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PhI(OCOCF$_3$)$_2$-Mediated Cyclization of *o*-(1-Alkynyl)benzamides: Metal-Free Synthesis of 3-Hydroxy-2,3-dihydroisoquinoline-1,4-dione

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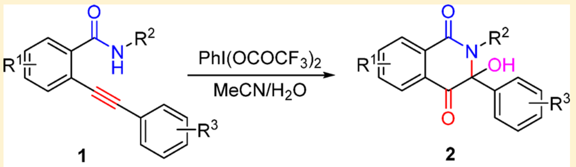
Supporting Information

ABSTRACT: The synthesis of an undocumented skeleton of 3-hydroxy-2,3-dihydroisoquinoline-1,4-diones has been discovered and reported. The reaction consists of an intramolecular cyclization of *o*-(1-alkynyl)benzamides in MeCN/H_2O, mediated by metal-free, hypervalent reagent of PhI(OCOCF$_3$)$_2$, followed by an oxidative hydroxylation reaction. The mechanism consisting of two pathways has been proposed and discussed.



The intramolecular cyclization of alkynes possessing a nucleophilic moiety in the proximity of the carbon−carbon triple bond[1] has been reported to be a convenient and effective process for the construction of a variety of heterocycles.[2] Among these transformations is the construction of N-containing heterocycles through intramolecular cyclization reactions between an amide moiety and the carbon−carbon triple bond. For this reason, during the past decades *o*-(1-alkynyl)benzamide derivatives have been widely studied as a basic enyne-amide system for exploring novel and useful cyclization transformations.[3] The existing strategies mainly involve the *N*-nucleophilic or *O*-nucleophilic attack of the amide group onto the nearby carbon−carbon triple bond, giving rise to the five- or six-membered heterocyclic compounds through *5-exo-dig* or *6-endo-dig* cyclization, respectively.[4] For examples, upon treatment with electrophilic oxidants such as I_2, ICl, NBS and PhSeCl, *o*-(1-alkynyl)benzamides could be converted into isobenzofuranimine and isochromenimine compounds, with the electrophilic E^+ being incorporated into the products (Figure 1, route a).[5] Interestingly, in the presence of AgSbF$_6$ or AgOTf as catalyst, the reaction provided isochomenimines with excellent regioselectivity with no formation of the five-membered isobenzofuranimine compounds (route b).[4c,d] On the other hand, in the presence of a base[4a] or mediated by AlCl$_3$ and acyl chlorides,[4b] *o*-(1-alkynyl)benzamides were converted into isoindolinone compounds **I**, obviously resulting from the nucleophilicity of the amide group instead while going through the similar reactions as in routes a and b (route c). Moreover, by the combining Cs$_2$CO$_3$ and catalytic amount of Cu(OAc)$_2$,[4e] or InBr$_3$[4f,g] as *Lewis* acids, *o*-(1-alkynyl)benzamides could be transformed into isoquinolinones **II** (route d). It was also reported that with ZnCl$_2$ as catalyst and DMF as solvent, and the reaction temperature at 100 °C, both **I** and **II** were formed.[6] It is worth noting that for *o*-(1-alkynyl)benzamide derivatives bearing certain types of R^2 substituents, cascade heteroannulation could occur leading to the formation of various fused heterocylic compounds such as indole[3, 2-*c*]isoquinoliones,[7] 3,4-dihydro-1*H*-benzo[*c*]-chromen-6(2*H*)-imine[8] derivatives, and indeno[1,2-*c*]azepin-3(2*H*)-ones[9] (not shown).

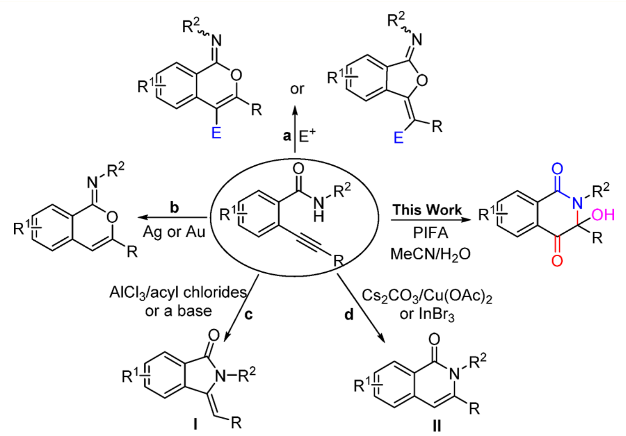


Figure 1. Existing intramolecular cyclization of *o*-(1-alkynyl)-benzamides.

These reported transformations showed that *o*-(1-alkynyl)-benzamides could be converted into various interesting heterocycles, the particular type of which depended on the reaction conditions and substitution pattern of the starting substrates. In this communication, we report a novel transformation, which yielded products carrying the skeleton of 3-hydroxy-2,3-dihydroisoquinoline-1,4-dione, a structure that has never been

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reported before to the best of our knowledge, by treating *o*-(1-alkynyl)benzamide derivatives with hypervalent iodine reagent,[10] i.e., phenyl iodide bistrifluoroacetate (PIFA) in a mixture of MeCN and H_2O as solvent.

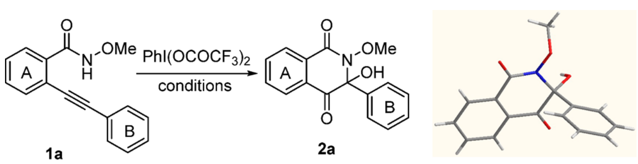
As part of our ongoing effort in searching for new methods to construct heterocyclic compounds utilizing hypervalent iodine reagents,[11] we launched the study of potential cyclization reactions of *o*-(1-alkynyl)benzamides mediated by suitable hypervalent iodine reagents.[12] During those first trials, we used the readily available *N*-methoxy-2-(phenylethynyl)benzamide **1a** (1.0 equiv) as the model substrate, PIFA (1.2 equiv) as the hypervalent iodine reagent, and DCE as the solvent, one of the most frequently chosen solvents for the types of reactions involving hypervalent iodine(III) reagents. However, the reaction provided a complex mixture of products. By switching the solvent to the more polar acetonitrile, the reaction furnished 3-hydroxy-2,3-dihydroisoquinoline-1,4-dione (the structure of which was unambiguously confirmed through X-ray crystallographic analysis) as the major product in 10% yield, with 80% of the starting material recovered. This initial result indicated that the reaction sequence involved not only a cyclization reaction, but also a sequential oxidative hydroxylation reaction. This finding gave rise to the synthesis of a brand new class of heterocyclic compounds, namely, the 3-hydroxy-2,3-dihydroisoquinoline-1,4-dione derivatives.

As the yield from the initial reactions were far from satisfactory, we set out the study of reaction conditions in order to maximize the yields. The results are summarized in Table 1. When 2.1 equiv of PIFA was used, the starting material **1a** was completely consumed with the product **2a** being obtained in 42% yield. To our surprise, when the pure, dried acetonitrile was used as the solvent, the reaction afforded a complex mixture with only trace of the desired product formed. This result suggested that the water in the original untreated acetonitrile had to be involved in the reactions and likely the source for the oxygen and hydroxyl groups in the products. This hypothesis was proven true based on the results from the following control experiments: when a solvent containing a mixture of acetonitrile and water was applied, the reaction yield was greatly improved. A satisfactory 85% yield of the desired product was achieved when the volume ratio of acetonitrile to water was 1:1 (Table 1, entry 7). Further solvents screening showed that the solvent system of 1,4-dioxane/water (1:1 v/v) gave only 10% yield of the product and reactions in methanol/water (1:1 v/v) or trifluoroethanol (TFE)/water (1:1 v/v) only provided a complex mixture with no desired product formed. Screens of other hypervalent iodine reagents were also carried out, but results showed that none of the ones tested (PIDA, PhIO and IBX) gave better yield than with PIFA.

Under the optimal conditions (Table 1, entry 7), a series of substituted *o*-(1-alkynyl)benzamides were prepared (see Supporting Information for details) to investigate the scope of this novel method (Table 2). Reaction-yield data show that the electronic effects of R^1 was insignificant, and that the method was applicable for substrates bearing electron-withdrawing R^3 groups, including strong electron-withdrawing groups such as nitro or trifluoromethyl groups. For the R^2 groups, when the methoxy group was replaced by an alkyl group such as *n*-Pr, *i*-Pr or cyclopropyl, the starting material could not be fully consumed, much to our surprise, even at high temperature of 70 °C. Further attempts to improve the reaction yield were successful: when the solvent was switched to TFE the reaction went to completion with the corresponding products being obtained in good to high yields (Table 2, entries 14−16).

While the electron-withdrawing R^3 groups exerted no significant influence on the substrates for the reaction, it was not the case for the electron-donating ones. Reactions involving substrates with R^3 being methyl, methoxyl, or 1-naphthyl, an inseparable mixture of the desired 3-hydroxy-2,3-dihydroisoqui-

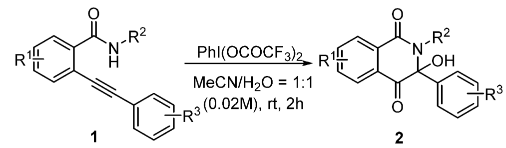
Table 1. Optimization of the Reaction Conditions[a]



entry	oxidant (equiv)	solvent (v/v)	time (h)	yield (%)[b]
1	PIFA (1.2)	DCE	1	–[c]
2	PIFA (1.2)	CH_3CN	1.5	10
3	PIFA (2.1)	CH_3CN	1.5	42
4	PIFA (2.1)	CH_3CN (dried)	1.5	–
5	PIFA (2.1)	CH_3CN/H_2O (10:1)	0.5	62
6	PIFA (2.1)	CH_3CN/H_2O (5:1)	0.5	78
7	PIFA (2.1)	CH_3CN/H_2O (1:1)	0.5	85
8	PIFA (2.1)	1,4-dioxane/H_2O (1:1)	0.5	10
9	PIFA (2.1)	MeOH/H_2O (1:1)	0.5	–
10	PIFA (2.1)	TFE/H_2O (1:1)	0.5	–
11	PIDA (2.1)	CH_3CN/H_2O (1:1)	2	68
12	PhIO (2.1)	CH_3CN/H_2O (1:1)	5	58
13	IBX (2.1)	CH_3CN/H_2O (1:1)	0.5	<5

[a]All reactions were carried out with **1a** (0.5 mmol) and oxidant in solvent (*c* = 0.05 M) at rt. [b]Isolated yields. [c]Not detected.

Table 2. Synthesis of 3-Hydroxy-2,3-dihydroisoquinoline-1,4-dione via PIFA-Mediated Cyclization and Oxidative Hydroxylation[a]



entry	R^1	R^2	R^3	product **2**	yield (%)[b]
1	H	OMe	H	**2a**	85
2	5-Me	OMe	H	**2b**	78
3	5-OMe	OMe	H	**2c**	85
4	5-F	OMe	H	**2d**	87
5	4-Cl	OMe	H	**2e**	88
6	H	OMe	4-Cl	**2f**	85
7	H	OMe	3-Cl	**2g**	90
8	H	OMe	4-F	**2h**	77
9	H	OMe	3-NO_2	**2i**	89
10	H	OMe	3-CF_3	**2j**	83
11	H	OMe	3,4-diCl	**2k**	78
12	5-Me	OMe	4-Cl	**2l**	70
13	4-Cl	OMe	4-Cl	**2m**	78
14[c]	H	*n*-Pr	3-Cl	**2n**	67
15[c]	H	*i*-Pr	3-CF_3	**2o**	87
16[c]	H	cyclo-Pr	4-Cl	**2p**	92

[a]Conditions: **1** (0.5 mmol), PIFA (2.1 mmol) in CH_3CN/H_2O (1:1 v/v) at rt for 0.5 h. [b]Isolated yield. [c]Reaction carried out in TFE/H_2O (1:1) at 50 °C.

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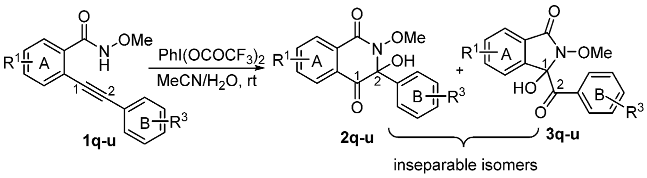
noline-1,4-diones **2** along with its 5-membered isomer 3-benzoyl-3-hydroxy-2-methoxyisoindolin-1-ones **3** were afforded in good to excellent total yields (Table 3). In addition, the ratios

Table 3. Formation of Inseparable Isomeric 3-Hydroxy-2,3-dihydroisoquinoline-1,4-diones and 3-Benzoyl-3-hydroxy-2-methoxyisoindolin-1-ones[a]



entry	substrate	R^1	R^3	2:3[b]	yield (%)[c]
1	**1q**	H	4-Me	5:1	81
2	**1r**	H	4-OMe	1:1	90
3	**1s**	H	3,4-diOMe	2:3	92
4	**1t**	H	1-naphthyl	1:2	88
5	**1u**	4-NO_2	H	3:1	78

[a]Conditions: **1** (0.5 mmol), PIFA (2.1 mmol) in CH_3CN/H_2O (1:1 v/v) at rt for 0.5 h. [b]The ratio was based on crude ^{1}H NMR. [c]Isolated yields.

of two products varied in different deuterium solvents as well as temperatures during the ^{1}H NMR experiments, which suggested that an isomeric equilibrium should exist between compounds **2** and **3**.[13] It is logical to suspect that the isomerization was probably due to the presence of the electron-donating R^3 group which would increase the nucleophilicity of the carbon−carbon triple bond as well as provide stability for the carbocation intermediate necessary for the formation of the 5-membered product **3**. Quantitative relationships between the relative yields of the two isomers and the electron-donating ability of R^3 provided support for the hypothesis, as results in Table 3 show that the amount of **3** relative to **2** consistently increased as R^3 became more and more electron-donating, namely, from methyl to methoxyl (singly substituted), to methoxyl (doubly substituted). We rationalized that if the "push" effect from R^3 had caused the formation of the 5-membered isomer, then the "pull" effect from R^1 should yield similar results. As expected, the reaction of **1u** yielded a mixture of compounds **2** and **3** in a ratio of 3:1.

To our disappointment, the method cannot be applied to the substrates in which R represents an alkyl group, or to the substrates in which R^2 is an H or aryl group. When substrates **1v**–**z** was subjected to the optimal conditions, the reaction provided no desired cyclized/hydroxylated product and an inseparable complex mixture was always obtained in each case (Figure 2).

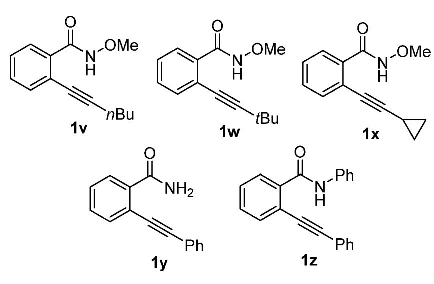
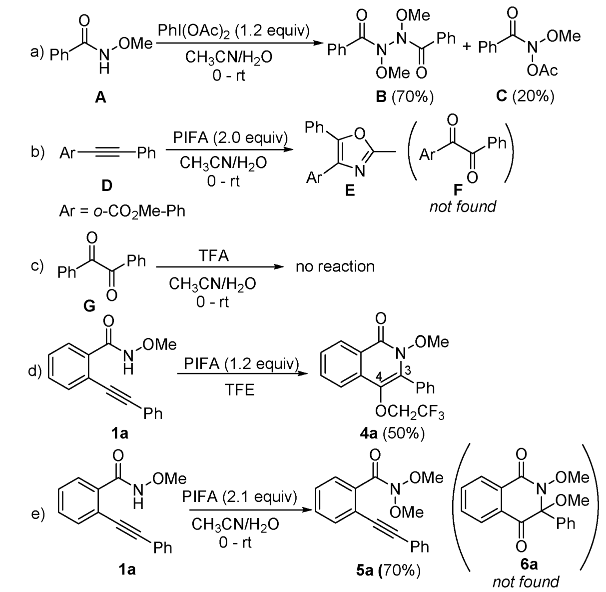


Figure 2. Other models that failed to cyclize.

Further studies were carried out in order to elucidate the reaction mechanism (Scheme 1). Since both the amide and

Scheme 1. Control Experiments



alkyne moieties can interact with the electrophilic hypervalent iodine reagent, our control reactions involved treating *N*-methoxybenzamide **A** and diphenylacetylene **D** separately with oxidants. A complex mixture was obtained from reactions between **A** and PIFA. By switching the oxidant to the less potent PIDA, **A** was converted to *N*′-benzoyl-*N*,*N*′-dimethoxybenzohydrazide **B**[14] and *N*-acetoxy-*N*-methoxybenzamide **C**, in 70% and 20% of the total yield, respectively[15] (Scheme 1a). Reaction between **D** and PIFA under our standard conditions yielded an oxazole derivative **E**,[16] instead of a diketone **F** as we had expected based on the report that 1,2-diphenylethyne derivatives could be converted into diketones under Vasil'eva's conditions (Scheme 1b).[17] Further studies showed that no reaction occurred between **G** and acetonitrile under acidic condition in TFA (Scheme 1c), a negative evidence that excluded the diketone pathway in the generation of **E**. All the control experiments unambiguously indicated that both the *N*-methoxyamide moiety and the alkyne moiety in **1a** were strong enough nucleophiles to react with the hypervalent iodine reagents applied.[18]

It is worthy to note that when substrate **1a** was subjected to PIFA (1.2 equiv) in trifluoroethanol (TFE), trifluoroethoxyl moiety was incorporated into the product and the reaction furnished 4-trifluoroethanolated isoquinolin-1(2*H*)-one product **4a** in 50% yield. Furthermore, one can envisage that by replacing water with the nucleophilic methanol, the reaction might provide the corresponding 3-methoxyl-2,3-dihydroisoquinoline-1,4-dione **6a**. However, when substrate **1a** was treated with PIFA in CH_3CN/MeOH (1:1 v/v), the reaction provided the *N*-methoxylated product **5a** as the major product, with no desired **6a** being detected.[19]

On the basis of the experimental evidence, both from literature[16,17] as well as this study, we propose a mechanism which consists of two plausible pathways in the initial stage of the reaction sequence (Scheme 2). In path a, the *N*-methoxyamide moiety, as the nucleophile, reacts with PIFA and gave intermediate **H**, accompanied by the loss of one molecule of trifluoroacetic acid.[20] Then an intramolecular cyclization occurs

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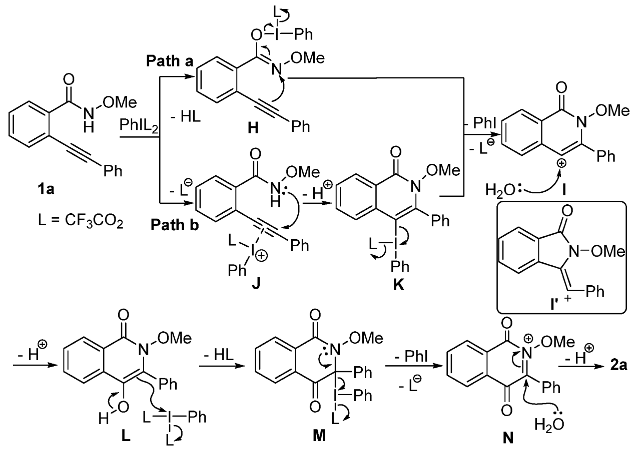
Scheme 2. Plausible Mechanistic Pathway



in **H**, giving rise to the cationic intermediate **I**, along with the release of one molecule of iodobenzene and a trifluoroacetate anion. In path b, it was the triple bond instead that serves as a nucleophile and initially activated by PIFA and forms the electrophilic intermediate **J**,[21] which reacts with the nucleophilic *N*-methoxyamide moiety to produce intermediate **K**. The elimination of the iodobenzene and trifluoroacetate anion from **K** leads to the same cationic intermediate **I**. Next, intermediate **L** was yielded from trapping a H_2O molecule, and is further oxidized by PIFA to furnish intermediate **M**.[22] Conversion to the iminium salt intermediate **N** after releasing an iodobenzene molecule and a trifluoroacetate anion, followed by the nucleophilic attack of water and the removal of one proton furnishes the title product **2a**. The proposed mechanism not only explains the indispensible involvement of water, but also the reasons why an electron-donating R^3 or an electron-withdrawing R^1 will facilitate the formation of the 5-membered isomer **3**. As the mechanism depicts, there is the possibility of forming an alternative five-membered isomeric cationic intermediate **I′** during the formation of intermediate **I**, via path a or path b. In comparison to intermediate **I**, this carbocation intermediate **I′** would particularly benefit from the stabilization received from the electron-donating R^1 or less destabilization caused by the electron-withdrawing R^3 group. The formation of **4a** and **5a** can also be well explained by the above reaction mechanism: when MeOH was present, it will competitively attack the electron-positive N center in **H** to give the *N*-methoxylated product **5a**, while when the less nucleophilic TFE was as the solvent, it captured the reactive intermediate **I** species to give the stable 4-trifluoroethanolated isoquinolin-1(2*H*)-one product **4a**.

In summary, we have reported an efficient method for the construction of some unprecedented new compounds containing the 3-hydroxy-2,3-dihydroisoquinoline-1,4-dione skeleton through hypervalent iodine-mediated intramolecular amidation of *o*-(1-alkynyl)benzamide compounds. A sound mechanism consisting of two pathways in the beginning of the reaction sequence has been proposed and is shown to agree with all experimental observations mentioned. Further studies on reaction mechanism are still in progress in our lab.

■ EXPERIMENTAL SECTION

1. General Information. All reactions were carried out at room temperature and stirred magnetically. ^{1}H and ^{13}C NMR spectra were recorded on a 600 MHz spectrometer (150 MHz for ^{13}C NMR) or 400 MHz spectrometer (100 MHz for ^{13}C NMR) at 25 °C. Chemical shifts values were given in ppm and referred to the internal standard TMS set as 0.00 ppm. The peak patterns were indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; qui, quintet; m, multiplet; td, triplet of doublets and dd, doublet of doublets. The coupling constants, *J*, are reported in Hertz (Hz). High resolution mass spectrometry (HRMS) was obtained on a Q-TOF microspectrometer. Melting points were determined with a micromelting point apparatus without corrections. TLC plates were visualized by exposure to ultraviolet light. Reagents and solvents were purchased as reagent grade and were used without further purification. All reactions were performed in standard glassware, heated at 70 °C for 3 h before use. Flash column chromatography was performed over silica gel 200−300 mesh and the eluent was a mixture of ethyl acetate (EA) and petroleum ether (PE).

2. General Procedure for the Synthesis of Amides 1. *Procedure A.*[23] To a mixture of $PdCl_2(PPh_3)_2$ (562 mg, 0.8 mmol) and CuI (76 mg, 0.4 mmol) in trimethylamine (100 mL) was added substitute 2-bromo methoxybenzoate (20 mmol). The flask was purged with N_2. After stirring for 5 min, ethynyltrimethylsilane (22 mmol) was added slowly and the reaction mixture was stirred at 40 °C for 2 h then at 70 °C for 5 h. After the completion of the reaction (monitored by TLC), the reaction mixture was cooled down to room temperature, filtered over Celite, washed with ethyl acetate, and evaporated. To the crude material, MeOH (40 mL), K_2CO_3 (3.5 g) and water (10 mL) were added and the mixture was stirred for 80 min at room temperature. After completion of the desilylation, water (200 mL) was added and the mixture was extracted with ethyl acetate (3 × 100 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product *o*-(1-alkynyl)benzoates can be used for the next step without any purification.

Procedure B.[24] To a mixture of the corresponding *o*-(1-alkynyl)-benzoates (20 mmol) and iodobenzene (30 mmol, 1.5 equiv) in Et_3N (80 mL) were added $PdCl_2(PPh_3)_2$ (28 mg, 2 mol %) and CuI (40 mg, 1 mol %). The resulting mixture was then heated under an N_2 atm at 55 °C. The reaction was monitored by TLC to establish completion. When the reaction was complete, the mixture was allowed to cool to room temperature, and the ammonium salt was removed by filtration. The solvent was removed under reduced pressure.[24a] The residue was dissolved in MeOH (40 mL) and KOH (aq.) (40 mL, 1.0 mol/L) was added to the solution slowly. The resulting mixture was then heated to 70 °C until TLC indicated the total consumption of the ester. After cooling, the reaction mixture was poured into crushed ice, acidified with 3 M HCl (15 mL) to pH 2−3 carefully and extracted with EtOAc (3 × 100 mL). The combined organic layer was dried over Na_2SO_4 and evaporated under reduced pressure.[24b]

To a solution of the corresponding *o*-(1-alkynyl)benzoic acid in DCM (0.3 M) was added a catalytic amount of DMF. At ambient temperature, oxalyl chloride (1.2 equiv) was added dropwise over a period of 0.5 h, forming a homogeneous solution. The resulting solution was kept at room temperature until TLC indicated the total consumption of the acid. Then, the solvent was removed under reduced pressure. The residue was dissolved in dry EA and slowly added dropwise to a solution of the $NH_2OMe{\cdot}HCl$ (1.2 equiv) and K_2CO_3 (3 equiv) in EA/H_2O = 2:1 (40 mL).[24c] The reaction mixture was maintained at ambient temperature and monitored by TLC. Upon completion, the mixture was extracted with EA (3 × 50 mL) and the combined organic phase was washed with NH_4Cl (1 × 80 mL) and brine (1 × 80 mL). Dried over Na_2SO_4 and evaporation of the solvent under reduced pressure and purification of the crude residue by flash column chromatography on silica gel (EA/PE) afforded the desired amides.

For **1n**, **1o**, **1p**,[24d] the acyl chloride residue was dissolved in dry DCM and slowly added dropwise to a solution of the appropriate aniline derivative (1.2 equiv) and Et_3N (2.5 equiv) in DCM (0.25 M). The reaction mixture was maintained at ambient temperature and monitored by TLC. Upon completion, the mixture was extracted with CH_2Cl_2 (3 × 50 mL) and the combined organic phase was washed with NH_4Cl (1 × 80 mL) and brine (1 × 80 mL). Dried over Na_2SO_4 and evaporation of the solvent under reduced pressure and purification of the crude residue by flash column chromatography on silica gel (EA/PE) afforded the desired amides.

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3. General Procedures for the Synthesis of 2. To a stirred solution of **1** (1.0 mmol) in MeCN/H_2O = 1:1 (50 mL) was added PIFA (2.1 mmol) slowly at 0 °C. The resulting mixture was kept at the same temperature until the TLC indicated that the total consumption of **1**. The reaction was quenched by sat. $NaHCO_3$ (50 mL) and extracted with ethyl acetate (3 × 20 mL). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4 and then evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel to afford the desired product **2**.

4. Procedures for the Synthesis of B and C. A mixture of **A** (1.0 mmol) and PIDA (1.0 mmol) in acetonitrile (20 mL) was stirred at the designated temperature. The reaction was monitored by TLC. After the reaction was completed, the reaction mixture was allowed to cool to room temperature, and EA (20 mL) was added. The resulting mixture was washed with saturated aqueous $Na_2S_2O_3$ (10 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and removed under reduced pressure. The residue was purified by flash column chromatography on silica gel.

5. Procedures for the Synthesis of E. A solution of **D** (1.0 mmol) and PIFA (2.0 mmol) in acetonitrile (20 mL) was stirred at the designated temperature. The reaction was monitored by TLC. After the reaction was completed, the reaction mixture was allowed to cool to room temperature, and EA (20 mL) was added. The resulting mixture was washed with saturated aqueous $NaHCO_3$ (20 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and removed under reduced pressure. The residue was purified by flash column chromatography on silica gel.

6. Spectroscopic Data of 1a–u. *N-Methoxy-2-(phenylethynyl)-benzamide (1a).* Following the general procedure, **1a** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 64%, 3.2 g, white solid, mp 107–109 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.64 (br s, 1H), 7.66–7.62 (m, 1H), 7.54–7.51 (m, 3H), 7.50–7.48 (m, 2H), 7.46–7.44 (m, 3H), 3.75 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.3, 136.7, 132.3, 131.2, 130.1, 129.0, 128.8, 128.7, 127.8, 122.2, 120.4, 92.6, 87.2, 63.2; HRMS (ESI) *m/z* calcd for $C_{16}H_{14}NO_2^+$ [M + H$^+$] 252.1019, found 252.1016.

N-Methoxy-5-methyl-2-(phenylethynyl)benzamide (1b). Following the general procedure, **1b** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 70%, 3.7 g, white solid, mp 123–125 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.61 (br s, 1H), 7.54–7.47 (m, 3H), 7.43 (d, J = 6.6 Hz, 3H), 7.37–7.28 (m, 2H), 3.73 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.3, 138.6, 136.6, 132.2, 131.1, 130.7, 128.8, 128.7, 128.3, 122.4, 117.4, 91.9, 87.4, 68.1, 63.2, 20.8; HRMS (ESI) *m/z* calcd for $C_{17}H_{16}NO_2^+$ [M + H$^+$] 266.1176, found 266.1176.

N,5-Dimethoxy-2-(phenylethynyl)benzamide (1c). Following the general procedure, **1c** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 57%, 0.9 g, white solid, mp 155–158 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.61 (s, 1H), 7.56 (d, J = 8.4 Hz, 1H), 7.48 (d, J = 6.1 Hz, 2H), 7.42 (d, J = 7.3 Hz, 3H), 7.09 (d, J = 8.2 Hz, 1H), 7.04 (s, 1H), 3.83 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 163.9, 159.1, 138.2, 133.9, 131.0, 128.7, 128.6, 122.6, 116.0, 113.2, 112.3, 91.1, 87.3, 63.2, 55.6; HRMS (ESI) *m/z* calcd for $C_{17}H_{16}NO_3^+$ [M + H$^+$] 282.1125, found 282.1127.

5-Fluoro-N-methoxy-2-(phenylethynyl)benzamide (1d). Following the general procedure, **1d** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 49%, 1.3 g, white solid, mp 133–135 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.71 (br s, 1H), 7.70 (dd, J = 7.9, 5.6 Hz, 1H), 7.55–7.48 (m, 2H), 7.44 (d, J = 4.9 Hz, 3H), 7.41 (d, J = 8.5 Hz, 2H), 3.74 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 162.9, 161.3 (d, J = 249.6 Hz), 138.9 (d, J = 7.4 Hz), 134.7 (d, J = 1.2 Hz), 131.2 (the two peaks overlapped), 129.0, 128.8, 122.0, 117.4 (d, J = 22.0 Hz), 116.9, 115.2 (d, J = 23.8 Hz), 92.3, 86.2, 63.4; HRMS (ESI) *m/z* calcd for $C_{16}H_{13}FNO_2^+$ [M + H$^+$] 270.0925, found 270.0925.

4-Chloro-N-methoxy-2-(phenylethynyl)benzamide (1e). Following the general procedure, **1e** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 65%, 1.8 g, white solid, mp 148–150 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.69 (br s, 1H), 7.74 (s, 1H), 7.58–7.55 (m, 1H), 7.52 (d, J = 8.2 Hz, 3H), 7.46 (d, J = 3.2 Hz, 3H), 3.74 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 163.3, 135.3, 134.6, 131.6, 131.4, 129.7, 129.3, 128.8, 128.7, 122.4, 121.7, 93.9, 85.9, 63.4; HRMS (ESI) *m/z* calcd for $C_{16}H_{13}ClNO_2^+$ [M + H$^+$] 286.0629, found 286.0626.

2-((4-Chlorophenyl)ethynyl)-N-methoxybenzamide (1f). Following the general procedure, **1f** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 55%, 1.5 g, white solid, mp 118–120 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.64 (br s, 1H), 7.64 (d, J = 7.6 Hz, 1H), 7.53–7.51 (m, 5H), 7.50 (d, J = 6.5 Hz, 2H), 3.73 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.2, 136.7, 133.7, 132.9, 132.3, 130.2, 129.0, 128.9, 127.9, 121.0, 120.0, 91.4, 88.3, 63.3; HRMS (ESI) *m/z* calcd for $C_{16}H_{13}ClNO_2^+$ [M + H$^+$] 286.0629, found 286.0629.

2-((3-Chlorophenyl)ethynyl)-N-methoxybenzamide (1g). Following the general procedure, **1g** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 60%, 1.7 g, white solid, mp 122–124 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.62 (br s, 1H), 7.65 (d, J = 7.6 Hz, 1H), 7.56 (s, 1H), 7.54 (dd, J = 7.7, 2.8 Hz, 1H), 7.52–7.50 (m, 3H), 7.48 (d, J = 5.0 Hz, 2H), 3.74 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.1, 136.8, 133.3, 132.4, 130.7, 130.6, 130.2, 129.9, 129.1, 129.0, 127.9, 124.2, 119.9, 91.0, 88.6, 63.2; HRMS (ESI) *m/z* calcd for $C_{16}H_{13}ClNO_2^+$ [M + H$^+$] 286.0629, found 286.0629.

2-((4-Fluorophenyl)ethynyl)-N-methoxybenzamide (1h). Following the general procedure, **1h** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 60%, 1.6 g, white solid, mp 148–150 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.60 (br s, 1H), 7.63 (d, J = 7.6 Hz, 1H), 7.57 (dd, J = 8.7, 5.5 Hz, 2H), 7.55–7.51 (m, 1H), 7.51–7.46 (m, 2H), 7.30 (t, J = 8.9 Hz, 2H), 3.74 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.2, 162.1 (d, J = 248.1 Hz), 136.7, 133.6 (d, J = 8.7 Hz), 132.3, 130.1, 128.7, 127.8, 120.2, 118.7 (d, J = 3.4 Hz), 116.1 (d, J = 22.4 Hz), 91.6, 87.0, 63.2; HRMS (ESI) *m/z* calcd for $C_{16}H_{13}FNO_2^+$ [M + H$^+$] 270.0925, found 270.0925.

N-Methoxy-2-((3-nitrophenyl)ethynyl)benzamide (1i). Following the general procedure, **1i** was purified by silica gel chromatography (EA/PE = 40/60). Yield: 20%, 0.6 g, white solid, mp 153–155 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.68 (br s, 1H), 8.29 (s, 1H), 7.94 (d, J = 7.6 Hz, 1H), 7.76 (t, J = 8.1 Hz, 1H), 7.72 (d, J = 7.5 Hz, 1H), 7.61–7.55 (m, 2H), 7.54 (s, 2H), 3.76 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.1, 147.9, 137.3, 136.8, 132.6, 130.6, 130.3, 129.3, 128.0, 125.6, 123.7, 119.5, 105.8, 90.3, 89.4, 63.2; HRMS (ESI) *m/z* calcd for $C_{16}H_{13}N_2O_4^+$ [M + H$^+$] 297.0870, found 297.0873.

N-Methoxy-2-((3-(trifluoromethyl)phenyl)ethynyl)benzamide (1j). Following the general procedure, **1j** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 75%, 2.23 g, white solid, mp 130–132 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.64 (br s, 1H), 7.84 (s, 1H), 7.83–7.79 (m, 2H), 7.72–7.68 (m, 2H), 7.58–7.54 (m, 1H), 7.52 (d, J = 7.0 Hz, 2H), 3.75 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.1, 136.8, 135.0, 132.5, 130.2, 130.1, 129.7 (q, J = 32.1 Hz), 129.1, 127.9, 127.6 (q, J = 3.6 Hz), 125.5 (q, J = 3.8 Hz), 123.7 (q, J = 272.7 Hz), 123.3, 119.8, 90.9, 88.9, 63.2; HRMS (ESI) *m/z* calcd for $C_{17}H_{13}F_3NO_2^+$ [M + H$^+$] 320.0893, found 320.0893.

2-((3,4-Dichlorophenyl)ethynyl)-N-methoxybenzamide (1k). Following the general procedure, **1k** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 45%, 1.4 g, white solid, mp 154–156 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.62 (br s, 1H), 7.76 (d, J = 1.8 Hz, 1H), 7.72 (d, J = 8.3 Hz, 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.55 (td, J = 7.6, 6.5, 3.2 Hz, 1H), 7.52 (d, J = 5.1 Hz, 2H), 7.49 (dd, J = 8.3, 1.9 Hz, 1H), 3.74 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.1, 136.7, 132.6, 132.5, 131.9, 131.6, 131.3, 131.1, 130.2, 129.2, 127.9, 122.8, 119.7, 90.2, 89.4, 63.3; HRMS (ESI) *m/z* calcd for $C_{16}H_{12}Cl_2NO_2^+$ [M + H$^+$] 320.0240, found 320.0245.

2-((4-Chlorophenyl)ethynyl)-N-methoxy-5-methylbenzamide (1l). Following the general procedure, **1l** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 64%, 1.9 g, white solid, mp 105–108 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.66 (br s, 1H), 7.58–7.56 (m, 5H), 7.42–7.35 (m, 2H), 3.77 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.2, 138.9, 136.6, 133.5, 132.8, 132.3, 130.8, 129.0, 128.4, 121.2, 117.1, 90.7, 88.5, 63.3, 20.8; HRMS (ESI) *m/z* calcd for $C_{17}H_{15}ClNO_2^+$ [M + H$^+$] 300.0786, found 300.0786.

4-Chloro-2-((4-chlorophenyl)ethynyl)-N-methoxybenzamide (1m). Following the general procedure, **1m** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 30%, 0.9 g, white solid, mp 146–148 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.72 (br s, 1H), 7.76

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J. Org. Chem. 2015, 80, 5320–5328

(s, 1H), 7.58 (dd, J = 8.3, 2.0 Hz, 1H), 7.55−7.53 (m, 5H), 3.74 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 163.3, 135.3, 134.7, 134.1, 133.0, 131.7, 129.7, 129.1, 129.0, 122.1, 120.6, 92.7, 86.9, 63.3; HRMS (ESI) m/z calcd for $C_{16}H_{12}Cl_2NO_2^+$ [M + H$^+$] 320.0240, found 320.0240.

2-((3-Chlorophenyl)ethynyl)-N-propylbenzamide (1n). Following the general procedure, **1n** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 57%, 1.7 g, white solid, mp 130−133 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.41 (br s, 1H), 7.63 (d, J = 5.6 Hz, 1H), 7.54−7.47 (m, 7H), 7.47 (s, 1H), 3.23 (q, J = 6.6 Hz, 2H), 1.53 (q, J = 7.2 Hz, 2H), 0.89 (t, J = 7.4 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 167.2, 140.1, 133.2, 132.5, 132.4, 130.7, 130.6, 129.8, 129.5, 128.9, 127.6, 124.3, 119.2, 90.8, 89.2, 40.8, 22.4, 11.5; HRMS (ESI) m/z calcd for $C_{18}H_{17}ClNO^+$ [M + H$^+$] 298.0993, found 298.0990.

N-Isopropyl-2-((3-(trifluoromethyl)phenyl)ethynyl)benzamide (1o). Following the general procedure, **1o** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 63%, 2 g, white solid, mp 118−120 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.32 (br s, 1H), 7.84 (s, 1H), 7.81 (t, J = 7.4 Hz, 2H), 7.70 (t, J = 7.8 Hz, 1H), 7.67−7.64 (m, 1H), 7.54−7.47 (m, 3H), 4.10 (d, J = 6.9 Hz, 1H), 1.15 (d, J = 6.6 Hz, 6H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 166.3, 140.2, 134.9, 132.4, 130.1, 129.6 (q, J = 32.3 Hz), 129.4, 127.6 (q, J = 3.4 Hz), 125.3 (q, J = 3.0 Hz), 124.6, 123.6 (q, J = 272.3 Hz) 123.5, 122.8, 119.0, 90.6, 89.5, 41.0, 22.2; HRMS (ESI) m/z calcd for $C_{19}H_{17}F_3NO^+$ [M + H$^+$] 332.1257, found 332.1255.

2-((4-Chlorophenyl)ethynyl)-N-cyclopropylbenzamide (1p). Following the general procedure, **1p** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 60%, 1.7 g, white solid, mp 152−154 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.46 (br s, 1H), 7.60 (dd, J = 7.6, 1.9 Hz, 1H), 7.51−7.54 (m, 4H), 7.51−7.44 (m, 3H), 2.86 (s, 1H), 0.69 (td, J = 7.0, 4.7 Hz, 2H), 0.59−0.46 (m, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.4, 139.7, 133.6, 132.8, 132.2, 129.5, 129.0, 128.8, 127.6, 121.2, 119.5, 91.2, 88.8, 22.7, 5.8; HRMS (ESI) m/z calcd for $C_{18}H_{15}ClNO^+$ [M + H$^+$] 296.0837, found 296.0835.

N-Methoxy-2-(p-tolylethynyl)benzamide (1q). Following the general procedure, **1q** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 50%, 2.5 g, white solid, mp 109−122 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.57 (br s, 1H), 7.61 (d, J = 7.5 Hz, 1H), 7.54−7.43 (m, 3H), 7.40 (d, J = 8.0 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 3.73 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.8, 139.3, 137.2, 132.7, 131.6, 130.5, 129.9, 129.0, 128.3, 121.0, 119.7, 93.3, 87.1, 63.7, 21.5; HRMS (ESI) m/z calcd for $C_{17}H_{16}NO_2^+$ [M + H$^+$] 266.1176, found 266.1174.

N-Methoxy-2-((4-methoxyphenyl)ethynyl)benzamide (1r). Following the general procedure, **1r** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 44%, 2.5 g, white solid, mp 119−121 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.56 (br s, 1H), 7.59 (d, J = 7.7 Hz, 1H), 7.50 (t, J = 7.4 Hz, 1H), 7.48−7.41 (m, 4H), 7.00 (d, J = 8.8 Hz, 2H), 3.80 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.4, 159.7, 136.5, 132.8, 132.0, 130.0, 128.2, 127.8, 120.8, 114.4, 114.1, 92.9, 85.9, 63.2, 55.3; HRMS (ESI) m/z calcd for $C_{17}H_{16}NO_3^+$ [M + H$^+$] 282.1125, found 282.1127.

2-((3,4-Dimethoxyphenyl)ethynyl)-N-methoxybenzamide (1s). Following the general procedure, **1s** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 57%, 3.5 g, white solid, mp 137−140 °C; ^{1}H NMR (600 MHz, CDCl$_3$) δ 9.86 (br s, 1H), 7.95 (s, 1H), 7.68−7.51 (m, 1H), 7.52−7.34 (m, 2H), 7.16 (ddd, J = 8.2, 4.5, 1.9 Hz, 1H), 7.04 (dd, J = 4.3, 1.9 Hz, 1H), 6.87 (dd, J = 8.3, 4.7 Hz, 1H), 3.91 (t, J = 5.3 Hz, 9H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 165.3, 150.2, 148.8, 133.4, 132.9, 131.0, 129.9, 128.7, 125.1, 120.1, 114.0, 111.1, 100.0, 95.8, 86.0, 64.7, 56.0; HRMS (ESI) m/z calcd for $C_{18}H_{18}NO_4^+$ [M + H$^+$] 312.1230, found 312.1230.

N-Methoxy-2-(naphthalen-2-ylethynyl)benzamide (1t). Following the general procedure, **1t** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 54%, 2.4 g, white solid, mp 156−158 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.70 (br s, 1H), 8.48 (d, J = 8.1 Hz, 1H), 8.02 (dd, J = 7.8, 2.6 Hz, 2H), 7.79 (t, J = 6.4 Hz, 2H), 7.70−7.49 (m, 6H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.0, 137.1, 133.3, 133.2, 133.0, 131.0, 130.7, 129.8, 129.2, 128.9, 128.3, 127.7, 127.3, 126.4, 126.1, 121.1, 120.2, 92.5, 91.2, 63.8; HRMS (ESI) m/z calcd for $C_{20}H_{16}NO_2^+$ [M + H$^+$] 302.1176, found 302.1175.

N-Methoxy-4-nitro-2-(phenylethynyl)benzamide (1u). Following the general procedure, **1u** was purified by silica gel chromatography (EA/PE = 40/60). Yield: 65%, 3.8 g, yellow solid, mp 127−130 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.91 (br s, 1H), 8.42 (s, 1H), 8.29 (dd, J = 8.4, 2.3 Hz, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.58 (dd, J = 6.7, 3.0 Hz, 2H), 7.48 (dd, J = 4.9, 2.1 Hz, 3H), 3.77 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 162.7, 148.1, 141.9, 131.5, 129.6, 129.5, 128.9, 126.8, 123.4, 122.1, 121.3, 94.7, 85.2, 63.5; HRMS (ESI) m/z calcd for $C_{16}H_{13}N_2O_4^+$ [M + H$^+$] 297.0870, found 297.0870.

2-(Hex-1-yn-1-yl)-N-methoxybenzamide (1v). Following the general procedure, it was purified by silica gel chromatography (EA/PE = 30/70). Yield: 56%, 2.5 g, white solid, mp 79−81 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.45 (s, 1H), 7.43 (m, 2H), 7.37 (m, 2H), 3.71 (s, 3H), 2.41 (t, J = 6.9 Hz, 2H), 1.53−1.47 (m, 2H), 1.43 (m, 2H), 0.89 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.4, 136.7, 132.3, 129.8, 127.7, 127.5, 121.3, 94.2, 78.2, 63.1, 30.1, 21.3, 18.4, 13.5; HRMS (ESI) m/z calcd for $C_{14}H_{18}NO_2^+$ [M + H$^+$] 232.1332, found 232.1330.

2-(3,3-Dimethylbut-1-yn-1-yl)-N-methoxybenzamide (1w). Following the general procedure, it was purified by silica gel chromatography (EA/PE = 30/70). Yield: 46%, 1.9 g, white solid, mp 85−87 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.44 (s, 1H), 7.41 (m, 2H), 7.37 (m, 2H), 3.73 (s, 3H), 1.26 (s, 9H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.4, 136.7, 132.1, 129.7, 127.7, 127.5, 121.1, 101.9, 76.7, 63.1, 30.5, 27.7; HRMS (ESI) m/z calcd for $C_{14}H_{18}NO_2^+$ [M + H$^+$] 232.1332, found 232.1330.

2-(Cyclopropylethynyl)-N-methoxybenzamide (1x). Following the general procedure, it was purified by silica gel chromatography (EA/PE = 30/70). Yield: 33%, 1.7 g, white solid, mp 80−82 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.39 (s, 1H), 7.41 (m, 2H), 7.36 (m, 2H), 3.71 (s, 3H), 1.52 (m, 1H), 0.95−0.84 (m, 2H), 0.76−0.65 (m, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.5, 136.8, 132.2, 129.8, 127.6, 127.6, 121.3, 97.6, 73.2, 63.1, 8.4 (one signal was missing due to the overlap of peaks); HRMS (ESI) m/z calcd for $C_{13}H_{14}NO_2^+$ [M + H$^+$] 216.1019, found 216.1015.

2-(Phenylethynyl)benzamide (1y). Following the general procedure, **1y** was purified by silica gel gel chromatography (EA/PE = 30/70). Yield: 30%, 226 mg, white solid, mp 145−147 °C; ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.10 (d, J = 7.5 Hz, 1H), 7.62 (d, J = 7.3 Hz, 1H), 7.57−7.51 (m, 2H), 7.45 (m, 3H), 7.40−7.33 (m, 3H), 6.71 (s, 1H). The ^{1}H NMR spectral data are in good agreement with the literature.[4d]

N-Phenyl-2-(phenylethynyl)benzamide (1z). Following the general procedure, **1z** was purified by silica gel gel chromatography (EA/PE = 10/90). Yield: 40%, 226 mg, white solid, mp 156−157 °C; ^{1}H NMR (600 MHz, Chloroform-d) δ 9.22 (s, 1H), 8.26−8.05 (m, 1H), 7.67 (d, J = 7.7 Hz, 3H), 7.49−7.52 (m, 4H), 7.33−7.40 (m, 5H), 7.15 (t, J = 7.4 Hz, 1H). The ^{1}H NMR spectral data are in good agreement with the literature.[4d]

7. Spectroscopic Data of 2a−u. *3-Hydroxy-2-methoxy-3-phenyl-2,3-dihydroisoquinoline-1,4-dione (2a).* Following the general procedure, **2a** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 80%, 226 mg, white solid, mp 138−140 °C; ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.40 (dd, J = 8.0, 1.3 Hz, 1H), 7.96 (dd, J = 7.7, 1.4 Hz, 1H), 7.84 (td, J = 7.7, 1.4 Hz, 1H), 7.69 (td, J = 7.5, 1.3 Hz, 1H), 7.46−7.38 (m, 2H), 7.31 (dd, J = 5.1, 2.2 Hz, 3H), 4.72 (s, 1H), 4.07 (s, 3H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 190.8, 161.5, 136.6, 135.8, 133.4, 130.9, 129.5, 129.2, 129.0, 128.8, 127.5, 126.4, 93.9, 65.4; HRMS (ESI) m/z calcd for $C_{16}H_{14}NO_4^+$ [M + H$^+$] 284.0917, found 284.0913.

3-Hydroxy-2-methoxy-7-methyl-3-phenyl-2,3-dihydroisoquinoline-1,4-dione (2b). Following the general procedure, **2b** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 78%, 232 mg, white solid, mp 123−125 °C; ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.19 (s, 1H), 7.85 (d, J = 7.9 Hz, 1H), 7.47 (d, J = 7.6 Hz, 1H), 7.41 (d, J = 7.9 Hz, 2H), 7.31 (d, J = 5.5 Hz, 3H), 4.87 (s, 1H), 4.06 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 190.6, 161.7, 147.6, 136.8, 134.3, 130.8, 129.4, 129.2, 129.0, 127.8, 126.7, 126.4, 93.8, 65.4, 22.2; HRMS (ESI) m/z calcd for $C_{17}H_{16}NO_4^+$ [M + H$^+$] 298.1074, found 298.1074.

3-Hydroxy-2,7-dimethoxy-3-phenyl-2,3-dihydroisoquinoline-1,4-dione (2c). Following the general procedure, **2c** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 85%, 243 mg, white solid, mp 148−151 °C; ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.90 (d, J = 8.5 Hz, 1H),

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J. Org. Chem. 2015, 80, 5320−5328

7.84 (s, 1H), 7.41 (d, J = 5.6 Hz, 2H), 7.31 (d, J = 4.8 Hz, 3H), 7.14 (d, J = 8.5 Hz, 1H), 4.82 (s, 1H), 4.06 (s, 3H), 3.98 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.6, 165.9, 161.2, 137.1, 133.6, 130.0, 129.3, 128.9, 126.3, 122.0, 120.7, 111.9, 93.6, 65.3, 56.2; HRMS (ESI) m/z calcd for $C_{17}H_{16}NO_5^+$ [M + H$^+$] 314.1023, found 314.1020.

*7-Fluoro-3-hydroxy-2-methoxy-3-phenyl-2,3-dihydroisoquinoline-1,4-dione (**2d**).* Following the general procedure, **2d** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 85%, 256 mg, white solid, mp 133−135 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (dt, J = 8.8, 2.9 Hz, 1H), 8.00 (td, J = 6.2, 5.4, 1.7 Hz, 1H), 7.40 (td, J = 5.8, 5.1, 3.4 Hz, 2H), 7.38−7.30 (m, 4H), 4.94−4.54 (m, 1H), 4.06 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.3, 167.3 (d, J = 260.7 Hz), 160.3, 136.4, 134.1 (d, J = 9.0 Hz), 130.9 (d, J = 9.4 Hz), 129.7, 129.1, 126.3, 125.7 (d, J = 1.2 Hz), 121.1 (d, J = 22.8 Hz), 115.8 (d, J = 26.4 Hz), 93.9, 65.4; HRMS (ESI) m/z calcd for $C_{16}H_{13}FNO_4^+$ [M + H$^+$] 302.0823, found 302.0823.

*6-Chloro-3-hydroxy-2-methoxy-3-phenyl-2,3-dihydroisoquinoline-1,4-dione (**2e**).* Following the general procedure, **2e** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 87%, 276 mg, white solid, mp 151−153 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.33 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 2.1 Hz, 1H), 7.77 (dd, J = 8.4, 2.1 Hz, 1H), 7.42−7.38 (m, 2H), 7.33 (dd, J = 5.1, 2.0 Hz, 3H), 4.63 (s, 1H), 4.06 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.6, 160.9, 140.3, 136.1, 135.8, 130.5, 129.8, 129.2, 129.1, 127.3, 126.4, 119.8, 94.1, 65.5; HRMS (ESI) m/z calcd for $C_{16}H_{13}ClNO_4^+$ [M + H$^+$] 318.0528, found 318.0528.

*3-(4-Chlorophenyl)-3-hydroxy-2-methoxy-2,3-dihydroisoquinoline-1,4-dione (**2f**).* Following the general procedure, **2f** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 85%, 269 mg, white solid, mp 175−178 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.35 (d, J = 7.8 Hz, 1H), 7.95 (d, J = 7.7 Hz, 1H), 7.84 (t, J = 7.5 Hz, 1H), 7.70 (t, J = 7.5 Hz, 1H), 7.35 (d, J = 8.6 Hz, 2H), 7.28 (d, J = 8.6 Hz, 2H), 4.99 (s, 1H), 4.05 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 190.6, 161.5, 136.0, 135.7, 135.2, 133.6, 130.7, 129.2, 129.0, 128.9, 128.0, 127.6, 93.5, 65.5; HRMS (ESI) m/z calcd for $C_{16}H_{13}ClNO_4^+$ [M + H$^+$] 318.0528, found 318.0525.

*3-(3-Chlorophenyl)-3-hydroxy-2-methoxy-2,3-dihydroisoquinoline-1,4-dione (**2g**).* Following the general procedure, **2g** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 90%, 285 mg, white solid, mp 152−155 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.39 (dd, J = 7.9, 1.2 Hz, 1H), 7.98 (dd, J = 7.7, 1.3 Hz, 1H), 7.86 (td, J = 7.6, 1.3 Hz, 1H), 7.71 (td, J = 7.6, 1.3 Hz, 1H), 7.48 (q, J = 1.4 Hz, 1H), 7.29−7.27 (m, 1H), 7.24−7.23 (m, 2H), 4.79 (s, 1H), 4.06 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 190.5, 161.3, 138.7, 136.1, 135.1, 133.6, 130.8, 130.1, 129.6, 129.0, 128.9, 127.6, 127.0, 124.5, 93.2, 65.5; HRMS (ESI) m/z calcd for $C_{16}H_{13}ClNO_4^+$ [M + H$^+$] 318.0528, found 318.0526.

*3-(4-Fluorophenyl)-3-hydroxy-2-methoxy-2,3-dihydroisoquinoline-1,4-dione (**2h**).* Following the general procedure, **2h** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 77%, 231 mg, white solid, mp 160−162 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.37 (d, J = 7.8 Hz, 1H), 7.96 (d, J = 7.7 Hz, 1H), 7.84 (t, J = 8.0 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 7.45−7.34 (m, 2H), 6.99 (t, J = 8.6 Hz, 2H), 4.82 (s, 1H), 4.06 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 190.7, 163.3 (d, J = 249.7 Hz), 161.4, 135.9, 133.6, 132.5 (d, J = 3.2 Hz), 130.8, 129.1, 128.8, 128.6 (d, J = 8.7 Hz), 127.6, 116.0 (d, J = 21.9 Hz), 93.4, 65.4; HRMS (ESI) m/z calcd for $C_{16}H_{13}FNO_4^+$ [M + H$^+$] 302.0823, found 302.0820.

*3-Hydroxy-2-methoxy-3-(3-nitrophenyl)-2,3-dihydroisoquinoline-1,4-dione (**2i**).* Following the general procedure, **2i** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 89%, 292 mg, yellow solid, mp 170−172 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.45 (d, J = 7.8 Hz, 1H), 8.39 (s, 1H), 8.19 (d, J = 9.3 Hz, 1H), 8.01 (d, J = 7.7 Hz, 1H), 7.91 (t, J = 8.1 Hz, 1H), 7.76 (t, J = 7.6 Hz, 1H), 7.67 (d, J = 7.9 Hz, 1H), 7.50 (t, J = 8.0 Hz, 1H), 4.82 (s, 1H), 4.06 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 190.3, 161.2, 148.7, 139.2, 136.5, 133.9, 132.1, 130.8, 129.9, 129.2, 128.8, 127.8, 124.4, 122.2, 92.8, 65.6; HRMS (ESI) m/z calcd for $C_{16}H_{13}N_2O_6^+$ [M + H$^+$] 329.0768, found 329.0768.

*3-Hydroxy-2-methoxy-3-(3-(trifluoromethyl)phenyl)-2,3-dihydroisoquinoline-1,4-dione (**2j**).* Following the general procedure, **2j** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 83%, 291 mg, white solid, mp 155−158 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.39 (d, J = 7.8 Hz, 1H), 7.98 (d, J = 7.7 Hz, 1H), 7.87 (t, J = 7.6 Hz, 1H), 7.80 (s, 1H), 7.72 (t, J = 7.5 Hz, 1H), 7.58 (d, J = 7.7 Hz, 1H), 7.52 (d, J = 7.9 Hz, 1H), 7.43 (t, J = 7.8 Hz, 1H), 4.93 (s, 1H), 4.04 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 190.5, 161.3, 138.0, 136.2, 133.7, 131.7 (q, J = 33.0 Hz), 130.8, 129.9 (q, J = 276.2 Hz), 129.5, 129.4, 129.0, 127.7, 126.4 (q, J = 3.0 Hz), 123.9 (q, J = 3.6 Hz), 93.2, 65.4; HRMS (ESI) m/z calcd for $C_{17}H_{13}F_3NO_4^+$ [M + H$^+$] 352.0791, found 352.0791.

*3-(3,4-Dichlorophenyl)-3-hydroxy-2-methoxy-2,3-dihydroisoquinoline-1,4-dione (**2k**).* Following the general procedure, **2k** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 88%, 308 mg, white solid, mp 165−168 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.38 (dd, J = 7.9, 1.2 Hz, 1H), 7.98 (dd, J = 7.7, 1.3 Hz, 1H), 7.87 (td, J = 7.7, 1.3 Hz, 1H), 7.73 (td, J = 7.6, 1.2 Hz, 1H), 7.58 (d, J = 2.3 Hz, 1H), 7.36 (d, J = 8.5 Hz, 1H), 7.18 (dd, J = 8.5, 2.3 Hz, 1H), 4.87 (s, 1H), 4.05 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 190.2, 161.2, 136.9, 136.2, 134.0, 133.7, 133.4, 130.8, 130.7, 129.0, 128.9, 128.9, 127.7, 125.6, 92.8, 65.5; HRMS (ESI) m/z calcd for $C_{16}H_{12}Cl_2NO_4^+$ [M + H$^+$] 352.0138, found 352.0138.

*3-(4-Chlorophenyl)-3-hydroxy-2-methoxy-7-methyl-2,3-dihydroisoquinoline-1,4-dione (**2l**).* Following the general procedure, **2l** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 70%, 231 mg, white solid, mp 158−160 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.86 (d, J = 7.8 Hz, 1H), 7.50 (d, J = 7.7 Hz, 1H), 7.34 (d, J = 8.6 Hz, 2H), 7.27 (d, J = 7.7 Hz, 2H), 4.84 (s, 1H), 4.06 (s, 3H), 2.53 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 190.3, 161.64 147.9, 135.6, 135.4, 134.5, 130.7, 129.3, 129.2, 127.9, 127.8, 126.5, 93.3, 65.5, 22.2; HRMS (ESI) m/z calcd for $C_{17}H_{15}ClNO_4^+$ [M + H$^+$] 332.0684, found 332.0682.

*6-Chloro-3-(4-chlorophenyl)-3-hydroxy-2-methoxy-2,3-dihydroisoquinoline-1,4-dione (**2m**).* Following the general procedure, **2m** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 77%, 273 mg, white solid, mp 166−168 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 2.0 Hz, 1H), 7.78 (dd, J = 8.4, 2.1 Hz, 1H), 7.36−7.28 (m, 4H), 4.74 (s, 1H), 4.04 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.4, 160.8, 140.5, 136.0, 135.9, 134.8, 130.5, 130.3, 129.3, 128.9, 128.0, 127.3, 93.6, 65.5; HRMS (ESI) m/z calcd for $C_{16}H_{12}Cl_2NO_4^+$ [M + H$^+$] 352.0138, found 352.0135.

*3-(3-Chlorophenyl)-3-hydroxy-2-propyl-2,3-dihydroisoquinoline-1,4-dione (**2n**).* Following the general procedure, **2n** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 67%, 220 mg, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (dd, J = 7.1, 1.2 Hz, 1H), 7.66−7.54 (m, 3H), 7.48−7.43 (m, 1H), 7.33−7.28 (m, 1H), 7.21−7.12 (m, 2H), 5.74 (s, 1H), 3.38 (ddd, J = 14.2, 9.8, 5.8 Hz, 1H), 3.16 (ddd, J = 14.2, 9.8, 6.1 Hz, 1H), 1.57−1.44 (m, 2H), 0.83 (t, J = 7.4 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.1, 168.5, 144.0, 135.2, 134.3, 133.6, 133.2, 131.9, 130.9, 130.1, 129.6, 127.2, 124.4, 122.5, 90.7, 41.7, 22.2, 11.5; HRMS (ESI) m/z calcd for $C_{18}H_{17}ClNO_3^+$ [M + H$^+$] 330.0891, found 330.0888.

*3-Hydroxy-2-isopropyl-3-(3-(trifluoromethyl)phenyl)-2,3-dihydroisoquinoline-1,4-dione (**2o**).* Following the general procedure, **2o** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 87%, 315 mg, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99−7.91 (m, 2H), 7.76−7.72 (m, 1H), 7.60 (td, J = 7.5, 1.1 Hz, 1H), 7.58−7.51 (m, 2H), 7.38 (t, J = 7.9 Hz, 1H), 7.28 (d, J = 1.1 Hz, 1H), 5.73 (s, 1H), 3.89−3.52 (m, 1H), 1.39 (d, J = 6.8 Hz, 3H), 1.21 (d, J = 6.9 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.3, 168.2, 143.8, 133.1, 132.8, 132.5, 132.4, 131.6 (q, J = 33.4 Hz), 130.6 (q, J = 3.5 Hz), 130.6, 129.5, 126.6 (q, J = 4.1 Hz), 123.2 (q, J = 261.2 Hz), 122.2, 91.4, 45.9, 20.6, 20.4; HRMS (ESI) m/z calcd for $C_{19}H_{17}F_3NO_3^+$ [M + H$^+$] 364.1155, found 364.1152.

*3-(4-Chlorophenyl)-2-cyclopropyl-3-hydroxy-2,3-dihydroisoquinoline-1,4-dione (**2p**).* Following the general procedure, **2p** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 92%, 300 mg, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (d, J = 7.4 Hz, 1H), 7.61−7.53 (m, 2H), 7.50−7.45 (m, 2H), 7.28−7.23 (m, 3H), 5.86 (s, 1H), 1.13 (dddd, J = 10.3, 6.6, 5.2, 4.0 Hz, 1H), 0.79−0.65 (m, 2H), 0.48 (dddd, J = 10.6, 6.8, 5.2, 3.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.3, 169.7, 144.2, 141.1, 133.4, 131.6, 130.8, 130.8, 130.4, 129.4, 124.5, 122.4, 91.5, 22.5, 4.8, 4.2; HRMS (ESI) m/z calcd for $C_{18}H_{15}ClNO_3^+$ [M + H$^+$] 328.0735, found 328.0733.

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*3-Hydroxy-2-methoxy-3-(p-tolyl)-2,3-dihydroisoquinoline-1,4-dione (**2q**) and 3-(3,4-Dimethoxybenzoyl)-3-hydroxy-2-methoxyisoindolin-1-one (**3q**).* Following the general procedure, **2q** and **3q** were purified by silica gel chromatography (EA/PE = 30/70): yield 81%, 240 mg, isomers (**2q**/**3q** ratio 5:1) are reported together, white solid; ^{1}H NMR (600 MHz, $CDCl_3$) major isomer **2q** δ 8.38 (d, J = 7.8 Hz, 1H), 7.95 (d, J = 7.7 Hz, 1H), 7.82 (t, J = 7.6 Hz, 1H), 7.67 (t, J = 7.5 Hz, 1H), 7.30 (d, J = 8.3 Hz, 2H), 7.11 (d, J = 8.1 Hz, 2H), 4.81 (s, 1H), 4.07 (s, 3H), 2.27 (s, 3H); minor isomer **3q** δ 7.92−7.91 (m, 1H), 7.62−7.56 (m, 2H), 7.38 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 2.5 Hz, 1H, peaks of two isomers overlapped), 7.07 (d, J = 8.2 Hz, 2H), 6.12 (s, 1H), 3.98 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.5, 190.8, 161.5, 139.6, 135.7, 133.7, 133.5, 133.4, 130.8, 130.8, 129.7, 129.6, 129.3, 129.2, 128.7, 127.5, 126.3, 124.3, 122.7, 93.9, 90.0, 66.1, 65.4, 21.7, 21.1; HRMS (ESI) m/z calcd for $C_{17}H_{16}NO_4^+$ [M + H$^+$] 298.1074, found 298.1074.

*3-Hydroxy-2-methoxy-3-(4-methoxyphenyl)-2,3-dihydroisoquinoline-1,4-dione (**2r**) and 3-Hydroxy-2-methoxy-3-(4-methylbenzoyl)isoindolin-1-one (**3r**).* Following the general procedure, **2r** and **3r** were purified by silica gel chromatography (EA/PE = 30/70): yield 90%, 282 mg, isomers (**2r**/**3r** ratio 1:1) are reported together, white solid; ^{1}H NMR (600 MHz, $CDCl_3$) isomer **2r** δ 8.38 (d, J = 7.8 Hz, 1H), 7.95 (d, J = 7.7 Hz, 1H), 7.82 (t, J = 7.6 Hz, 1H), 7.67 (t, J = 7.5 Hz, 1H), 7.33 (d, J = 8.9 Hz, 2H), 6.81 (d, J = 8.9 Hz, 2H), 4.73 (s, 1H), 4.07 (s, 3H), 3.73 (s, 3H), isomer **3r** δ 7.94−7.90 (m, 1H), 7.61−7.56 (m, 2H), 7.54 (d, J = 9.0 Hz, 2H), 7.31−7.28 (m, 1H), 6.75 (d, J = 9.0 Hz, 2H), 6.19 (s, 1H), 3.98 (s, 3H), 3.77 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.6, 190.7, 164.4, 161.5, 160.5, 142.0, 135.6, 133.7, 133.4, 132.0, 130.8, 130.7, 129.4, 129.3, 128.7, 128.4, 127.9, 127.5, 124.6, 124.4, 122.7, 114.4, 114.2, 93.8, 89.8, 66.0, 65.1, 55.5, 55.3; HRMS (ESI) m/z calcd for $C_{17}H_{16}NO_5^+$ [M + H$^+$] 314.1023, found 314.1020.

*3-(3,4-Dimethoxyphenyl)-3-hydroxy-2-methoxy-2,3-dihydroisoquinoline-1,4-dione (**2s**) and 3-(3,4-Dimethoxybenzoyl)-3-hydroxy-2-methoxyisoindolin-1-one (**3s**).* Following the general procedure, **2s** and **3s** were purified by silica gel chromatography (EA/PE = 20/80): yield 92%, 316 mg, isomers (**2s**/**3s** ratio 2:3) are reported together, white solid; ^{1}H NMR (600 MHz, $CDCl_3$) major isomer **3s** δ 7.93 (d, J = 7.7 Hz, 1H), 7.60 (p, J = 7.3 Hz, 2H), 7.33−7.32 (d, J = 8.3 Hz, 1H)7.16 (d, J = 8.3 Hz, 2H), 6.70 (d, J = 8.3 Hz, 1H), 6.24 (s, 1H), 4.00 (s, 3H), 3.85 (s, 3H), 3.73 (s, 3H), minor isomer **2s** δ 8.37 (d, J = 7.7 Hz, 1H), 7.96 (d, J = 7.6 Hz, 1H), 7.82 (t, J = 7.3 Hz, 1H), 7.68 (t, J = 7.5 Hz, 1H), 7.01 (s, 1H), 6.88 (d, J = 8.5 Hz, 1H), 6.74 (d, J = 8.5 Hz, 1H), 4.99 (s, 1H), 4.07 (s, 3H), 3.83 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.4, 190.5, 164.3, 161.6, 154.3, 149.9, 149.3, 148.7, 142.1, 137.4, 135.6, 133.8, 133.4, 130.8, 130.7, 129.4, 129.2, 128.7, 128.6, 127.5, 124.6, 124.5, 124.2, 122.8, 119.0, 111.6, 110.9, 110.5, 109.5, 93.8, 89.9, 66.2, 65.4, 56.1, 55.9, 55.9, 55.8; HRMS (ESI) m/z calcd for $C_{18}H_{18}NO_6^+$ [M + H$^+$] 344.1129, found 344.1130.

*3-Hydroxy-2-methoxy-3-(naphthalen-2-yl)-2,3-dihydroisoquinoline-1,4-dione (**2t**) and 3-(2-Naphthoyl)-3-hydroxy-2-methoxyisoindolin-1-one (**3t**).* Following the general procedure, **2t** and **3t** were purified by silica gel chromatography (EA/PE = 20/80): yield 88%, 293 mg, isomers (**2t**/**3t** ratio 1:2) are reported together, white solid; some peaks of two isomers overlapped ^{1}H NMR (600 MHz, $CDCl_3$) major isomer **3t** δ7.84−7.89 (m, 3H), 7.67−7.75 (m, 2H), 7.39−7.52 (m, 4H), 7.21−7.24 (m, 2H), 6.03 (s, 1H), 4.12 (s, 3H); minor isomer **2t** δ 8.40 (d, J = 7.8 Hz, 1H), δ 8.01 (d, J = 7.6 Hz, 1H), 7.81−7.89 (m, 2H), 7.67−7.75 (m, 1H), 7.39−7.52 (m, 4H), 7.21−7.24 (m, 2H), 4.62 (s, 1H), 3.57 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.2, 164.4, 144.6, 139.7, 133.7, 133.5, 133.3, 132.5, 130.9, 130.8, 130.2, 129.9, 129.2, 128.7, 128.5, 127.7, 127.6, 126.7, 126.5, 126.3, 125.8, 125.2, 125.1, 124.5, 124.2, 123.9, 122.4, 91.8, 66.6, 64.6; HRMS (ESI) m/z calcd for $C_{20}H_{16}NO_4^+$ [M + H$^+$] 334.1074, found 334.1070.

*3-Hydroxy-2-methoxy-6-nitro-3-phenyl-2,3-dihydroisoquinoline-1,4-dione (**2u**) and 3-Benzoyl-3-hydroxy-2-methoxy-5-nitroisoindolin-1-one (**3u**).* Following the general procedure, **2u** and **3u** were purified by silica gel chromatography (EA/PE = 20/80): yield 78%, 256 mg, isomers (**2u**/**3u** ratio 3:1) are reported together, white solid; ^{1}H NMR (600 MHz, $CDCl_3$) major isomer **2u** δ 8.75 (s, 1H), 8.61 (q, J = 8.6 Hz, 2H), 7.40 (s, 2H), 7.38−7.33 (m, 3H), 4.88 (s, 1H), 4.09 (s, 3H), minor isomer **3u** δ 8.46 (d, J = 8.3 Hz, 1H), 8.17 (s, 1H), 8.09 (d, J = 8.3 Hz, 1H), 7.53 (t, J = 7.5 Hz, 1H), 7.50 (d, J = 7.9 Hz, 2H), 7.32 (d, J = 7.8 Hz, 2H), 6.20 (s, 1H), 4.06 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 188.5, 159.7, 150.7, 135.5, 135.0, 134.7, 130.7, 130.5, 130.1, 129.5, 129.3, 129.2, 128.9, 126.4, 125.6, 122.8, 118.4, 94.3, 89.9, 66.5, 65.6; HRMS (ESI) m/z calcd for $C_{16}H_{13}N_2O_6^+$ [M + H$^+$] 329.0768, found 329.0766.

*N′-Benzoyl-N,N′-dimethoxybenzohydrazide (**B**).*[3] Following the general procedure, **B** was purified by silica gel chromatography (EA/PE = 10/90). Yield: 70%, 210 mg, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 (d, J = 7.6 Hz, 4H), 7.53−7.49 (m, 2H), 7.39 (t, J = 7.4 Hz, 4H), 3.86 (s, 6H).

*N-Acetoxy-N-methoxybenzamide (**C**).* Following the general procedure, **C** was purified by silica gel chromatography (EA/PE = 5/95). Yield: 20%, 42 mg, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88−7.72 (m, 2H), 7.56 (t, J = 7.5 Hz, 1H), 7.44 (t, J = 7.9 Hz, 2H), 3.96 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.1, 168.2, 132.9, 131.5, 129.0, 128.4, 62.6, 18.8; HRMS (ESI) m/z calcd for $C_{10}H_{12}NO_4^+$ [M + H$^+$] 210.0761, found 210.0760.

*Methyl 2-(2-methyl-5-phenyloxazol-4-yl)benzoate (**E**).* Following the general procedure, **E** was purified by silica gel chromatography (EA/PE = 10/90). Yield: 85%, 248 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00−7.88 (m, 1H), 7.59−7.42 (m, 3H), 7.41−7.34 (m, 2H), 7.31−7.18 (m, 3H), 3.61 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 159.6, 145.5, 134.3, 133.4, 131.9, 131.3, 131.1, 130.5, 128.6, 128.6, 128.5, 127.9, 125.2, 52.0, 14.0; HRMS (ESI) m/z calcd for $C_{18}H_{16}NO_3^+$ [M + H$^+$] 294.1125, found 294.1125.

*2-Methoxy-3-phenyl-4-(2,2,2-trifluoroethoxy)isoquinolin-1(2H)-one (**4a**).* Following the general procedure, **4a** was purified by silica gel chromatography (EA/PE = 5/95). Yield: 50%, 98 mg, white solid, mp 105−108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 7.6 Hz, 1H), 7.69−7.50 (m, 5H), 7.34 (t, J = 7.5 Hz, 1H), 7.24−7.16 (m, 1H), 6.45 (d, J = 8.0 Hz, 1H), 4.17 (s, 3H), 4.02 (q, J = 8.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.6, 138.5, 132.8, 131.9, 131.3, 131.0, 130.7, 129.6, 128.4, 126.3, 123.5, 123.1 (q, J = 278.2 Hz), 121.7, 121.2, 66.4 (q, J = 35.1 Hz), 65.2; ^{19}F NMR (566 MHz, $CDCl_3$) δ −73.76 (s, 3F); HRMS (ESI) m/z calcd for $C_{18}H_{15}F_3NO_3^+$ [M + H$^+$] 350.0999, found 350.1004.

*N,N-Dimethoxy-2-(phenylethynyl)benzamide (**5a**).* Following the general procedure, **5a** was purified by silica gel chromatography (EA/PE = 5/95). Yield: 70%, 126 mg, white solid, mp 156−158 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61 (d, J = 7.0 Hz, 1H), 7.53 (m, 2H), 7.50−7.41 (m, 2H), 7.39 (d, J = 6.7 Hz, 1H), 7.38−7.35 (m, 3H) 3.83 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.00, 136.6, 132.7, 131.7, 130.2, 128.7, 128.4, 127.9, 127.5, 122.8, 121.3, 93.6, 86.8, 61.2; HRMS (ESI) m/z calcd for $C_{17}H_{16}NO_3^+$ [M + H$^+$] 282.1125, found 282.1125.

■ ASSOCIATED CONTENT

Supporting Information

Spectral data for all new compounds. The material is available free of charge via the Internet at The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00576.

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Notes

The authors declare no competing financial interest.

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