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Oxidative Radical Cyclization of *N*-methyl-*N*-arylpropiolamide to Isatins via Cleavage of the Carbon-carbon Triple Bond

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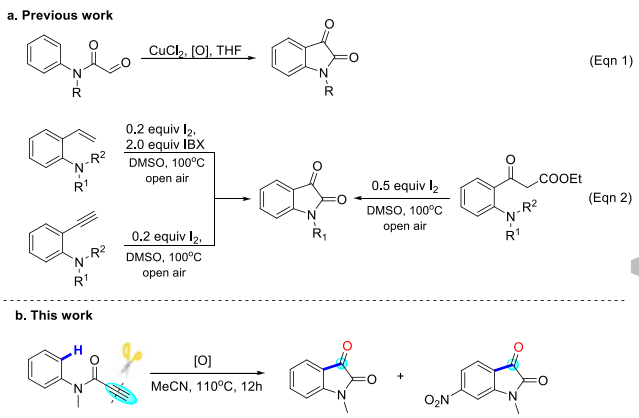
Abstract. A radical cyclization of *N*-methyl-*N*-arylpropiolamide to isatins via an oxidative cleavage of a carbon-carbon triple bond has been developed. In the presence of oxone and $NaNO_2$, a variety of *N*-methyl-*N*-arylpropiolamides were smoothly transformed into isatins. A nitration reaction proceeded along with the oxidative cyclization; both nitrated and non-nitrated isatins were obtained in a one-pot reaction with moderate to good total yields. This is the first example for the synthesis of isatins via the oxidative radical cleavage of a carbon-carbon triple bond.

Keywords: Radical reaction; Oxidation; Cyclization; Isatin; Nitration

Introduction

The carbon-carbon triple bond is an extremely useful synthetic building block for a diverse number of chemical transformations.[1] Considerable attention has been paid to the cyclization,[2a,b] difunctionalization,[2c,d] and oxidation of alkynes[2e-h] for the construction of a diverse array of molecules. In recent years, the oxidative cleavage of carbon-carbon triple bonds has emerged as a powerful tool for a variety of chemical reactions.[3] Significant effort has been devoted to the oxidative cleavage of the carbon-carbon triple bond into the corresponding oxo-compounds.[3a] For example, the Jiang group[3b] disclosed an efficient transformation of internal alkynes to carboxylic esters via a palladium-catalyzed cleavage of carbon-carbon triple bonds. Xie developed a facile and convenient Rh(III)-catalyzed acylation of the Csp^2–H bond of *N*-phenoxyacetamide with a number of alkynes under mild conditions; the alkynes are employed as a novel acyl source.[3h] In addition, the transformation of the alkyne group to the corresponding nitrile functionality has been achieved through a C–C bond cleavage.[3d-f] For example, the Jiao group[3d] reported the first direct conversion of alkynes into nitriles via a Ag-catalyzed nitrogenation of alkynes. Inspired by this intriguing alkyne chemistry, we envisioned that isatins could be synthesized from *N*-methyl-*N*-arylpropiolamide via a cyclization that proceeds through an oxidative radical cleavage of the carbon-carbon triple bond (Scheme 1b). Due to the high chemical bond energy of the carbon-carbon triple bond and the relatively electron deficient environment resulting from the electron withdrawing effect of the carbonyl group, the oxidative cleavage of the terminal triple bond in propiolamide remains challenging.



Scheme 1. Synthetic methods for isatins

Application of this new chemistry for the preparation of isatins is of great interest. Isatins are an important class of indolone derivative which are commonly found in natural products,[4] pharmaceuticals (such as

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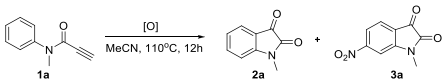
anti-allergenic, antimalarial, and anti-HIV compounds, etc.),[5] and dyes.[6] In addition, isatins are important skeletons for drug design and functional materials development.[7] Owing to the synthetic utility of isatins, the development of efficient methods for the synthesis of such compounds has become a prominent area of research. In the past few decades, the Sandmeyer, Stollé, and Martinet methodologies have been commonly used for the synthesis of isatins.[8] However, these traditional methods possess several disadvantages, such as narrow substrate scope, poor yields, and the need for strong acids, thus are insufficient for the preparation of a diverse range of isatins. In 2010, the Li group[9] reported an intriguing method for the synthesis of isatins via a Cu-catalyzed intramolecular C-H oxidative acylation of formyl-*N*-arylformamides using O_2 as a terminal oxidant (Scheme 1a, Eqn 1). In 2015, the Ilangovan group[10] developed an efficient iodine-promoted synthesis of isatins from 2′-aminophenylacetylenes, 2′-aminostyrenes, and 2′-amino-β-ketoesters through oxidative processes (Scheme 1a, Eqn 2). Although progress has been made in the synthesis of isatins over recent years, efficient synthetic methods for their preparation remain scarce. In order to enrich the diversity of the isatins that can be prepared, the development of efficient synthetic methods with good functional groups tolerance are desired. Herein we report the preparation of isatins via a new radical cyclization of *N*-methyl-*N*-arylpropiolamide through oxidative cleavage of a carbon-carbon triple bond in the presence of oxone and $NaNO_2$ (Scheme 1b).

Results and Discussion

Our study began with the reaction of *N*-methyl-*N*-arylpropiolamide (**1a**) with radical oxidants. The inexpensive $NaNO_2$ is an oxidative radical initiator.[11] It was assumed that a combination of peroxide and $NaNO_2$ is expected to be a radical system for the cleavage of carbon-carbon triple bonds. Thus, combinations of $NaNO_2$ with different peroxides, including $K_2S_2O_8$, $(NH_4)_2S_2O_8$, oxone, DCP (Dicumyl peroxide), BPO (Benzoyl peroxide), DTBP (Di-*tert*-butyl peroxide), and H_2O_2 were examined (entries 1-7). The results show that a nitration reaction occurs along with the oxidative cyclization of **1a**, leading to the formation of non-nitrated and nitrated products **2a** and **3a**, respectively. $NaNO_2$ adopts the role of a radical initiator and a nitro source.[12e, 16a] The treatment of **1a** with $NaNO_2$ (1 equiv) and $K_2S_2O_8$ (0.5 equiv) gave products **2a** and **3a** in yields of 13% and 29%, respectively (entry 1). $(NH_4)_2S_2O_8$ is ineffective in this reaction (entry 2). Compared with $K_2S_2O_8$, oxone is more effective for the reaction, and the yield of product **2a** could be improved to 22%. Next, other organic peroxides, such as DCP, BPO, DTBP, and H_2O_2, were also evaluated. However, these oxidants were all ineffective, and the starting material was mostly recovered. In order to improve the reaction efficiency and selectivity, the quantity of $NaNO_2$ needed for the reaction was examined (entries 8-11). Encouragingly, products **2a** and **3a** could be obtained in a total yield of 86% (yields of 32% and 54%, respectively) when **1a** was treated with oxone (0.5 eq) and $NaNO_2$ (1.3 equiv) (entry 8).

Table 1. Screening of optimal conditions [a].



Entry	Oxidant (eq)	$NaNO_2$ (eq)	Solvent	Yield (%)	
				2a	**3a**
1	$K_2S_2O_8$ (0.5)	$NaNO_2$ (1)	MeCN	13	29
2	$(NH_4)_2S_2O_8$ (0.5)	$NaNO_2$ (1)	MeCN	trace	trace
3	Oxone (0.5)	$NaNO_2$ (1)	MeCN	22	30
4	DCP (0.5)	$NaNO_2$ (1)	MeCN	0	0
5	BPO (0.5)	$NaNO_2$ (1)	MeCN	0	0
6	DTBP (0.5)	$NaNO_2$ (1)	MeCN	0	0
7	H_2O_2 (0.5)	$NaNO_2$ (1)	MeCN	trace	trace
8	Oxone (0.5)	$NaNO_2$ (1.3)	MeCN	32	54
9	Oxone (0.5)	$NaNO_2$ (1.7)	MeCN	27	50
10	Oxone (0.5)	$NaNO_2$ (2)	MeCN	26	48
11	Oxone (0.5)	$NaNO_2$ (3)	MeCN	17	25
12	Oxone (0.5)	—	MeCN	0	0
13	—	$NaNO_2$ (1.3)	MeCN	0	0
14	Oxone (0.1)	$NaNO_2$ (1.3)	MeCN	trace	trace
15	Oxone (0.2)	$NaNO_2$ (1.3)	MeCN	10	28
16	Oxone (1)	$NaNO_2$ (1.3)	MeCN	19	35
17	Oxone (0.5)	$NaNO_2$ (1.3)	Toluene	trace	0
18	Oxone (0.5)	$NaNO_2$ (1.3)	dioxane	trace	0
19	Oxone (0.5)	$NaNO_2$ (1.3)	Acetone	0	0
20	Oxone (0.5)	$NaNO_2$ (1.3)	H_2O	0	0
21	Oxone (0.5)	$NaNO_2$ (1.3)	HFIP	trace	trace
22	Oxone (0.5)	$NaNO_2$ (1.3)	DMF	0	0
23[b]	Oxone (0.5)	$NaNO_2$ (1.3)	MeCN	trace	14
24[c]	Oxone (0.5)	$NaNO_2$ (1.3)	MeCN	27	32
25[d]	Oxone (0.5)	$NaNO_2$ (1.3)	MeCN	32	50
26[e]	Oxone (0.5)	$NaNO_2$ (1.3)	MeCN	11	15
27[f]	Oxone (0.5)	$NaNO_2$ (1.3)	MeCN	15	47

[a] *Reaction conditions*: **1a** (0.1 mmol), solvent (1 mL), at 110 °C for 12 h. [b] at 70 °C. [c] at 90 °C. [d] at 130 °C. [e] under N_2. [f] under O_2.

Unexpectedly, the reaction yield began to decrease when more than 1.3 equivalents of $NaNO_2$ were used (entries 9-11); the high concentration of $NaNO_2$ led to the formation of unknown by-products. In addition to $NaNO_2$, the reaction yield is also dependent on the amount of oxone. In the absence of oxone, no product was obtained (entry 13). Compared with conducting the reaction with 0.5 equiv of oxone, increasing or decreasing the amount of oxone led to a decrease in yield (entries 14-16). Next, different solvents, including toluene, 1,4-dioxane, acetone, H_2O, HFIP and DMF, were investigated (entries 17-22). Compound **1a** was almost completely recovered when the reaction was carried out in acetone, H_2O, or HFIP. The starting material was consumed when the reaction was conducted in toluene, 1,4-dioxane, and DMF, but the reaction was messy and none of the target product was isolated. The results show that the reaction temperature is also crucial for this

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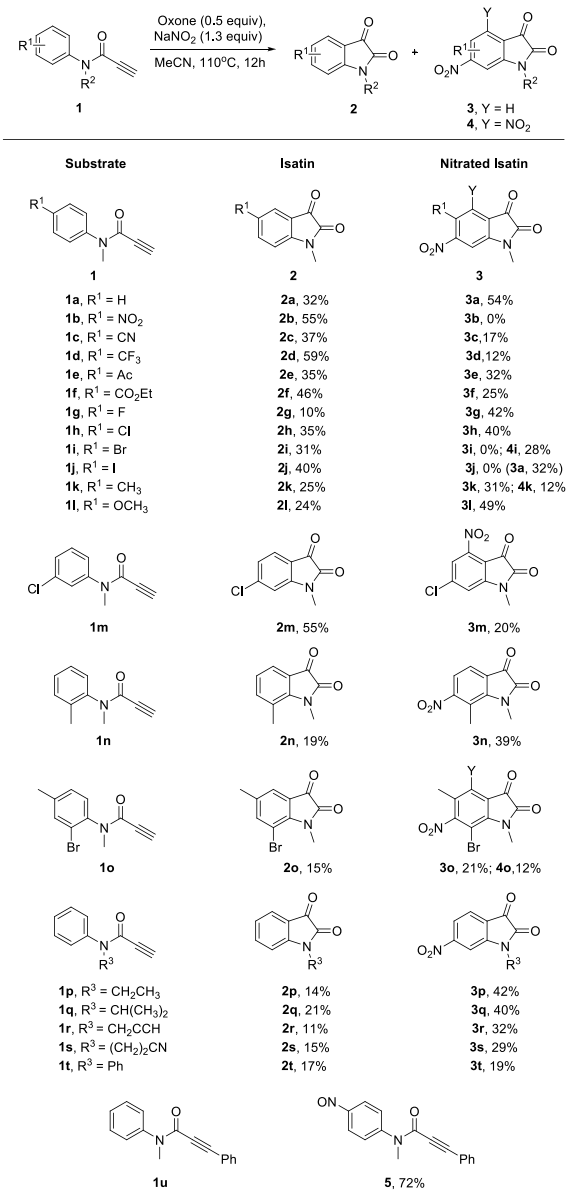
transformation (entries 23-25). Reaction at 70 °C only gave product **3a** in 14% yield with none of product **2a** being observed. This result indicates that the formation of **2a** by hydrogen elimination requires more energy than nitration (entry 23). Reactivity was greatly surpressed when the reaction was carried out under a nitrogen atmosphere, resulting in a low yield of the desired product (entry 26). An oxygen atmosphere was favorable to the formation of product **3a**, but the total yield of products **2a** and **3a** was lower (entry 27).

With the optimal reaction conditions in hand, the reaction scope was investigated (Table 2). The results show that substrates bearing electron-withdrawing groups, including nitro, cyano, trifluoromethyl, acetyl, ester, fluoro, chloro, bromo, and iodo substituents, are all tolerated well with the corresponding products being obtained in moderate to good total yields (Table 2, substrates **1a-j**, **1m**). All of these functional groups are synthetically useful in medicinal chemistry. Substrates bearing a strong electron-withdrawing group lead to the formation of the corresponding non-nitrated product **2** because the electron-deficient aromatic rings disfavor the nitration reaction. For example, nitro substituted compound **1b** only gave its corresponding product **2b** in 55% yield. A substrate bearing a trifluoromethyl group afforded product **2d** in 59% yield, with **3d** being obtained in 12% yield. The structure of product **3d** was confirmed by single crystal X-ray diffraction (see ESI).[13] Interestingly, a substrate bearing a bromo group gave the dinitrated product **4i** rather than the *mono*-nitrated product **3i**. Iodo-substrate **1j** was amenable to the reaction conditions giving product **2j** in 40% yield. However, product **3j** underwent deiodination during column chromatography purification, affording **3a** in 32% yield. When a chloro group was present at the *meta*-position of substrate **1m**, the 4-nitro substituted product **3m** was obtained in 20% yield. NOE NMR experiments were conducted on products **3f** and **3m** in order to confirm the selectivity of the nitration (See ESI). The *ortho* methyl substituted substrate underwent reaction smoothly to give products **2n** and **3n** in 19% and 39% yields, respectively. For the reaction of substrate **1o** bearing both a methyl and a bromo group, in addition to the formation of products **2o** and **3o**, a dinitrated product **4o** was also isolated. Susbtrates in which the methyl substituent at the nitrogen atom was replaced with an ethyl, isopropyl, prop-2-ynyl, cyanopropyl or phenyl group, also performed well to give their corresponding products in moderate total yields (Products **1p-t**). Finally, *N*-methyl-*N*,3-diphenylpropiolamide was subjected to our reaction conditions; however, cyclization of the interal alkyne was unsuccessful. Instead, nitrosation occurred at the *para*-position of the acylamino group, affording product **5** in 72% yield.

Table 2. Substrates scope [a].



[a] *Reaction conditions:* reaction conditions: **1a** (0.2 mmol), Oxone (0.1 mmol, 0.5 equiv), $NaNO_2$ (0.26 mmol, 1.3 equiv), at 110 °C in MeCN for 12 h.

Next, a gram-scale reaction was conducted with substrate **1a** (7 mmol and 15 mmol, respectively). The reactions proceeded well to give products **2a** and **3a** in moderate total yields (Scheme 2, eqn 1). It is important to note that isatins bearing a nitro group are important compounds because the nitro group can be reduced to an amino group, a process that is useful for further derivatization.[12] In the presence of iron powder (3.0 equiv) and HCl (37%, conc.), the nitro functionality was reduced to an amino group in a mixed solvent system of H_2O/MeOH, providing product **6** in 84% yield (Scheme 2, Eqn 2).

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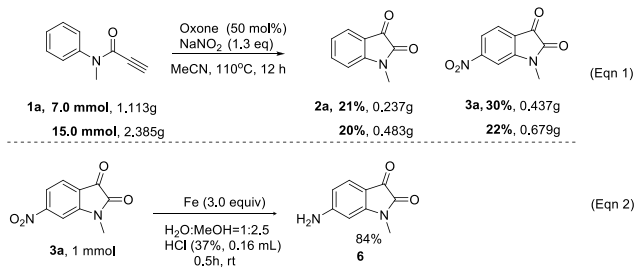
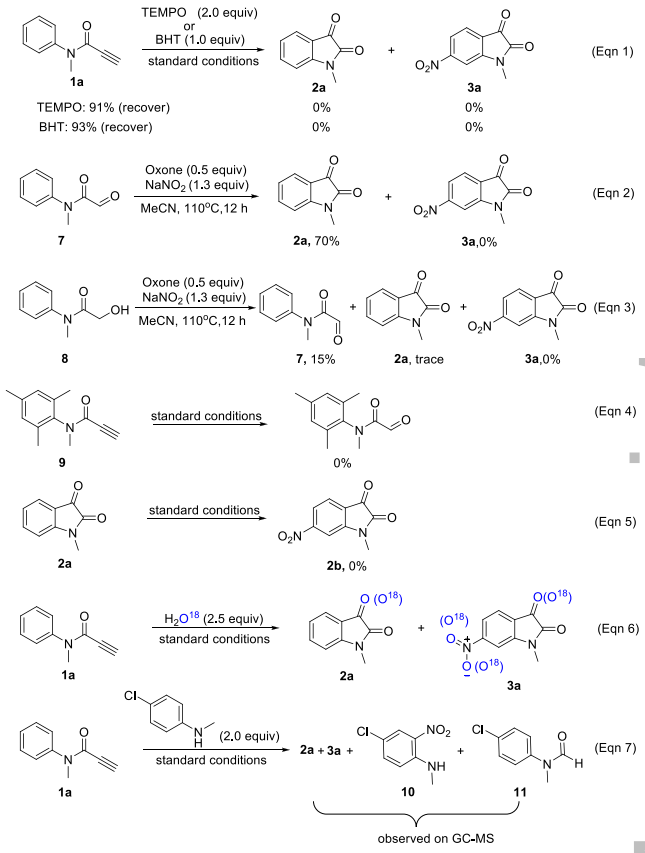


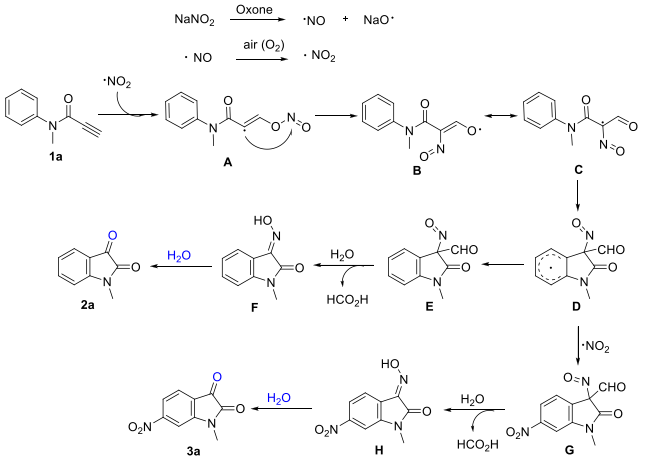
Scheme 2. Gram-scale reaction and the reduction of nitro group.

To better understand the reaction mechanism, control experiments were conducted. Initially, radical scavengers such as 2,6-di-tertbutyl-4-methylphenol (BHT) and 2,2,6,6-Tetramethylpiperidinooxy (TEMPO) were added to the reaction. In the presence of BHT or TEMPO, the reaction was completely inhibited and the starting material was recovered in 93% and 91% yields, respectively (Scheme 3, Eqn 1). These results suggest that the reaction proceeds through a radical process. Classically, alkynes can be transformed into ketones or a compound with one less carbon atom by the cleavage of a carbon-carbon triple bond under oxidative conditions.[14] We speculated that the compound **7** may be the reaction intermediate that is obtained from the oxidation of the terminal alkyne. However, compound **7** was not detected by GC-MS analysis. Additionally, the reaction of compound **7** under standard conditions only gave product **2a** in 70% yield; the nitrated product **3a** was not observed (Scheme 3, Eqn 2). This result suggests that compound **7** may not be the reaction intermediate. Based on previous reports,[15] the generation of compound **8** from **1a** is possible. However, none of the desired product was formed for the reaction of compound **8** under the reaction conditions, with only compound **7** being obtained in 15% yield (Scheme 3, Eqn 3). To better understand the chemical transformation of the terminal alkyne, compound **9** was prepared and subjected to the reaction conditions; no oxidized product was formed (Scheme 3, Eqn 4). In order to gain a better understanding of the nitration step, product **2a** was subjected to the reaction conditions, but no nitration occurred (Scheme 3, Eqn 5). The results suggest that the oxidative cyclization and nitration may be a collaborative pathway. Next, the source of the oxygen atoms in the carbonyl and nitro groups was studied by adding H_2O^{18} to the reaction mixture (Scheme 3, Eqn 6). The O^{18}-labelled product **2a** was obtained as the major product. A mixture of product **3a,** possessing one or two O^{18}-labelled atoms, was observed in a 1:1 ratio, suggesting that the oxygen atoms in the carbonyl and nitro groups originate from the H_2O. We envisaged that the cleavage of the carbon-carbon triple bond may produce an active carbonyl species which can be trapped by an amine. Thus, 4-chloro-*N*-methylaniline was added to the reaction mixture in order to trap the active carbonyl species. Fortunately, a small amount of *N*-(4-chlorophenyl)-*N*-methylformamide **11** was observed by GC-MS analysis (Scheme 3, Eqn 7)



Scheme 3. Control experiments.

According to the present results and previous reports,[16] a possible reaction mechanism has been proposed (Scheme 4). Initially, $NaNO_2$ is quickly converted to an NO radical via the assistance of oxone at high temperature. The NO radical may be further oxidized to an NO_2 radical for the nitration reaction. The NO_2 radical can be trapped by the C−C triple bond to afford intermediate **A**, which can undergo isomerization to give intermediate **B** that also has a resonance structure **C**.[17] Subsequently, a rapid cyclization occurs to give intermediate **D**. Hydrogen radical elimination of **D** leads to intermediate **E**, which undergoes a decarbonylation reaction to produce intermediate **F**. Alternatively, intermediate **D** could be trapped by the NO_2 radical to give intermediate **G**. A subsequent decarbonylation of **G** gives intermediate **H**. Finally, both intermediates **F** and **H** undergo hydrolysis to afford **2a** and **3a**, respectively. Intermediates **E**, **F**, **G**, and **H** may all be unstable under the reaction conditions or electrospraying environment - these compounds were not observed by LC-MS analysis. A more detailed reaction mechanism remains to be uncovered.



Scheme 4. A possible mechanism.

Conclusion

In summary, a novel method for the oxidative radical cyclization of *N*-methyl-*N*-arylpropiolamide into isatins, in the presence of $NaNO_2$ and oxone, has been developed. This represents the first example for the synthesis of isatins through a sequential radical oxidative cleavage and cyclization of a terminal carbon-carbon triple bond. Although perfect selectivity for the formation of isatins or nitrated isatins has not been achieved, the preparation of two different isatins in a one-pot reaction is of interest to the synthetic community. It is noteworthy that isatins bearing a nitro group cannot be easily prepared using other methodologies. Moreover, the nitro group can be readily transformed into an amino group allowing for further diversification. This study provides an alternative protocol for the preparation of isatins, particularly for the synthesis of nitro and amino derivatives.

Experimental Section

General remarks

^1H and ^{13}C NMR spectra were measured on a Bruker Avance-III 500 instrument (600MHz for ^1H, 151 MHz for ^{13}C NMR spectroscopy) using $CDCl_3$ as the solvent. Chemical shifts for ^1H and ^{13}C NMR were referred to internal Me_4Si (0 ppm) as the standard. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Mass spectra were measured on an Agilent GC-MS-5975C Plus spectrometer (EI). HRMS (ESI) analysis was measured on a Thermo Scientific LTQ Orbitrap XL.

Typical Experimental Procedure To a flame-dried Schlenk tube with a magnetic stirring bar was charged **1a** (0.2 mmol), oxone (0.1 mmol), $NaNO_2$ (0.26 mmol) and MeCN (2 mL) under an air atmosphere. The reaction mixture was stirred at 110 °C for 12 hours. After reaction completion, the mixture was poured into ethyl acetate and washed with saturated Na_2CO_3.The aqueous layer was extracted with ethyl acetate and the combined organic layers were dried over anhydrous Na_2SO_4 and evaporated under vacuum. The residue was purified by flash column chromatography (hexane/ethyl acetate) to afford the desired products **2a** and **3a**.

1-methylindoline-2,3-dione (2a)[9]**.** Yield: 10.3 mg (32%), Crimson solid, m.p. 124.1–125.0 °C (lit. 121.7–124.5 °C). ^1H NMR (600 MHz, $CDCl_3$) δ=7.65–7.58 (m, 2H), 7.14 (t, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 7.8 Hz, 1H), 3.26 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 183.3, 158.2, 151.5, 138.4, 125.2, 123.8, 117.5, 109.9, 26.2. IR (KBr) δ= 1742, 1727, 1609, 1471, 1327cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 161 (83), 133 (32), 105 (59), 104 (100), 78 (35).

1-methyl-6-nitroindoline-2,3-dione (3a). Yield: 22.2 mg (54%), Crimson solid, m.p. 117.9–118.3 °C (CAS No. 108726-52-9). ^1H NMR (600 MHz, $CDCl_3$) δ = 8.03 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.75 (d, *J* = 1.4 Hz, 1H), 3.38 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 182.0, 157.2, 153.7, 152.0, 126.1, 120.9, 119.2, 105.2, 26.8. IR (KBr) δ = 1748, 1724, 1603, 1468, 1324 cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 206 (100), 178 (56), 150 (79), 104 (74), 77 (44), 63 (47).

1-methyl-5-nitroindoline-2,3-dione (2b)[12a]. Yield: 22.7 mg (55%), Yellow solid, m.p. 201.1–202.3 °C (lit. 201–202 °C). LRMS (EI, 70 eV) *m/z* (%): 206 (100), 178 (73), 150 (66), 149 (43), 120 (23), 104 (58), 77 (45), 63(35). ^1H NMR (600 MHz, $CDCl_3$) δ = 8.58 (dd, *J* = 8.7, 2.4 Hz, 1H), 8.49 (d, *J* = 2.3 Hz, 1H), 7.08 (d, *J* = 8.7 Hz, 1H), 3.38 (s, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ = 179.9, 156.7, 154.3, 143.1, 132.5, 119.8, 115.9, 109.0, 25.7.

1-methyl-2,3-dioxoindoline-5-carbonitrile (2c)[18a]**.** Yield: 13.8 mg (37%), Crimson solid, m.p. 191.8–192.6 °C (lit. 157.6–160°C). ^1H NMR (600 MHz, Acetone) δ = 8.07 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.93 (d, *J* = 1.4 Hz, 1H), 7.35 (d, *J* = 8.3 Hz, 1H), 3.29 (s, 3H). ^{13}C NMR (151 MHz, Acetone) δ=181.8, 157.9, 154.7, 141.8, 127.6, 118.0, 117.6, 111.3, 106.5, 25.8. IR (KBr) δ = 1763, 1742, 1739, 1624, 1592, 1489, 1468, 1339 cm^{-1}. LRMS (EI, 70 eV) *m/z* (%) 186(69), 158(35), 130(73), 129(100), 103(38).

1-methyl-6-nitro-2,3-dioxoindoline-5-carbonitrile (3c). Yield: 7.8 mg (17%), Crimson solid, m.p. 196.0–197.0 °C. ^1H NMR (600 MHz, Acetone) δ 8.22 (s, 1H), 8.08 (s, 1H), 3.42 (s, 3H). ^{13}C NMR (151 MHz, Acetone) δ 180.6, 157.5, 155.4, 130.2, 128.7, 120.5, 114.3, 107.6, 101.5, 26.3. IR (KBr) δ = 1765, 1746, 1735, 1621, 1598, 1487, 1465 cm^{-1}.

1-methyl-5-(trifluoromethyl)indoline-2,3-dione (2d)[9]. Yield: 27.0 mg (59%), Yellow solid, m.p. 124.9–125.5 °C (lit. 126.7–128.2°C). ^1H NMR (600 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.3 Hz, 1H), 7.85 (s, 1H), 7.05 (d, *J* = 8.3 Hz, 1H), 3.32 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 181.98, 157.81, 153.70, 135.3 (q, *J* = 3.6 Hz, 1C), 126.4 (q, *J* = 33.9 Hz, 1C), 123.4 (q, *J* = 272.1 Hz, 1C), 122.4 (q, *J* = 3.6 Hz, 1C), 117.2, 110.2, 26.52. IR (KBr) δ = 1742, 1624, 1598, 1324, 1283, 1162cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 229 (53), 201 (25), 173 (50), 172 (100), 146 (24), 145 (24).

1-methyl-6-nitro-5-(trifluoromethyl)indoline-2,3-dione (3d). Yield: 6.6 mg (12%), Yellow solid, m.p. 163.1–163.7 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.32 (s, 1H), 3.38 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 180.1, 156.8, 154.7, 154.1, 125.0(q, *J* = 5.1 Hz, 1C), 121.4(q, *J* = 273.8 Hz, 1C) 118.7(q, *J* = 35.6 Hz, 1C), 118.1, 106.5, 27.0. IR (KBr) δ = 1757, 1742, 1633, 1598, 1551, 1365, 1292cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 274 (45), 246 (30), 229 (26), 218(31), 201 (22), 173 (34), 172 (100), 152 (22), 145 (52). HRMS (ESI) m/z calcd for $C_{10}H_6F_3N_2O_4^+$ $(M+H)^+$ 275.02742, found 275.02661.

5-acetyl-1-methylindoline-2,3-dione (2e)[9]**.** Yield: 14.2 mg (35%), Yellow solid, m.p. 140.2–140.7 °C (lit. 145.3–148.4 °C). ^1H NMR (600 MHz, Acetone) δ = 8.32 (dd, *J* = 8.3, 1.8 Hz, 1H), 8.10 (d, *J* = 1.8 Hz, 1H), 7.26 (d, *J* = 8.3 Hz, 1H), 3.29 (s, 3H), 2.60 (s, 3H). ^{13}C NMR (151 MHz, Acetone) δ = 195.1, 182.9, 158.4, 155.0, 138.3, 132.7,

124.0, 117.4, 110.2, 25.7, 25.6. IR (KBr) δ = 1756, 1683, 1622, 1371, 1321, 1265 cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 203 (58), 160 (100), 132 (54).

5-acetyl-1-methyl-6-nitroindoline-2,3-dione (3e). Yield: 15.9 mg (32%), Yellow solid, m.p. 218.1–219.2 °C. ^1H NMR (600 MHz, DMSO) δ = 8.20 (s, 1H), 7.78 (s, 1H), 3.18 (s, 3H), 2.62 (s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 196.4, 181.4, 159.0, 154.9, 153.8, 126.2, 126.0, 119.5, 106.7, 28.8, 27.1. IR (KBr) δ = 1758, 1734, 1685, 1629, 1376, 1325, 1261 cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 248 (47), 233 (45), 205 (100), 175 (21), 131 (35), 103 (22).

Ethyl 1-methyl-2,3-dioxoindoline-5-carboxylate (2f). Yield: 21.4 mg (46%), Yellow solid, m.p. 136.6–136.8 °C. ^1H NMR (600 MHz, $CDCl_3$) δ = 8.35 (dd, *J* = 8.3, 1.5 Hz, 1H), 8.28 (d, *J* = 1.2 Hz, 1H), 6.98 (d, *J* = 8.3 Hz, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 3.32 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.4, 164.9, 158.3, 154.4, 134.0, 126.5, 126.4, 117.1, 109.7, 61.5, 26.5, 14.3. IR (KBr) δ = 1754, 1739, 1709, 1612, 1592, 1321, 1268, 1238 cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 233(97), 205 (48), 188 (27), 176 (34), 160 (100), 149 (36), 148 (35), 132 (89), 104 (30), 77 (27), 63 (21).

Ethyl 1-methyl-6-nitro-2,3-dioxoindoline-5-carboxylate (3f). Yield: 13.9 mg (25%), Yellow solid, m.p. 159.8–160.0 °C. ^1H NMR (600 MHz, $CDCl_3$) δ = 8.13 (s, 1H), 7.18 (s, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.36 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ = 180.7, 162.5, 157.2, 155.6, 154.3, 127.8, 120.7, 118.1, 105.4, 62.9, 26.2, 13.8. IR (KBr) δ = 1754, 1724, 1627, 1551, 1359, 1315, 1283 cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 278 (100), 250 (61), 248 (37), 233 (41), 222 (54), 205 (94), 194 (24), 177 (65), 176 (60), 174 (45), 148 (38), 131 (30), 104 (24), 103 (25), 81 (29), 62 (25). HRMS (ESI) m/z: calcd for $C_{12}H_{11}N_2O_6^+$ $(M+H)^+$ 279.06116, found 279.06137.

5-fluoro-1-methylindoline-2,3-dione (2g)[9]**.** Yield: 7.2 mg (10 %), Deep crimson solid, m.p. 142.5–143.5 °C (lit. 150.7-152.5 °C). ^1H NMR (600 MHz, $CDCl_3$) δ = 7.37 – 7.29 (m, 2H), 6.87 (dd, *J* = 8.2, 3.5 Hz, 1H), 3.26 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.8, 159.4 (d, *J* = 246.1 Hz, 1C), 158.0, 147.5, 124.7(d, *J* = 24.2 Hz, 1C), 118.0, 117.8, 112.4 (d, *J* = 24.2 Hz, 1C), 111.1(d, *J* = 3.2 Hz, 1C), 26.4. LRMS (EI, 70 eV) *m/z* (%): 179 (63), 151 (27), 123 (46), 122 (100), 96 (30).

5-fluoro-1-methyl-6-nitroindoline-2,3-dione (3g). Yield: 18.9 mg (42 %), Deep crimson solid, m.p. 147.4–148.2 °C. ^1H NMR (600 MHz, $CDCl_3$) δ = 7.56 (d, *J* = 8.1 Hz, 1H), 7.50 (d, *J* = 5.1 Hz, 1H), 3.34 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 181.2, 156.7, 152.3(d, *J* = 265 Hz, 1C), 146.7, 142.68, 142.6, 120.7, 115.6 (d, *J* = 24.0, 1C), 106.9, 26.8. IR (KBr) δ = 1769, 1748, 1639, 1606, 1536, 1462, 1442, 1345cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 224 (98), 196 (47), 194 (44), 168 (77), 167 (31), 138 (33), 137 (44), 123 (23), 122 (89), 95 (48), 81(100).

5-chloro-1-methylindoline-2,3-dione (2h)[9]**.** Yield: 13.4 mg (35%), Crimson solid, m.p. 171.9–172.6 °C (lit. 165.1–166.8 °C). ^1H NMR (600 MHz, $CDCl_3$) δ=7.61–7.56 (m, 2H), 6.88 (d, *J* = 8.0 Hz, 1H), 3.27 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.3, 157.7, 149.7, 137.7, 129.7, 125.2, 118.3, 111.2, 26.4. IR (KBr) δ = 1748, 1733, 1725, 1610, 1483, 1468, 1445, 1327 cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 197 (23), 195 (76), 169 (13), 167 (39), 141 (23), 140 (39), 139 (72), 138 (100), 114 (10), 112 (30).

5-chloro-1-methyl-6-nitroindoline-2,3-dione (3h). Yield: 19.4 mg (40%), Yellow solid, m.p. 205.1–205.7 °C. ^1H NMR (600 MHz, $CDCl_3$) δ = 7.78 (s, 1H), 7.29 (s, 1H), 3.33 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 180.8, 156.6, 149.8, 128.3, 122.1, 119.3, 106.8, 100.0, 26.8. IR (KBr) δ=1762, 1754, 1736, 1616, 1554, 1412, 1350 cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 242 (34), 240 (100), 214 (21), 212 (70), 186 (31), 184 (100), 140 (26), 138 (79), 111 (30), 103 (33), 102 (46), 99 (39), 88 (29), 74 (25), 62 (22). HRMS (ESI) m/z calcd for $C_9H_5ClN_2O_4Na^+$ $(M+Na)^+$ 262.98301, found 262.98331.

5-bromo-1-methylindoline-2,3-dione (2i)[18b]**.** Yield: 14.9 mg (31%), Crimson solid, m.p. 161.8–162.3 °C (lit. 163–164 °C). ^1H NMR (600 MHz, $CDCl_3$) δ = 7.76-7.70 (m, 2H), 6.83 (d, *J* = 8.3 Hz, 1H), 3.26 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.1, 157.5, 150.1, 140.6, 128.1, 118.6, 116.6, 111.6, 26.3. IR (KBr) δ = 1751, 1733, 1722, 1607, 1474, 1442, 1327 cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 241 (74), 239 (75), 213 (64), 211 (61), 186 (67), 185 (97), 183 (75), 182 (100), 159 (22), 156 (26), 77 (38), 76 (20), 75 (31), 74 (27), 63 (38).

5-bromo-1-methyl-6-nitroindoline-2,3-dione (4i). Yield: 16.0 mg (28%), Yellow solid, m.p. 212.6–213.5 °C. ^1H NMR (600 MHz, $CDCl_3$) δ = 7.94 (s, 1H), 3.33 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.7, 156.5, 155.2, 150.5, 131.3, 119.5, 108.4, 106.9, 26.8. IR (KBr) δ = 1748, 1621, 1542, 1409, 1345, 1306 cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 331(4), 329 (6), 286 (56), 284 (50), 258 (46), 256 (70), 254 (41), 230 (46), 228 (28), 199 (27), 197 (70), 184 (39), 182 (45), 143 (34), 141 (41), 115 (34),103 (100), 88 (55), 83 (40).

5-iodo-1-methylindoline-2,3-dione (2j)[18d]**.** Yield: 26.6 mg (40%), Crimson solid, m.p. 166.4–167.0 °C (lit. 150–152 °C). ^1H NMR (600 MHz, $CDCl_3$) δ = 7.92 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.88 (d, *J* = 1.4 Hz, 1H), 6.72 (d, *J* = 8.2 Hz, 1H), 3.25 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 181.9, 157.2, 150.7, 146.4, 133.7, 119.0, 112.1, 86.0, 26.3. IR (KBr) δ= 1751, 1724, 1601, 1483, 1456, 11427, 1324 cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 287 (100), 259 (56), 231 (59), 230 (65), 104 (20), 77 (24), 63 (23).

1,5-dimethylindoline-2,3-dione (2k)[9]**.** Yield: 8.7 mg (25%), Crimson solid, m.p.147.5–149.3 °C (lit. 150.5–151.2 °C). ^1H NMR (600 MHz, $CDCl_3$) δ = 7.42 (d, *J* = 7.6 Hz, 2H), 6.80 (d, *J* = 8.5 Hz, 1H), 3.24 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 183.6, 158.4, 149.3, 138.7, 133.7, 125.7, 117.5, 109.7, 26.2, 20.7. LRMS (EI, 70 eV) *m/z* (%):175 (67), 147 (32), 119 (52), 118 (100), 91 (29).

1,5-dimethyl-6-nitroindoline-2,3-dione (3k). Yield: 13.6 mg (31%), Crimson solid, m.p. 180.4–181.5°C. ^1H NMR (600 MHz, DMSO) δ 7.68 (d, *J* = 15.1 Hz, 2H), 3.16 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 182.8, 158.4, 154.5, 150.0, 128.3, 126.9, 120.7, 106.2, 26.9, 18.4. LRMS (EI, 70 eV) *m/z* (%): 220 (100), 207 (26), 190 (25), 175 (39), 147 (85), 119 (38), 118 (24), 117 (42), 92 (42), 91 (54), 77 (53), 65 (28), 65 (28).

1,5-dimethyl-4,6-dinitroindoline-2,3-dione (4k). Yield: 6.4 mg (12%), Crimson solid, m.p. 214.5–215.5 °C. ^1H NMR (600 MHz, Acetone) δ = 7.93 (s, 1H), 3.39 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (151 MHz, Acetone) δ = 183.0, 161.9, 161.2, 156.0, 150.4, 122.7, 115.3, 113.3, 31.6, 16.9. LRMS (EI, 70 eV) *m/z* (%): 265 (30), 235 (52), 160 (33), 145 (22), 133 (23), 117 (27), 93 (70).

5-methoxy-1-methylindoline-2,3-dione (2l)[9]**.** Yield: 9.2 mg (24%), Deep red solid, m.p. 163.9–164.6 °C (lit. 171.2–172.5 °C). ^1H NMR (600 MHz, $CDCl_3$) δ 7.17 (dd, *J* = 8.0, 2.1 Hz, 2H), 6.83 (dd, *J* = 7.4, 1.6 Hz, 1H), 3.82 (s, 3H), 3.24 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 183.7, 158.3, 156.6, 145.4, 124.6, 117.9, 110.8, 109.6, 56.0, 26.2. IR (KBr) δ = 1742, 1724, 1627, 1486, 1292 cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 191 (100), 148 (48), 135 (57), 134 (70), 120 (85), 92 (22).

5-methoxy-1-methyl-6-nitroindoline-2,3-dione (3l). Yield: 23.1 mg (49%), Crimson solid, m.p.193.4–194.6 °C. ^1H NMR (600 MHz, $CDCl_3$) δ = 7.41 (s, 1H), 7.26 (s, 1H), 3.98 (s, 3H), 3.29 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 182.3, 157.1, 149.6, 144.1, 119.7, 111.1, 106.8, 99.8, 57.4, 26.6. LRMS (EI, 70 eV) *m/z* (%): 236 (100), 208 (61), 180

(33), 106 (23), 91 (20), 77 (28). HRMS (ESI) m/z calcd for $C_{10}H_9N_2O_5^+$ $(M+H)^+$ 237.05060, found 237.05031.

6-chloro-1-methylindoline-2,3-dione (2m)[18b]**.** Yield: 21.4 mg (55%), Crimson solid, m.p. 171.6–172.4 °C (lit. 177-178 °C). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.0 Hz, 1H), 7.12 (dd, *J* = 7.9, 0.9 Hz, 1H), 6.92 (s, 1H), 3.26 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.8, 158.2, 152.4, 144.9, 126.3, 124.0, 115.8, 110.8, 26.4. LRMS (EI, 70 eV) *m/z* (%): 197 (31), 195 (90), 167 (38), 141 (24), 140 (36), 139 (73), 138 (100), 126 (23), 112 (30), 75 (25).

6-chloro-1-methyl-4-nitroindoline-2,3-dione (3m). Yield: 9.7 mg (20%), Crimson solid, m.p. 163.1–163.7 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.95 (d, *J* = 1.7 Hz, 1H), 7.63 (d, *J* = 1.6 Hz, 1H), 3.38 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 179.0, 156.4, 153.3, 153.0, 134.8, 120.7, 117.6, 103.3, 26.9. LRMS (EI, 70 eV) *m/z* (%): 242 (34), 240 (100), 214 (19), 212 (64), 186 (24), 184 (76), 140 (24), 138 (71), 111 (30), 103 (45), 102 (42), 99 (24), 97 (36), 88 (38), 75 (23), 74 (26), 62 (20). HRMS (ESI) m/z calcd for $C_9H_5ClN_2O_4Na^+$ $(M+Na)^+$ 262.98301, found 262.98367.

1,7-dimethylindoline-2,3-dione (2n)[9]**.** Yield: 6.7 mg (19%), Deep red solid, m.p. 157.8–158.3 °C (lit. 162.3–164.8 °C). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.3 Hz, 1H), 7.37–7.31 (m, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 3.53 (s, 3H), 2.57 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 183.7, 159.2, 149.0, 142.2, 123.9, 123.4, 121.9, 118.5, 29.7, 18.8. IR (KBr) δ = 1736, 1598, 1453, 1436, 1362, 1315cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 175 (87), 147 (27), 119 (67), 118 (100), 91 (41).

1,7-dimethyl-6-nitroindoline-2,3-dione (3n). Yield: 17.2 mg (39%), Crimson solid, m.p. 154.0–154.8 °C. LRMS (EI, 70 eV) *m/z* (%): 220 (100), 203 (24), 175 (36), 147 (45), 119 (24), 118 (25), 117 (48), 91 (35), 77 (34). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.61 (d, *J* = 7.9 Hz, 1H), 7.37 (d, *J* = 7.9 Hz, 1H), 3.62 (s, 3H), 2.57 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ=182.2, 158.5, 158.3, 150.9, 123.8, 119.7, 119.0, 116.0, 30.7, 13.7. IR (KBr) δ = 1756, 1733, 1598, 1530, 1448, 1357, 1303cm^{-1}. HRMS (ESI) m/z calcd for $C_{10}H_9N_2O_4^+$$(M+H)^+$ 221.05568, found 221.05505.

7-bromo-1,5-dimethylindoline-2,3-dione (2o). Yield: 7.7 mg (15%), Crimson solid, m.p. 150.7–151.6 °C (CAS No. 906660-35-3). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.54 (s, 1H), 7.39 (s, 1H), 3.63 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 182.8, 158.7, 146.0, 143.7, 135.4, 125.1,120.4, 103.9, 29.6, 20.1. IR (KBr) δ = 1742, 1621, 1569, 1474, 1438cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 255 (63), 253 (59), 227 (23), 225 (24), 199 (45), 198 (37), 197 (44), 196 (38), 118 (100), 117 (22), 103 (21), 91 (29), 89 (32), 63 (20).

7-bromo-1,5-dimethyl-6-nitroindoline-2,3-dione (3o). Yield: 12.5 mg (21%), Crimson solid, m.p. 161.5–162.3 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.47 (s, 1H), 3.61 (s, 3H), 2.24 (s, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ = 181.3, 158.0, 157.8, 147.7, 127.2, 126.8, 119.5, 95.9, 29.9, 16.9. IR (KBr) δ = 1751, 1624, 1548, 1542, 1460cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 300 (99), 298 (100), 254 (26), 253 (30), 227 (33), 225 (67), 207 (31), 191 (26), 146 (26), 145 (41), 116 (26), 118 (32), 117 (58), 76 (55), 75 (45).

7-bromo-1,5-dimethyl-4,6-dintroindoline-2,3-dione (4o) Yield: 8.3 mg (12%), Crimson solid, m.p. 202.1–203.1 °C. ^{1}H NMR (600 MHz, Acetone) δ = 3.72 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (151 MHz, Acetone) δ = 176.9, 158.0, 157.4, 149.3, 144.3, 117.3, 110.7, 97.6, 29.6, 11.0. IR (KBr) δ = 1745, 1630, 1542, 1451, 1380, 1365, 1289 cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 345 (40), 343 (34), 315 (54), 313 (57), 241 (29), 239 (30),181 (34),174 (23), 173 (41), 172 (25), 171 (31), 160 (65), 144 (100), 132 (43), 131 (32), 130 (33), 129 (46), 117 (32), 116 (51), 104 (42), 101 (36), 92 (46).

1-ethylindoline-2,3-dione (2p)[18b]**.** Yield: 5.0 mg (14%), Crimson solid, m.p. 93.0–93.9 °C(lit. 92–94 °C). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.60 (dd, *J* = 12.3, 4.4 Hz, 2H), 7.12 (t, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 7.8 Hz, 1H), 3.80 (q, *J* = 7.3 Hz, 2H), 1.32 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 183.7, 157.9, 150.7, 138.3, 125.5, 123.6, 117.7, 110.0, 35.0, 12.5. IR (KBr) δ = 1739, 1727, 1613, 1471, 1374, 1350cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 175 (100), 132 (42), 119 (63), 118 (78), 104 (61), 90 (28), 77 (34).

1-ethyl-6-nitroindoline-2,3-dione (3p) Yield: 18.5 mg (42%), Crimson solid, m.p. 159.6–159.8 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.01 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.74 (d, *J* = 1.7 Hz, 1H), 3.90 (q, *J* = 7.3 Hz, 2H), 1.39 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.3, 156.8, 153.7,151.3, 126.2, 121.1, 118.9, 105.1, 35.6, 12.3. IR (KBr) δ = 1756, 1736, 1624, 1603, 1542, 1439, 1342cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 220 (100), 175 (40), 147 (27), 145 (23), 119 (31), 118 (21), 117 (38), 92 (45), 77 (33). HRMS (ESI) m/z calcd for $C_{10}H_9N_2O_4^+$ $(M+H)^+$ 221.05568, found 221.05603.

1-isopropylindoline-2,3-dione (2q)[18a]. Yield: 8.0 mg (21%), Crimson solid, m.p. 113.9–114.5 °C(lit. 124.4–125.7 °C). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.4 Hz, 1H), 7.57 (td, *J* = 8.0, 1.3 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 4.55 (dt, *J* = 14.0, 7.0 Hz, 1H), 1.53 (d, *J* = 7.0 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 183.8, 157.8, 150.5, 138.0, 125.6, 123.2, 118.0, 111.3, 44.8, 19.4. IR (KBr) δ = 1739, 1719, 1607, 1598, 1465, 1351cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 189 (66), 146 (100), 132 (64), 92 (20), 90 (27).

1-isopropyl-6-nitroindoline-2,3-dione (3q). Yield: 18.9 mg (40%), Yellow solid, m.p. 161.9–162.7 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.98 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.85 (d, *J* = 1.8 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 1H), 4.58 (dt, *J* = 14.0, 7.0 Hz, 1H), 1.59 (d, *J* = 7.0 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 182.5, 156.8, 153.5, 151.1, 126.2, 121.3, 118.6, 106.2, 45.8, 19.2. IR (KBr) δ = 1754, 1736, 1267, 1601, 1536, 1439, 1345 cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 234 (95), 191 (100), 177 (23), 161 (48), 145 (70), 133 (22). HRMS (ESI) m/z calcd for $C_{11}H_{11}N_2O_4^+$ $(M+H)^+$ 235.07133, found 235.07153.

1-(prop-2-ynyl)indoline-2,3-dione (2r)[18e]**.** Yield: 4.1 mg (11%), Crimson solid, m.p. 142.3–144.9 °C (lit. 144–146 °C). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.71–7.62 (m, 2H), 7.19 (m, 2H), 4.56 (d, *J* = 2.5 Hz, 2H), 2.32 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 182.5, 157.2, 149.6, 138.4, 125.5, 124.2, 117.7, 111.1, 75.7, 73.3, 29.7. IR (KBr) δ = 3261, 2917, 2843, 2124, 1745, 1616, 1465, 1348 cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 185 (45), 156 (30), 146 (22), 129 (100), 102 (56), 90 (45).

6-nitro-1-(prop-2-ynyl)indoline-2,3-dione (3r). Yield: 14.7 mg (32%), Crimson solid, m.p. 186.5–187.1 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12 – 8.05 (m, 2H), 7.91 (d, *J* = 8.1 Hz, 1H), 4.78 (d, *J* = 2.5 Hz, 2H), 2.98 (t, *J* = 2.5 Hz, 1H). ^{13}C NMR (151 MHz, Acetone) δ 181.8, 156.6, 153.4, 150.5, 125.4, 122.0, 118.9, 106.0, 76.0, 73.9. IR (KBr) δ = 3264, 2975, 2922, 2124, 1745, 1624, 1601, 1536, 1445, 1345 cm^{-1}. LRMS (EI, 70 eV) m/z (%): 230 (100), 174 (60), 156 (28), 145 (47), 128 (62), 117 (33), 101 (46), 89 (32), 75 (31). HRMS (ESI) m/z calcd for $C_{11}H_7N_2O_4^+$ $(M+H)^+$ 231.04003, found 231.04012.

3-(2,3-dioxoindolin-1-yl)propanenitrile (2s)[18f]**.** Yield: 6.0 mg (15%), Crimson solid, m.p. 127.1–127.9 °C (lit. 101.1 °C). ^{1}H NMR (600 MHz, Acetone) δ = 7.73 (td, *J* = 7.9, 1.2 Hz, 1H), 7.60 (dd, *J* = 7.4, 0.5 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 4.16 (t, *J* = 6.8 Hz, 2H), 2.98 (t, *J* = 6.8 Hz, 2H). ^{13}C NMR (151 MHz, Acetone) δ = 182.9, 158.1, 150.4, 138.3, 124.6, 123.6, 117.9,117.5,110.7, 36.0, 15.7. IR (KBr) δ = 1736, 1615, 1465, 1359, 1321cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 200 (27), 132 (100), 77 (19).

3-(6-nitro-2,3-dioxoindolin-1-yl)propanenitrile (3s). Yield: 14.2 mg (29%), Yellow solid, m.p. 178.6–179.5 °C. ^{1}H NMR (600 MHz, Acetone) δ = 8.20 (d, *J* = 1.9 Hz, 1H), 8.06 (dd, *J* = 8.1, 1.9 Hz, 1H), 7.88 (d, *J* = 8.1 Hz, 1H), 4.33 (t, *J* = 6.8 Hz, 2H), 3.02 (t, *J* = 6.8 Hz, 2H). ^{13}C NMR (151 MHz, Acetone) δ = 182.0, 157.6, 153.6, 151.1, 125.4, 121.9, 118.7, 117.6, 105.8, 36.4, 15.7. IR (KBr) δ= 1756, 1742, 1627, 1616, 1536, 1439, 1351cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 245 (28), 177 (100), 147 (32), 131 (48), 119 (24).

1-phenylindoline-2,3-dione (2t)[18c]. Yield: 7.6 mg (17%), Crimson solid, m.p. 135.3–136.1 °C (lit.137–139 °C). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.71 (m, 1H), 7.61–7.52 (m, 3H), 7.50-7.40 (m, 3H), 7.19 (td, *J* = 7.5, 0.8 Hz, 1H), 6.91 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.9, 157.3, 151.7, 138.3, 132.9, 130.0, 128.8, 126.0, 125.6, 124.3, 117.5, 111.3. IR (KBr) δ = 1739, 1613, 1468, 1365, 1294cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 223 (17), 195 (100), 167 (31).

6-nitro-1-phenylindoline-2,3-dione (3t). Yield: 10.2 mg (19%), Crimson solid, m.p. 177.9–178.3 °C (CAS No. 681467-58-3). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.06 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.70 (d, *J* = 1.5 Hz, 1H), 7.65 (t, *J* = 7.8 Hz, 2H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.44 (d, *J* = 7.5 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ=181.7, 156.2, 153.6, 152.3, 132.0, 130.5, 129.7, 126.5, 125.9, 120.8, 119.5, 106.4. IR (KBr) δ= 1751, 1622, 1607, 1530, 1347, 1262 cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 268 (24), 240 (100), 194 (33), 166 (58), 139 (23), 77 (31).

***N*-methyl-*N*-(4-nitrosophenyl)-3-phenylpropiolamide (5)**. Yield: 38.0 mg (72%), Yellow solid, m.p. 163.2–164.2 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.46 (dd, *J* = 10.7, 4.3 Hz, 1H), 7.38 (t, *J* = 7.8 Hz, 2H), 7.31-7.27 (m, 2H), 6.64 (d, *J* = 10.2 Hz, 2H), 6.57 (d, *J* = 10.2 Hz, 2H), 2.92 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ= 183.0, 160.0, 150.0, 142.1, 134.4, 131.6, 129.4, 127.5, 127.4, 126.6, 65.5, 26.4. IR (KBr) δ = 1978, 1742, 1722, 1669, 1527, 1383, 1362 cm^{-1}. LRMS (EI, 70 eV) *m/z* (%): 264 (67), 233(87), 197 (21), 186 (30), 164 (23), 79 (27), 66 (100), 53 (46). HRMS (ESI) m/z calcd for $C_{16}H_{13}N_2O_2^+$ $(M+H)^+$ 265.09715, found 265.09787.

Ethyl 4-(N-methylpropiolamido)benzoate **(1f)**
Colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.09 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 4.39 (dd, *J* = 13.9, 6.9 Hz, 2H), 3.35 (s, 3H), 2.86 (s, 1H), 1.40 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.7, 152.6, 146.4, 130.6, 130.0, 126.9, 79.9, 76.1, 61.3, 36.3, 14.3. LRMS (EI, 70 eV) *m/z* (%): 231 (41), 186 (39), 159 (37), 158 (61), 130 (57), 104 (25), 77 (30), 66 (100). HRMS (ESI) m/z calcd for $C_{13}H_{14}NO_3^+$ $(M+H)^+$ 232.09682, found 232.09669.

N-isopropyl-*N*-phenylpropiolamide **(1q)**
While solid, m.p. 105.2–106.2 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 – 7.39 (m, 3H), 7.23 – 7.14 (m, 2H), 5.06 – 4.87 (m, 1H), 2.73 (d, *J* = 0.8 Hz, 1H), 1.10 (dd, *J* = 6.8, 1.2 Hz, 6H).^{13}C NMR (151 MHz, $CDCl_3$) δ 152.8, 137.7, 130.6, 128.9, 128.7, 79.4, 76.7, 46.7, 20.7. LRMS (EI, 70 eV) *m/z* (%): 187 (100), 172 (82), 145 (33), 144 (55), 120 (73), 118 (42), 117 (66), 104 (48), 94 (22), 77 (78). HRMS (ESI) m/z calcd for $C_{12}H_{14}NO^+$ $(M+H)^+$ 188.10699, found 188.10730.

N-phenyl-*N*(pro-2-ynyl)propiolamide **(1r)**
Colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 – 7.37 (m, 3H), 7.36 – 7.32 (m, 2H), 4.47 (d, *J* = 2.5 Hz, 2H), 2.83 (s, 1H), 2.22 (t, *J* = 2.5 Hz, 1H).^{13}C NMR (151 MHz, $CDCl_3$) δ 152.5, 140.4, 129.3, 128.8, 128.3, 80.6, 77.9, 75.7, 72.9, 37.9. LRMS (EI, 70 eV) *m/z* (%): 183 (33), 154 (100), 130 (30), 104 (25), 77 (51). HRMS (ESI) m/z calcd for $C_{12}H_{10}NO^+$ $(M+H)^+$ 184.07569, found 184.07574.

6-amino-1-methylindoline-2,3-dione **(6)**
Crisom oil. ^{1}H NMR (600 MHz, DMSO) δ = 7.23 (d, *J* = 8.4 Hz, 1H), 7.15 (s, 2H), 6.17 (dd, *J* = 8.4, 1.7 Hz, 1H), 6.11 (d, *J* = 1.6 Hz, 1H), 3.04 (s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 177.6, 161.7, 159.4, 154.7, 127.9, 108.0, 106.0, 94.3, 26.0. LRMS (EI, 70 eV) *m/z* (%): 176 (100), 148 (49), 147 (26), 120 (50), 119 (62), 93 (23). HRMS (ESI) m/z calcd for $C_9H_9N_2O_2^+$ $(M+H)^+$ 177.06585, found 177.06538.

N-mesityl-*N*-methylpropiolamide **(9)**
While solid, m.p. 108.3–108.9 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.92 (s, 2H), 3.15 (s, 3H), 2.64 (s, 1H), 2.29 (s, 3H), 2.19 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.8, 138.4, 137.6, 136.0, 129.3, 79.4, 76.1, 34.0, 21.0, 17.5. LRMS (EI, 70 eV) *m/z* (%): 201 (93), 186 (40), 184 (32), 148 (39), 91 (31), 66 (100). HRMS (ESI) m/z calcd for $C_{13}H_6NO^+$ $(M+H)^+$ 202.12264, found 202.12282.

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Oxidative Radical Cyclization of *N*-methyl-*N*-arylpropiolamide to Isatins via Cleavage of Carbon-carbon Triple Bond

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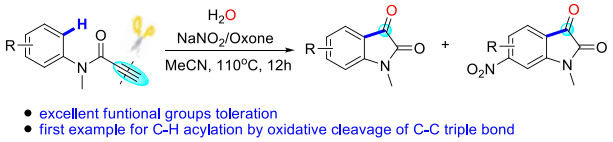

- excellent funtional groups toleration
- first example for C-H acylation by oxidative cleavage of C-C triple bond