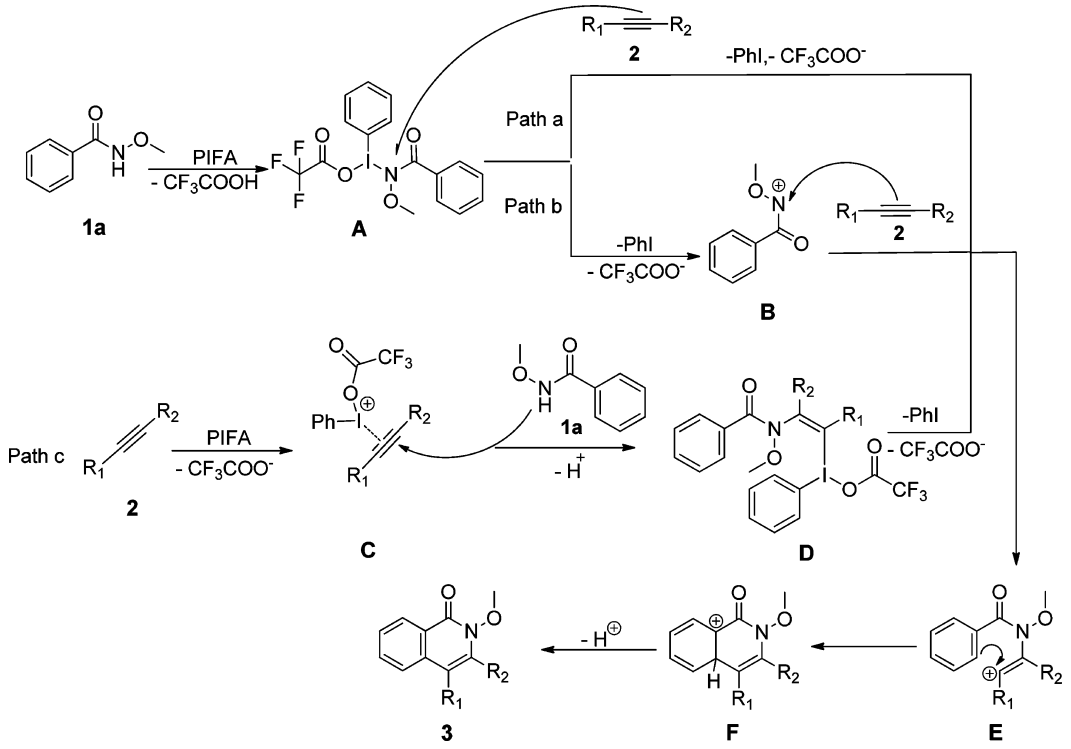
Scheme 7. Plausible Mechanistic Pathway



regioselectivity. Studies toward the spirocyclization reaction are currently underway in our laboratory.

EXPERIMENTAL SECTION

General Methods. All NMR solvents were used as received. Other solvents used in reactions were distilled and purified by standard procedures. The hypervalent iodine reagents PIDA,[21] PIFA,[22] and iodosylbenzene[23] were prepared according to literature methods. Amide substrates[24] and alkynes[25] were synthesized according to the reported procedures. Chemical shifts of NMR spectra were reported in ppm downfield shift from internal Me_4Si. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; qui, quintet; m, multiplet; dd, doublet of doublets. The high-resolution mass spectra were recorded in positive-ion mode on a Q-TOF instrument equipped with an ESI ion source.

General Procedure for the Synthesis of Amide 1. To a solution of the carboxylic acid (3.3 mmol, 1 equiv) in dry DCM (10 mL) was added oxalyl chloride (0.34 mL, 4.0 mmol, 1.2 equiv) dropwise at 0 °C, followed by a catalytic amount of dry DMF (2 drops). The reaction was stirred at room temperature until the acid was completely consumed (typically 8 h). The solvent was removed under vacuum to afford the corresponding crude acyl chloride.

Methoxyamine hydrochloride (334.1 mg, 4.0 mmol, 1.2 equiv) was added to a biphasic mixture of K_2CO_3 (912.1 mg, 6.6 mmol, 2 equiv) in a mixture of EtOAc (24 mL) and H_2O (12 mL). The mixture was cooled to 0 °C, and then acyl chloride in a minimum amount of EtOAc was added dropwise. The reaction was stirred 8 h at room temperature. The organic phase was separated, and the aqueous phase was extracted twice with EtOAc and dried over $MgSO_4$. The solvent was evaporated to give the product.

General Procedure for the Synthesis of Alkyne 2. *Method A: Symmetrical Diarylacetylene.* To an oven-dried 25 mL round-bottom flask were added $Pd(PPh_3)_2Cl_2$ (67.4 mg, 6 mol %), CuI (30.5 mg, 10 mol %), and either iodide or bromine compound (1.6 mmol, 1 equiv), and the flask was purged with argon. Argon-sparged anhydrous toluene (8 mL) and DBU (1.43 mL, 6 equiv) were added successively by syringe. Ice-chilled trimethylsilylethyne (104.5 μL, 0.50 equiv) was then added by syringe, followed immediately by distilled water (11.5 μL, 40 mol %). The reaction flask was covered by aluminum foil and stirred at a high rate of speed for 18 h at a designated temperature (0 °C, 60 °C, or 80 °C). Then the reaction mixture was partitioned in ethyl ether and distilled water (50 mL each). The organic layer was washed with 10% HCl (3 × 75 mL) and saturated aqueous NaCl (75 mL) and dried over $MgSO_4$. The crude product was purified by silica gel column chromatography (eluent: EtOAc/petroleum ether).

Method B: Unsymmetrical Diarylacetylene. To an oven-dried 25 mL round-bottom flask were added $Pd(PPh_3)_2Cl_2$ (67.4 mg, 6 mol %), CuI (30.5 mg, 10 mol %), and iodoarene (1 equiv, 1.6 mmol), and the flask was purged with argon. Argon-sparged anhydrous toluene (8 mL) and NEt_3 (1.34 mL, 6 equiv) were added successively by syringe. Ice-chilled trimethylsilylethyne (219.4 μL, 1.05 equiv) was then added by syringe. The reaction flask was covered in aluminum foil and stirred at a high rate of speed for 18 h. After that, another iodoarene (0.8 equiv, 1.28 mmol), DBU (2.87 mL, 12 equiv), and distilled water (11.5 μL, 40 mol %) were added. The mixture was stirred for another 18 h and then partitioned in ethyl ether and distilled water (50 mL each). The organic layer was washed with 10% HCl (3 × 75 mL) and saturated aqueous NaCl (75 mL) and dried over $MgSO_4$. The crude product was purified by silica gel column chromatography (eluent: EtOAc/petroleum ether).

*(3-Methoxy-1-propynyl)benzene (**2j**).* 3-Phenyl-2-propyn-1-ol (200.0 mg, 1.51 mmol) and 60% NaH (120.8 mg, 3.02 mmol) were added to 5 mL of anhydrous THF, and the system was cooled to 0 °C. After CH_3I (428.7 mg, 3.02 mmol) was added dropwise, the reaction was stirred at room temperature and monitored by TLC. Upon completion, saturated NH_4Cl was added at 0 °C, and the reaction was extracted with DCM (3 × 10 mL). The combined organic layer was washed with water and brine and dried with Na_2SO_4. The solvent was evaporated to give the product. Yellow oil, 179.2 mg, 81% yield, R_f = 0.16 (petroleum ether). ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 (dd, J = 4.0, 2.0 Hz, 2H), 7.26−7.21 (m, 3H), 4.25 (s, 2H), 3.38 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.8, 128.5, 128.3, 122.7, 86.4, 84.9, 60.4, 57.7.

*3-Phenylpropiolaldehyde (**2k**).* To a solution of DDQ (34.3 mg, 0.151 mmol) in 5 mL of DCM and 0.5 mL of AcOH was added 3-phenylprop-2-yn-1-ol (200.0 mg, 1.51 mmol), followed by $NaNO_2$ (10.4 mg, 0.151 mmol). The solution was stirred under oxygen

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atmosphere for 10 h. Upon completion, the solvent was concentrated in vacuo, and the product was further purified by column chromatography (R_f = 0.38, EtOAc/petroleum ether = 1:15) to afford 3-phenylpropiolaldehyde (139.8 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.42 (s, 1H), 7.60 (t, J = 7.6 Hz, 2H), 7.48 (t, J = 8.4 Hz, 1H), 7.42 (d, J = 7.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.9, 133.3, 131.4, 128.8, 119.4, 95.2, 88.5.

General Procedure for the Oxidative Annuluation Reaction. To an oven-dried 10 mL reaction tube were added amide **1** (0.25 mmol, 1.5 equiv) and alkyne **2** (0.17 mmol, 1 equiv) under argon atmosphere. Dry DCM (2 mL) was then added by syringe, and the resultant mixture was cooled to −20 °C. A solution of PIFA (0.34 mmol, 2 equiv) and TFA (0.85 mmol, 5 equiv) in 1.4 mL of dry DCM was then dropped into the reaction. After that, the mixture was stirred at designated temperature (−20 °C or room temperature) and monitored by TLC. Upon completion, 3 mL of saturated $NaHCO_3$ was added, the mixture was stirred for 10 min and extracted with DCM (3 × 5 mL). The combined organic layer was washed with brine (20 mL) and dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by silica gel chromatography (eluent: EtOAc/petroleum ether) to afford the desired product **3**.

Procedure for the Synthesis of 4a. To a solution of **3aa** (0.2 mmol, 65 mg) in 2 mL of DMF was added NaH (0.6 mmol, 14.4 mg), and the resultant mixture was heated at 120 °C for 2 h. After the reaction was completed, the mixture was cooled to room temperature, 5 mL of H_2O was added and extracted with DCM (3 × 5 mL), and the organic layer was combined and dried over Na_2SO_4. Futher purification by silica gel chromatography (eluent: EtOAc/petroleum ether) afforded 3,4-diphenylisoquinolin-1(2*H*)-one (**4a**) as a white amorphous solid (51.4 mg, 87% yield). R_f = 0.15 (EtOAc/petroleum ether = 1/3), mp 249−251 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.50 (s, 1H), 8.47 (d, J = 7.8 Hz, 1H), 7.64−7.56 (m, 1H), 7.50 (t, J = 7.2 Hz, 1H), 7.40−7.14 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 138.7, 137.1, 135.8, 135.1, 132.7, 131.9, 129.3, 128.7, 128.4, 128.4, 127.5, 127.3, 126.6, 125.7, 125.1, 171.3. FT-IR: ν = 3025, 2889, 1647, 1607, 1553, 1490, 1346, 1313, 1265, 1155, 1030 cm^{-1}. HRMS-ESI [M + H]$^+$ calcd for $C_{21}H_{16}NO$: 298.1232, found 298.1232.

***N*-Methoxybenzamide (1a).** White amorphous solid, 458.9 mg, 92% yield, R_f = 0.21 (EtOAc/petroleum ether = 1/2), mp 61−62 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.78−7.76 (m, 2H), 7.50 (t, J = 7.2 Hz, 1H), 7.40 (t, J = 7.6 Hz, 2H), 3.84 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 132.0, 131.8, 128.6, 127.1, 64.4.

***N*-Methoxy-4-methylbenzamide (1b).** White amorphous solid, 485.2 mg, 89% yield, R_f = 0.21 (EtOAc/petroleum ether = 1/2), mp 69−70 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (s, 1H), 7.58 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 7.6 Hz, 2H), 3.74 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 141.5, 128.2, 127.9, 126.1, 63.3, 20.5.

4-*tert*-Butyl-*N*-methoxybenzamide (1c). White amorphous solid, 581.4 mg, 85% yield, R_f = 0.26 (EtOAc/petroleum ether = 1/2), mp 62−63 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.45 (s, 1H), 7.63 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.8 Hz, 2H), 3.77 (s, 3H), 1.23 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 155.6, 128.9, 126.9, 125.6, 64.4, 35.0, 31.1.

4-Chloro-*N*-methoxybenzamide(1d). White amorphous solid, 502.3 mg, 82% yield, R_f = 0.23 (EtOAc/petroleum ether = 1/2), mp 104−105 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.64 (s, 1H), 7.57 (d, J = 4.0 Hz, 2H), 7.23 (d, J = 8.4 Hz, 2H), 3.69 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 138.3, 130.1, 128.9, 128.6, 64.4.

4-Bromo-*N*-methoxybenzamide (1e). White amorphous solid, 584.6 mg, 77% yield, R_f = 0.23 (EtOAc/petroleum ether = 1/2), mp 113−115 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.33 (s, 1H), 7.62 (d, J = 8.4 Hz, 2H), 7.54 (d, J = 8.4 Hz, 2H), 3.85 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.8, 132.0, 130.6, 128.8, 126.9, 64.6.

4-Iodo-*N*-methoxybenzamide (1f). White amorphous solid, 740.6 mg, 81% yield, R_f = 0.24 (EtOAc/petroleum ether = 1/2), mp 135−136 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 (s, 1H), 7.79 (d, J = 7.2 Hz, 2H), 7.50 (d, J = 6.8 Hz, 2H), 3.86 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 137.90, 131.2, 128.7, 99.2, 64.5.

***N*-Methoxy-2-methylbenzamide (1g).** White amorphous solid, 457.9 mg, 84% yield, R_f = 0.24 (EtOAc/petroleum ether = 1/2), mp 104−105 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 7.34 (m, 2H), 7.26−7.16 (m, 2H), 3.88 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 136.8, 132.6, 130.9, 130.4, 127.2, 125.6, 64.4, 19.4.

2-Chloro-*N*-methoxybenzamide (1h). White amorphous solid, 465.5 mg, 76% yield, R_f = 0.26 (EtOAc/petroleum ether = 1/2), mp 112−113 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 7.43 (d, J = 6.8 Hz, 1H), 7.27−7.20 (m, 2H), 7.19−7.13 (m, 1H), 3.75 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 132.2, 131.9, 131.1, 130.3, 130.2, 127.1, 64.7.

2-Iodo-*N*-methoxybenzamide (1i). White amorphous solid, 749.7 mg, 82% yield, R_f = 0.24 (EtOAc/petroleum ether = 1/2), mp 96−98 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.26 (s, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.29−7.17 (m, 2H), 7.01 (t, 7.2 Hz, 1H), 3.77 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 139.8, 138.5, 131.7, 128.7, 128.1, 93.2, 64.4.

***N*-Methoxy-3-methylbenzamide (1j).** Colorless oil, 474.3 mg, 87% yield, R_f = 0.27 (EtOAc/petroleum ether = 1/2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (s, 1H), 7.51−7.46 (m, 2H), 7.21−7.15 (m, 2H), 3.73 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 138.4, 132.7, 131.7, 128.4, 127.9, 124.2, 64.2, 21.3.

***N*-Methoxybiphenyl-4-carboxamide (1k).** White amorphous solid, 570.0 mg, 76% yield, R_f = 0.20 (EtOAc/petroleum ether = 1/2), mp 175−176 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 7.60 (d, J = 8.0 Hz, 2H), 7.42 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 7.6 Hz, 2H), 7.24 (t, J = 7.2 Hz, 2H), 7.17 (t, J = 7.2 Hz, 1H), 3.69 (s, 3H), ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 145.0, 139.8, 130.5, 129.0, 128.2, 127.6, 127.4, 127.2, 64.7.

***N*-Methoxy-2-naphthamide (1l).** White amorphous solid, 451.5 mg, 68% yield, R_f = 0.21 (EtOAc/petroleum ether = 1/2), mp 127−128 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.43 (s, 1H), 8.18 (s, 1H), 7.76−7.69 (m, 4H), 7.49−7.41 (m, 2H), 3.82 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 134.9, 132.5, 129.0, 128.9, 128.6, 127.9, 127.9, 127.8, 126.9, 123.4, 64.6.

***N*-Methoxythiophene-3-carboxamide (1m).** White amorphous solid, 352.7 mg, 68% yield, R_f = 0.26 (EtOAc/petroleum ether = 1/2), mp 84−85 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.01 (s, 1H), 7.95 (s, 1H), 7.40 (d, J = 4.8 Hz, 1H), 7.25 (dd, J = 4.8, 2.8 Hz, 1H), 3.75 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 134.0, 129.4, 126.5, 126.2, 64.5.

***N*-Methoxy-4-methoxylbenzamide (1n).** White amorphous solid, 460.4 mg, 77% yield, R_f = 0.15 (EtOAc/petroleum ether = 1/1), mp 100−101 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.61 (s, 1H), 7.72 (d, J = 8.4 Hz, 2H), 7.01 (d, J = 8.4 Hz, 2H), 3.79 (s, 3H), 3.69 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 164.3, 162.3, 129.3, 124.8, 114.2, 63.7, 55.8.

1,2-Diphenylethyne (2a). Method A, white crystalline solid, 91.3 mg, 64% yield, R_f = 0.64 (petroleum ether), mp 58−59 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66−7.56 (m, 4H), 7.50−7.36 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.7, 128.4, 128.3, 123.3, 89.4.

1,2-Di-*p*-tolylethyne (2b). Method A, yellow crystalline solid, 138.6 mg, 84% yield, R_f = 0.48 (petroleum ether), mp 135−137 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.0 Hz, 4H), 7.16 (d, J = 7.6 Hz, 4H), 2.36 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.2, 131.5, 129.1, 120.4, 88.9, 21.6.

1,2-Bis(4-methoxyphenyl)ethyne (2c). Method A, yellow amorphous solid, 133.4 mg, 70% yield, R_f = 0.42 (EtOAc/petroleum ether = 1/95), mp 144−145 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (t, J = 8.8 Hz, 4H), 6.79 (d, J = 8.8 Hz, 4H), 3.75 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 132.9, 115.7, 114.0, 88.0, 55.3.

1,2-Bis(4-chlorophenyl)ethyne (2d). Method A, yellow amorphous solid, 177.9 mg, 90% yield, R_f = 0.79 (petroleum ether), mp 176−178 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 8.5 Hz, 4H), 7.25 (d, J = 8.4 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.5, 132.8, 128.8, 121.4, 89.2.

1,2-Bis(4-bromophenyl)ethyne (2e). Method A, gray amorphous solid, 201.6 mg, 75% yield, R_f = 0.76 (petroleum ether), mp 182−184 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 8.0 Hz, 4H),

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7.38 (d, J = 8.4 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.0, 131.7, 122.8, 121.9, 89.4.

1,2-Di(thiophen-2-yl)ethyne (2f). Method A, white amorphous solid, 130.9 mg, 86% yield, R_f = 0.62 (petroleum ether), mp 97−99 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.17 (m, 4H), 6.92 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 132.2, 127.7, 127.2, 122.9, 86.3

2-(Phenylethynyl)thiophene (2g). Method B, red amorphous solid, 150.9 mg, 64% yield, R_f = 0.53 (petroleum ether), mp 48−50 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51−7.44 (m, 2H), 7.34−7.27 (m, 3H), 7.24 (s, 2H), 6.99−6.95 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.9, 131.44 128.4, 128.4, 127.3, 127.1, 123.3, 122.9, 93.1, 82.6.

1-Methoxy-4-(phenylethynyl)benzene (2h). Method B, green amorphous solid, 181.3 mg, 68% yield, R_f = 0.14 (petroleum ether), mp 57−59 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47−7.37 (m, 4H), 7.28−7.22 (m, 3H), 6.83−6.78 (m, 2H), 3.76 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 133.1, 131.5, 128.3, 128.0, 123.6, 115.4, 114.0, 89.4, 88.1, 55.3.

1-chloro-4-(phenylethynyl)benzene (2i). Method B, white amorphous solid, 215.1 mg, 79% yield, R_f = 0.55 (petroleum ether), mp 82−84 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 7.2 Hz, 2H), 7.49 (d, J = 8.2 Hz, 2H), 7.43−7.32 (m, 5H). ^{13}C NMR (101 MHz,$CDCl_3$) δ 134.2, 132.8, 131.6, 128.7, 128.5, 128.4, 122.9, 121.8, 90.3, 88.3.

2-Methoxy-3,4-diphenylisoquinolin-1(2*H*)-one (3aa). White amorphous solid, 46.8 mg, 84% yield, R_f = 0.35 (EtOAc/petroleum ether = 1/5), mp 188−190 °C. ^{1}H NMR (400 MHz, acetone-d_6) δ 8.47 (d, J = 7.6 Hz, 1H), 7.66 (t, J = 7.2 Hz, 1H), 7.58 (t, J = 3.2 Hz, 1H), 7.43−7.39 (m 2H), 7.30−7.15 (m, 9H), 3.74 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2, 140.0, 136.5, 135.5, 132.3, 131.7, 131.6, 130.7, 128.3, 128.1, 127.8,127.5, 127.2, 126.8, 126.4, 125.8, 118.3, 63.5. FT-IR: ν = 3061, 2932, 1663, 1606, 1553, 1491, 1480, 1444, 1322, 1265, 1175, 1003, 971 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for $C_{22}H_{18}NO_2$: 328.1338, found 328.1328. (When 1 mmol of substrate **2a** was used, 271.2 mg of **3aa** was obtained in a yield of 83%.)

2-Methoxy-6-methyl-3,4-diphenylisoquinolin-1(2*H*)-one (3ba). White amorphous solid, 48.2 mg, 83% yield, R_f = 0.24 (EtOAc/petroleum ether = 1/5), mp 196−198 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.41 (d, J = 8.4 Hz, 1H), 7.29−7.22 (m, 8H), 7.19 (d, J = 8.4 Hz, 1H), 7.12 (d, J = 7.2 Hz, 2H), 3.75 (s, 3H), 2.54 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2, 139.0, 137.0, 135.6, 134.2, 133.8, 131.7, 131.6, 130.8, 128.2, 128.1, 127.5, 127.4, 127.1, 126.3, 125.8, 118.4, 63.4, 21.3. FT-IR: ν = 3163, 2934, 1663, 1630, 1591, 1496, 1443, 1414, 1334, 998 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for $C_{23}H_{20}NO_2$: 342.1494, found 342.1486.

6-*tert*-Butyl-2-methoxy-3,4-diphenylisoquinolin-1(2*H*)-one (3ca). White amorphous solid, 44.3 mg, 68% yield, R_f = 0.26 (EtOAc/petroleum ether = 1/5), mp 203−205 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, J = 1.6 Hz, 1H), 7.66 (dd, J = 8.4, 2.0 Hz, 1H), 7.27−7.20 (m, 9H), 7.11 (d, J = 2 Hz, 2H), 3.75 (s, 3H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4, 150.3, 139.2, 135.6, 134.2, 131.7, 131.6, 130.8, 130.3, 128.2, 128.1, 127.5, 127.1, 126.1, 125.7, 123.6, 118.2, 63.4, 35.0, 31.3. FT-IR: ν = 3058, 2962, 1665, 1612, 1588, 1493, 1442, 1333, 1264, 1178 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for $C_{26}H_{26}NO_2$: 384.1964, found 384.1956.

6-Chloro-2-methoxy-3,4-diphenylisoquinolin-1(2*H*)-one (3da). Yellow amorphous solid, 29.5 mg, 48% yield, R_f = 0.55 (EtOAc/petroleum ether = 1/5), mp 155−157 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, J = 2 Hz, 1H), 7.52 (dd, J = 8.4, 2 Hz, 1H), 7.28−7.21 (m, 9H), 7.13−7.08 (m, 2H), 3.76 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.2, 140.3, 135.0, 134.9, 133.0, 132.7, 131.5, 131.3, 130.6, 128.5, 128.3, 127.6, 127.5, 127.5, 127.4, 127.2, 117.9, 63.6. FT-IR: ν = 3059, 2934, 1666, 1589, 1492, 1477, 1443, 1329, 1173, 1129, 1074, 1032, 1015 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for $C_{22}H_{17}ClNO_2$: 362.0948, found 362.0948.

6-Bromo-2-methoxy-3,4-diphenylisoquinolin-1(2*H*)-one (3ea). White amorphous solid, 35.2 mg, 51% yield, R_f = 0.38 (EtOAc/petroleum ether = 1/5), mp 191−193 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, J = 2 Hz, 1H), 7.65 (dd, J = 8.4, 1.6 Hz, 1H), 7.29−7.22 (m, 8H), 7.15 (d, J = 8.8 Hz, 1H), 7.10 (d, J = 7.2 Hz, 2H), 3.75 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.0, 144.3, 140.5, 135.4, 135.3, 135.0, 131.5, 131.3, 130.6, 130.3, 128.5, 128.3, 127.7, 127.6, 127.4, 120.9, 117.9, 63.6. FT-IR: ν = 3058, 2933, 1665, 1618, 1491, 1474, 1327, 1266, 1172, 1032, 1014, 971 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for $C_{22}H_{17}BrNO_2$: 406.0443, found 406.0431.

6-Iodo-2-methoxy-3,4-diphenylisoquinolin-1(2*H*)-one (3fa). Yellow amorphous solid, 47.0 mg, 61% yield, R_f = 0.42 (EtOAc/petroleum ether = 1/5), mp 139−142 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (d, J = 1.6 Hz, 1H), 7.84 (dd, J = 8.8, 1.6 Hz, 1H), 7.27−7.21 (m, 8H), 7.11−7.06 (m, 2H), 7.00 (d, J = 8.4 Hz, 1H), 3.74 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.9, 141.0, 140.8, 136.5, 135.7, 134.9, 131.5, 131.3, 130.5, 128.5, 128.2, 127.8, 127.6, 127.5, 127.4, 118.0, 91.9, 63.6. FT-IR: ν = 3058, 2930, 1665, 1588, 1490, 1471, 1443, 1323, 1173, 1126, 1072, 1031, 1011, 969 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for $C_{22}H_{17}INO_2$: 454.0304, found 454.0291.

2-Methoxy-8-methyl-3,4-diphenylisoquinolin-1(2*H*)-one (3ga). White amorphous solid, 24.4 mg, 42% yield, R_f = 0.18 (EtOAc/petroleum ether = 1/5), mp 187−189 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (dd, J = 7.6, 1.6 Hz, 1H), 7.45−7.37 (m, 2H), 7.21−7.14 (m, 5H), 7.13−7.10 (m, 3H), 7.07 (m, 2H), 3.76 (s, 3H), 1.76 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2, 140.6, 138.8, 136.6, 135.5, 134.5, 132.2, 132.0, 130.5, 127.9, 127.8, 127.5, 127.3, 126.9, 126.6, 126.6, 118.1, 63.5, 23.9. FT-IR: ν = 3053, 2939, 1653, 1586, 1490, 1444, 1351, 1323, 1310, 1027, 1001 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for $C_{23}H_{20}NO_2$: 342.1494, found 342.1485.

8-Chloro-2-methoxy-3,4-diphenylisoquinolin-1(2*H*)-one (3ha). Yellow amorphous solid, 32.6 mg, 53% yield, R_f = 0.22 (EtOAc/petroleum ether = 1/5), mp 175−177 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 8.0 Hz, 1H), 7.64 (d, J = 7.6 Hz, 1H), 7.43 (t, J = 8 Hz, 1H), 7.21−7.13 (m, 5H), 7.11−7.07 (m, 3H), 7.05−7.01 (m, 2H), 3.76 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4, 142.2, 137.1, 136.2, 132.8, 132.0, 131.6, 131.2, 130.3, 129.1, 128.2, 127.4, 127.4, 127.3, 127.0, 126.9, 116.6, 63.6. FT-IR: ν = 3057, 2929, 1663, 1593, 1576, 1491, 1442, 1303, 1125, 1013 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for $C_{22}H_{17}ClNO_2$: 362.0948, found 362.0947.

8-Iodo-2-methoxy-3,4-diphenylisoquinolin-1(2*H*)-one (3ia). Yellow amorphous solid, 39.3 mg, 51% yield, R_f = 0.34 (EtOAc/petroleum ether = 1/5), mp 159−161 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (dd, J = 8.0, 1.2 Hz, 1H), 8.34 (dd, J = 7.6, 1.2 Hz, 1H), 7.22−7.18 (m, 3H), 7.16−7.11 (m, 6H), 6.98−7.01 (m, 2H), 3.79 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4, 148.6, 142.3, 135.8, 135.1, 134.0, 131.9, 130.3, 129.0, 128.8, 128.1, 127.7, 127.6, 127.6, 127.4, 118.2, 91.1, 63.6. FT-IR: ν = 3056, 2934, 1662, 1586, 1568, 1536, 1492, 1442, 1353, 1298, 1170, 1102, 1010 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for $C_{22}H_{17}INO_2$: 454.0304, found 454.0289.

2-Methoxy-3,4,6-triphenylisoquinolin-1(2*H*)-one (3ka). White amorphous solid, 46.6 mg, 68% yield, R_f = 0.20 (EtOAc/petroleum ether = 1/5), mp 195−197 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, J = 1.6 Hz, 1H), 7.76−7.74 (dd, J = 8.8, 1.6 Hz, 1H), 7.66 (d, J = 7.6 Hz, 2H), 7.41 (t, J = 7.6 Hz, 2H), 7.32 (t, J = 7.2 Hz, 1H), 7.28 (d, J = 8.4 Hz, 1H), 7.18−7.17 (m, 8H), 7.05 (d, J = 6 Hz, 2H), 3.68 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3, 139.9, 139.7, 139.6, 135.5, 135.4, 131.6, 131.2, 130.7, 129.0, 128.3, 128.2, 127.9, 127.5, 127.3, 127.2, 126.7, 126.4, 125.8, 118.2, 63.5. FT-IR: ν = 3058, 2929, 2852, 1664, 1616, 1483, 1443, 1335, 1276, 1157, 1072 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for $C_{28}H_{22}NO_2$: 404.1651, found 404.1641.

3-Methoxy-1,2-diphenylbenzo[*f*]isoquinolin-1(2*H*)-one (3la). Gray amorphous solid, 28.2 mg, 44% yield, R_f = 0.16 (EtOAc/petroleum ether = 1/5), mp 165−167 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.47−8.43 (m, 1H), 8.08−7.99 (m, 2H), 7.58−7.48 (m, 1H), 7.36−7.31 (m, 2H), 7.28−7.19 (m, 7H), 7.19−7.12 (m, 2H), 7.10−7.01 (m, 1H), 3.77 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 157.1, 142.7, 139.4, 136.4, 134.4, 132.6, 131.8, 130.7, 129.5, 129.2, 128.9, 128.8, 128.5, 128.3, 127.8, 127.7, 126.0, 125.4, 123.5, 117.6, 63.7. FT-IR: ν = 3057, 2932, 1654, 1540, 1491, 1443, 1355 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for $C_{26}H_{20}NO_2$: 378.1494, found 378.1485.

5-Methoxy-6,7-diphenylthieno[3,2-*c*]pyridin-4-one (3ma). White amorphous solid, 23.2 mg, 41% yield, R_f = 0.12 (EtOAc/petroleum ether = 1/5), mp 211−213 °C. ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.43 (d, J = 5.2 Hz, 1H), 7.24 (d, J = 5.6 Hz, 1H), 7.21−7.18 (m, 5H), 7.17−7.14 (m, 3H), 7.12−7.08 (m, 2H), 3.64 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.0, 149.2, 139.5, 136.1, 131.0, 130.9, 130.3, 130.2, 128.7, 128.4, 127.8, 127.7, 125.7, 125.5, 115.7, 63.7. FT-IR: ν = 3059, 2930, 1665, 1491, 1443, 1174, 1075, 1020, 952 cm^{-1}. HRMS-ESI [M + H]$^+$ calcd for $C_{20}H_{16}NO_2S$: 334.0902, found 334.0891.

2-Methoxy-3,4-diphenyl-2-azaspiro[4.5]deca-3,6,9-triene-1,8-dione (3na). White amorphous solid, 28.0 mg, 48% yield, R_f = 0.31 (EtOAc/petroleum ether = 1/3), mp 158−162 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.31 (m, 5H), 7.05 (m, 3H), 6.91 (dd, J = 1.6, 1.2 Hz, 2H), 6.73 (d, J = 10.0 Hz, 2H), 6.53 (d, J = 10.0 Hz, 2H), 3.64 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.0, 167.7, 143.5, 140.4, 133.1, 131.9, 130.0, 129.7, 128.8, 128.5, 128.1, 127.8, 127.6, 115.4, 64.4, 58.0. FT-IR: ν = 3056, 2937, 1731, 1664, 1622, 1598, 1498, 1444, 1397, 1345, 1248, 1180, 1111, 1074, 1025 cm^{-1}. HRMS-ESI [M + H]$^+$ calcd for $C_{22}H_{18}NO_3$: 344.1287, found 344.1278.

2-Methoxy-3,4-di-*p*-tolylisoquinolin-1(2*H*)-one (3ab). White amorphous solid, 52.6 mg, 87% yield, R_f = 0.53 (EtOAc/petroleum ether = 1/5), mp 152−154 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (dd, J = 7.6, 1.2 Hz, 1H), 7.59−7.49 (m 2H), 7.27 (d, J = 8.4 Hz, 1H), 7.15 (d, J = 8.0 Hz, 2H), 7.06 (t, J = 8 Hz, 4H), 7.00 (d, J = 8 Hz, 2H), 3.74 (s, 3H), 2.32 (d, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2, 140.0, 138.0, 136.8, 136.6, 132.5, 132.2, 131.4, 130.5, 128.8, 128.7, 128.2, 127.7, 126.6, 126.3, 125.8, 118.3, 63.4, 21.4, 21.2. FT-IR: ν = 3025, 2932, 1664, 1606, 1510, 1479, 1324, 1176, 1003, 973 cm^{-1}. HRMS-ESI [M + H]$^+$ calcd for $C_{24}H_{22}NO_2$: 356.1651, found 356.1640.

2-Methoxy-3,4-bis(4-methoxyphenyl)isoquinolin-1(2*H*)-one (3ac). White amorphous solid, 52.7 mg, 80% yield, R_f = 0.35 (EtOAc/petroleum ether = 1/3), mp 193−195 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, J = 7.6 Hz, 1H), 7.60−7.48 (m, 2H), 7.30 (d, J = 8.0 Hz, 1H), 7.18 (d, J = 8.4 Hz, 2H), 7.03 (d, J = 8.0 Hz, 2H), 6.85−6.74 (m, 4H), 3.80 (d, 6H), 3.73 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 158.5, 158.2, 139.9, 136.9, 132.7, 132.2, 132.0, 127.8, 127.8, 126.6, 126.3, 125.7, 124.0, 118.0, 113.6, 113.0, 63.3, 55.2, 55.1. FT-IR: ν = 2933, 2837, 1662, 1610, 1510, 1248, 1177, 1032, 972 cm^{-1}. HRMS-ESI [M + H]$^+$ calcd for $C_{24}H_{22}NO_4$: 388.1549, found 388.1540.

3,4-Bis(4-chlorophenyl)-2-methoxyisoquinolin-1(2*H*)-one (3ad). White amorphous solid, 41.8 mg, 62% yield, R_f = 0.25 (EtOAc/petroleum ether = 1/5), mp 172−174 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, J = 8.0 Hz, 1H), 7.55−7.44 (m, 2H), 7.20−7.08 (m, 7H), 6.96 (d, J = 8.0 Hz, 2H), 3.66 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0, 139.0, 136.0, 134.7, 133.7, 133.5, 132.8, 132.6, 131.9, 129.8, 128.7, 128.1, 128.0, 127.2, 126.5, 125.5, 117.2, 63.6. FT-IR: ν = 3066, 2932, 1665, 1607, 1490, 1324, 1176, 1090, 1017, 971 cm^{-1}. HRMS-ESI [M + H]$^+$ calcd for $C_{22}H_{16}Cl_2NO_2$: 396.0558, found 396.0549.

3,4-Bis(4-bromophenyl)-2-methoxyisoquinolin-1(2*H*)-one (3ae). White amorphous solid, 42.1 mg, 51% yield, R_f = 0.38 (EtOAc/petroleum ether = 1/5), mp 203−205 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (dd, J = 7.6, 1.2 Hz, 1H), 7.61−7.51 (m, 2H), 7.42 (dd, J = 8.4, 2.4 Hz, 4H), 7.20 (d, J = 8.0 Hz, 1H), 7.11 (d, J = 8.4 Hz, 2H), 6.97 (d, J = 8.4 Hz, 2H), 3.72 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0, 138.9, 136.0, 134.1, 133.2, 132.6, 132.2, 131.7, 131.1, 130.2, 128.0, 127.2, 126.5, 125.5, 123.0, 121.8, 117.2, 63.6. FT-IR: ν = 3064, 2932, 1665, 1608, 1485, 1323, 1175, 1070, 1013, 971 cm^{-1}. HRMS-ESI [M + H]$^+$ calcd for $C_{22}H_{16}Br_2NO_2$: 483.9548, found 483.9532.

2-Methoxy-3,4-di(thiophen-2-yl)isoquinolin-1(2*H*)-one (3af). White amorphous solid, 45.0 mg, 78% yield, R_f = 0.28 (EtOAc/petroleum ether = 1/2), mp 180−182 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 7.6 Hz, 1H), 7.62 (t, J = 8.0 Hz, 1H), 7.54 (t, J = 7.2 Hz, 1H), 7.46 (d, J = 8.0 Hz, 1H), 7.39 (d, J = 4.8 Hz, 1H), 7.32 (d, J = 4.8 Hz, 1H), 7.08 (d, J = 2.8 Hz, 1H), 7.01−6.99 (m, 1H), 6.95−6.93 (m, 2H), 3.84 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2, 136.6, 136.2, 135.3, 132.6, 131.3, 131.0, 130.2, 128.3, 127.8, 127.4, 127.0, 126.8, 126.3, 126.1, 125.9, 112.7, 63.9. FT-IR: ν = 3073, 2933, 1666, 1604, 1478, 1328, 1247, 1225, 1167, 995 cm^{-1}. HRMS-ESI [M + H]$^+$ calcd for $C_{18}H_{14}NO_2S_2$: 340.0466, found 340.0455.

2-Methoxy-3-phenyl-4-(thiophen-2-yl)isoquinolin-1(2*H*)-one (3ag). White amorphous solid, 40.2 mg, 71% yield, R_f = 0.41 (EtOAc/petroleum ether = 1/5), mp 199−201 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61−8.56 (d, J = 7.6 Hz, 1H), 7.68−7.61 (m, 1H), 7.60−7.53 (m, 1H), 7.50−7.45 (m, 1H), 7.33 (d, J = 5.9 Hz, 5H), 7.29−7.24 (m, 1H), 6.98−6.91 (m, 1H), 6.87−6.82 (m, 1H), 3.76 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2, 142.1, 137.0, 136.1, 132.6, 131.5, 130.3, 130.1, 128.6, 127.7, 127.6, 127.0, 126.8, 126.7, 126.1, 125.6, 110.6, 63.6. FT-IR: ν = 3084, 2935, 1664, 1606, 1478, 1332, 1227, 1171, 1002 cm^{-1}. HRMS-ESI [M + H]$^+$ calcd for $C_{20}H_{16}NO_2S$: 334.0902, found 334.0897.

2-Methoxy-3-(4-methoxyphenyl)-4-phenylisoquinolin-1(2*H*)-one (3ah). White amorphous solid, 43.7 mg, 72% yield, R_f = 0.35 (EtOAc/petroleum ether = 1/3), mp 152−154 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, J = 8.0 Hz, 1H), 7.63−7.52 (m, 2H), 7.34−7.26 (m, 6H), 7.04 (d, J = 8.0 Hz, 2H), 6.80 (d, J = 8.4 Hz, 2H), 3.80 (s, 3H), 3.75 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5, 158.2, 140.1, 136.9, 132.7, 132.3, 131.8, 130.7, 128.2, 127.8, 127.5, 127.6, 126.8, 126.4, 125.8, 118.0, 113.6, 63.5, 55.2. FT-IR: ν = 3055, 2919, 1662, 1640, 1617, 1512, 1479, 1324, 1246, 1175, 1032, 1004, 911 cm^{-1}. HRMS-ESI [M + H]$^+$ calcd for $C_{23}H_{20}NO_3$: 358.1443, found 358.1437.

4-(4-Chlorophenyl)-2-methoxy-3-phenylisoquinolin-1(2*H*)-one (3ai). White amorphous solid, 16.0 mg, 26% yield, R_f = 0.17 (EtOAc/petroleum ether = 1/5), mp 144−146 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, J = 7.6 Hz, 1H), 7.63−7.52 (m, 2H), 7.−7.25 (m, 5H), 7.24−7.20 (m, 3H), 7.15−7.08 (m, 2H), 3.75 (s, 3H). ^{13}C NMR (101 MHz,$CDCl_3$) δ 158.1, 138.6, 136.3, 135.1, 134.4, 132.4, 132.1, 131.5, 130.0, 128.3, 127.9, 127.8, 127.4, 127.1, 126.5, 125.9, 118.6, 63.5. FT-IR: ν = 3060, 2934, 1665, 1605, 1489, 1323, 1265, 1175, 1090, 1017, 1001, 971 cm^{-1}. HRMS-ESI [M + H]$^+$ calcd for $C_{22}H_{17}ClNO_2$: 362.0948, found 362.0945.

3-(4-Chlorophenyl)-2-methoxy-4-phenylisoquinolin-1(2*H*)-one (3ai′). White amorphous solid, 30.1 mg, 49% yield, R_f = 0.14 (EtOAc/petroleum ether = 1/5), mp 189−191 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 7.6 Hz, 1H), 7.58 (m, 2H), 7.34−7.20 (m, 8H), 7.07 (d, J = 7.2 Hz, 2H), 3.76 (s, 3H).^{13}C NMR (101 MHz,$CDCl_3$) δ 158.1, 140.3, 136.2, 134.0, 133.2, 132.9, 132.5, 131.3, 130.6, 128.6, 128.5, 127.9, 127.7, 127.0, 126.4, 125.4, 117.0, 63.6. FT-IR: ν = 3062, 2934, 1665, 1606, 1491, 1323, 1175, 1090, 1016, 1003, 971 cm^{-1}. HRMS-ESI [M + H]$^+$ calcd for $C_{22}H_{17}ClNO_2$: 362.0948, found 362.0949.

2-Methoxy-3-(methoxymethyl)-4-phenylisoquinolin-1(2*H*)-one (3aj). White amorphous solid, 21.0 mg, 12% yield, R_f = 0.21 (EtOAc/petroleum ether = 1/5), mp 108−110 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55−8.51 (m, 1H), 7.57−7.46 (m, 5H), 7.36−7.31 (dd, J = 2.4 Hz, 2H), 7.16−7.14 (m, 1H), 4.28 (s, 2H), 4.23 (s, 3H), 3.30 (s, 3H). ^{13}C NMR (101 MHz,$CDCl_3$) δ 158.4, 136.1, 135.9, 135.1, 132.2, 131.1, 128.6, 128.1, 127.7, 127.1, 126.8, 126.1, 120.1, 66.9, 64.6, 58.3. FT-IR: ν = 2988, 2816, 1666, 1597, 1494, 1445, 1390, 1323, 1248, 1099, 984 cm^{-1}. HRMS-ESI [M + H]$^+$ calcd for $C_{18}H_{18}NO_3$: 296.1287, found 296.1284.

2-Methoxy-1-oxo-4-phenyl-1,2-dihydroisoquinoline-3-carbaldehyde (3ak). White amorphous solid, 10.0 mg, 21% yield, R_f = 0.33 (EtOAc/petroleum ether = 1/5), mp 117−119 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.61 (s, 1H), 8.62−8.58 (m, 1H), 7.71−7.62 (m, 2H), 7.57−7.53 (m, 3H), 7.40−7.36 (m, 2H), 7.30 (dd, J = 8.4, 7.0 Hz, 1H), 4.27 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.7, 158.2, 135.1, 133.3, 132.8, 131.8, 131.2, 129.9, 129.1, 128.8, 128.5, 128.4, 128.2, 127.1, 65.3. FT-IR: ν = 3060, 2934, 1717, 1691, 1669, 1601, 1580, 1466, 1265, 1177, 1113, 1021 cm^{-1}. HRMS-ESI [M + H]$^+$ calcd for $C_{17}H_{14}NO_3$: 280.0974, found 280.0970.

2-Methoxy-6-methyl-3,4-di-*p*-tolylisoquinolin-1(2*H*)-one (3bb). White amorphous solid, 54.6 mg, 87% yield, R_f = 0.23 (EtOAc/petroleum ether = 1/5), mp 135−137 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.36 (dd, J = 8.4, 1.6 Hz, 1H), 7.17−7.10 (m, 2H), 7.02 (t, J = 7.6 Hz, 5H), 6.97 (d, J = 8 Hz, 2H), 3.70 (s, 3H), 2.49 (s, 3H), 2.29 (d, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2, 139.0, 137.9, 136.8, 136.5, 134.5, 133.7, 132.7, 131.4, 130.6, 128.8, 128.8, 128.2, 127.3, 126.2, 125.8, 118.2, 63.3, 21.3, 21.3, 21.2. FT-IR: ν

= 3025, 2924, 2855, 1664, 1617, 1509, 1495, 1454, 1332, 1033, 973 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for $C_{25}H_{24}NO_2$: 370.1807, found 370.1797.

2-Methoxy-3,4-bis(4-methoxyphenyl)-6-methylisoquinolin-1(2*H*)-one (3bc). White amorphous solid, 48.5 mg, 71% yield, R_f = 0.36 (EtOAc/petroleum ether = 1/3), mp 174−176 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.37 (d, J = 8.4 Hz, 1H), 7.16 (t, J = 8.0 Hz, 3H), 6.99 (d, J = 8.4 Hz, 2H), 6.7 (dd, J = 12, 8.8 Hz, 4H), 3.78 (d, 6H), 3.70 (s, 3H), 2.49 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 158.4, 158.2, 138.9, 136.8, 134.6, 133.7, 132.6, 132.1, 128.0, 127.3, 126.2, 125.7, 124.1, 118.0, 113.6, 113.0, 63.3, 55.1, 55.1, 21.3. FT-IR: ν = 2934, 2837, 1661, 1612, 1510, 1461, 1290, 1178, 1034 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for $C_{25}H_{24}NO_4$: 402.1705, found 402.1695.

3,4-Bis(4-chlorophenyl)-2-methoxy-6-methylisoquinolin-1(2*H*)-one (3bd). White amorphous solid, 39.8 mg, 57% yield, R_f = 0.40 (EtOAc/petroleum ether = 1/3), mp 107−109 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.42 (d, J = 8.4 Hz, 1H), 7.29−7.24 (m, 4H), 7.19 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 8.4 Hz, 1H), 7.04 (d, J = 8.0 Hz, 2H), 3.74 (s, 3H), 2.53 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0, 137.9, 137.5, 134.6, 134.0, 133.8, 133.7, 133.4, 132.8, 132.0, 129.9, 128.6, 128.1, 127.5, 126.4, 125.5, 117.2, 63.5, 21.3. FT-IR: ν = 3055, 2926, 2854, 1665, 1613, 1492, 1332, 1265, 1091, 1017, 972 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for $C_{23}H_{18}Cl_2NO_2$: 410.0715, found 410.0705.

6-*tert*-Butyl-2-methoxy-3,4-di-*p*-tolylisoquinolin-1(2*H*)-one (3cb). White amorphous solid, 46.9 mg, 67% yield, R_f = 0.31 (EtOAc/petroleum ether = 1/5), mp 190−192 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 2.0 Hz, 1H), 7.61 (dd, J = 8.8, 2.4 Hz, 1H), 7.20 (d, J = 8.8 Hz, 1H), 7.11 (d, J = 8.0 Hz, 2H), 7.03 (t, J = 8.4 Hz, 4H), 6.97 (d, J = 7.6 Hz, 2H), 3.70 (s, 3H), 2.30 (d, 6H), 1.40 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4, 150.0, 139.2, 137.9, 136.5, 134.5, 132.7, 131.4, 130.6, 130.2, 128.8, 128.8, 128.2, 126.0, 125.7, 123.5, 118.0, 63.3, 35.0, 31.3, 21.4, 21.0. FT-IR: ν = 2962, 2930, 1665, 1594, 1509, 1494, 1332, 1265, 1180, 1023, 974 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for $C_{28}H_{30}NO_2$: 412.2277, found 412.2266.

6-*tert*-Butyl-2-methoxy-3,4-bis(4-methoxyphenyl)-isoquinolin-1(2*H*)-one (3cc). White amorphous solid, 56.6 mg, 75% yield, R_f = 0.23 (EtOAc/petroleum ether = 1/5), mp 191−193 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 2.0 Hz, 1H), 7.55 (dd, J = 8.4, 2.0 Hz, 1H), 7.17 (t, J = 8.4 Hz, 1H), 7.07 (d, J = 8.4 Hz, 2H), 6.93 (d, J = 8.4 Hz, 2H), 6.69 (dd, J = 12.4, 8.8 Hz, 4H), 3.71 (d, 6H), 3.63 (s, 3H), 1.33 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1,158.4, 158.4, 150.0, 139.1, 134.6, 132.6, 132.1, 130.2, 128.0, 125.9, 125.6, 124.1, 123.6, 117.8, 113.5, 112.9, 63.3, 55.2, 55.1, 35.0, 31.3. FT-IR: ν = 2960, 2932, 1868, 1663, 1612, 1510, 1463, 1290, 1248, 1177, 1034, 973 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for: $C_{28}H_{30}NO_4$: 444.2175, found 444.2162.

6-Chloro-2-methoxy-3,4-di-*p*-tolylisoquinolin-1(2*H*)-one (3db). White amorphous solid, 40.4 mg, 61% yield, R_f = 0.32 (EtOAc/petroleum ether = 1/5), mp 176−178 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 2.0 Hz, 1H), 7.46 (dd, J = 8.8, 2.4 Hz, 1H), 7.19 (d, J = 8.8 Hz, 1H), 7.11 (d, J = 8.8 Hz, 2H), 7.04 (t, J = 7.6 Hz, 4H), 6.95 (d, J = 8.0 Hz, 2H), 3.71 (s, 3H), 2.30 (d, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.2, 140.3, 138.2, 136.9, 135.2, 132.8, 132.6, 132.1, 131.3, 130.5, 129.0, 128.4, 128.3, 127.5, 127.4, 127.1, 117.8, 63.5, 21.4, 21.2. FT-IR: ν = 2924, 2854, 1650, 1511, 1462, 1337, 1286, 1184, 1125, 1075, 817 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for $C_{24}H_{21}ClNO_2$: 390.1261, found 390.1250.

6-Bromo-2-methoxy-3,4-di-*p*-tolylisoquinolin-1(2*H*)-one (3eb). White amorphous solid, 48.0 mg, 65% yield, R_f = 0.53 (EtOAc/petroleum ether = 1/5), mp 166−168 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, J = 2.4 Hz, 1H), 7.60 (dd, J = 8.8, 2.0 Hz, 1H), 7.14−7.09 (m, 3H), 7.03 (t, J = 7.2 Hz, 4H), 6.94 (d, J = 7.6 Hz, 2H), 3.70 (s, 3H), 2.30 (d, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.1, 140.5, 138.2, 136.9, 135.5, 135.3, 132.0, 131.3, 130.4, 130.2, 129.0, 128.4, 128.3, 127.7, 120.7, 117.8, 100., 63.5, 21.4, 21.2. FT-IR: ν = 2926, 2855, 1667, 1592, 1509, 1474, 1325, 1172, 1025, 1012, 972 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for $C_{24}H_{21}BrNO_2$: 434.0756, found 434.0745.

6-Iodo-2-methoxy-3,4-di-*p*-tolylisoquinolin-1(2*H*)-one (3fb). White amorphous solid, 50.7 mg, 62% yield, R_f = 0.48 (EtOAc/petroleum ether = 1/5), mp 202−204 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.90 (d, J = 1.7 Hz, 1H), 7.78 (dd, J = 8.8, 2.0 Hz, 1H), 7.11 (d, J = 8.0 Hz, 2H), 7.03 (t, J = 7.2 Hz, 5H), 6.95 (m, 2H), 3.70 (s, 3H), 2.30 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.9, 140.8, 138.2, 136.9, 136.4, 135.93, 131.9, 131.3, 130.4, 129.0, 128.4, 128.3, 127.7, 127.6, 123.3, 117.9, 91.7, 63.5, 21.4, 21.3. FT-IR: ν = 2922, 2852, 1665, 1588, 1507, 1470, 1321, 1172, 1025, 1010, 972 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for $C_{24}H_{21}INO_2$: 482.0617, found 482.0605.

3,4-Bis(4-chlorophenyl)-6-iodo-2-methoxyisoquinolin-1(2*H*)-one (3fd). White amorphous solid, 50.6 mg, 57% yield, R_f = 0.38 (EtOAc/petroleum ether = 1/5), mp 119−121 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.93 (d, J = 2.0 Hz, 1H), 7.86 (dd, J = 8.8, 2.0 Hz, 1H), 7.29−7.26 (m, 4H), 7.18 (d, J = 8.4 Hz, 2H), 7.02 (d, J = 8.4 Hz, 2H), 6.95 (d, J = 10.8 Hz, 1H), 3.74 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.7, 141.3, 139.7, 136.7, 135.1, 134.9, 133.8, 133.1, 132.7, 131.8, 129.4, 128.8, 128.2, 127.9, 127.2, 116.9, 92.4, 63.7. FT-IR: ν = 3063, 2932, 1665, 1581, 1560, 1490, 1389, 1323, 1174, 1090, 1018, 970 cm^{-1}. HRMS-ESI $[M + H]^+$ calcd for $C_{22}H_{15}Cl_2INO_2$: 521.9525, found 521.9504.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of NMR, X-ray data, and optimization of the reaction conditions. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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