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Electrocatalytic C–H/N–H Coupling of 2′-Aminoacetophenones for the Synthesis of Isatins

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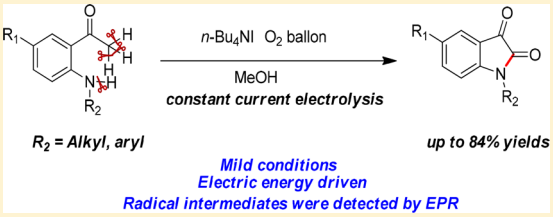
Supporting Information

ABSTRACT: 2′-Aminoacetophenones undergo a C(sp^3)–H oxidation followed by intramolecular C–N bond formation by virtue of a simple electrochemical oxidation in the presence of *n*-Bu_4NI, providing various isatins with moderate to good yields. The reaction intermediates were detected, and a radical-based pathway was proposed.



Isatins represent an important skeleton of heterocyclic compounds and widely exist in natural products and pharmaceuticals,[1] which have been extensively used in various reactions in the past few decades.[2] As a result, substantial attention has been paid to the development of the preparation of isatins. Traditionally, the pioneering work of the synthesis of isatins was mainly developed by Sandmeyer,[3] Stollé,[4] and Martinet.[5] However, the scope of substrates and regioselectivity restricted the wide application of these methods. Recently, these methods have been gradually replaced by several improved protocols, including aryne-based methods,[6] Sandmeyer modifications,[7] sulfurylide mediated carbonyl homologation,[8] metal-catalyzed oxidations,[9] and metal-free mediated domino reactions.[10] For instance, Zhu et al. and Wu et al. developed copper-catalyzed synthesis of isatins from 2′-aminoacetophenones, utilizing O_2[9c] and I_2[9d] as oxidants, respectively. Although considerable progress has been made in these reported methodologies, metal catalyst, peroxides, and elevated temperature were usually involved in most of these methods, resulting in concerns about the environmental impact. Therefore, a mild and green approach to synthesize various isatins is still attractive and valuable.

Electrochemical synthesis features sustainability and environmentally friendly properties and has been widely applied to constructing all kinds of chemical bonds.[11,12] As part of our continuing interest in C–H functionalization under electrochemical conditions,[13] we recently realized the synthesis of α-ketoamides,[14] α-ketoesters,[15] α-enaminones,[16] β-enaminones,[17] and the difunctionalization of arylketones with malonate esters.[18] Therefore, we envisaged that isatins may also be synthesized from 2′-aminoacetophenones via an electrochemically oxidative amidation of sp^3 C–H bonds. Herein, we found that the electrochemically oxidative cyclization of 2′-aminoacetophenones could be indeed conducted by using *n*-Bu_4NI as a redox catalyst and the reaction can be carried out smoothly at room temperature.

Initially, 1-(2-(benzylamino)phenyl)ethanone (**1a**) was chosen as the model substrate in an undivided cell equipped with a pair of platinum-plate electrodes (1.5 × 1.5 cm^2) in the presence of KI as electrolyte and MeOH as solvent under an oxygen atmosphere. To our delight, the desired product **2a** was obtained in 67% yield (Table 1, entry 1) after the electricity quantity of 14.9 F was consumed at room temperature. Later, other different supporting electrolytes, such as Me_4NI, Et_4NI, *n*-Bu_4NI, NaBr, and $LiClO_4$, were examined in the reaction (Table 1, entries 2–6). All of the iodine salts could conduct this reaction smoothly while NaBr and $LiClO_4$ hardly worked for this reaction, which indicated that iodine salts were crucial for the reaction. Of the counterions, *n*-Bu_4N^+ gave a superior result to K^+, Me_4N^+, or Et_4N^+, perhaps due to the good solubility of *n*-Bu_4NI in MeOH.[19] Then we screened the reaction current density, and a better yield was obtained when the current density was 8.9 mA/cm^2 (Table 1, entry 4 vs 7 and 8). After testing various solvents, it was found that MeOH was the best solvent. When other solvents were employed, the yield of the desired product decreased sharply, and only a trace amount of product was detected through thin layer chromatography (TLC) analysis and the ^1H NMR of the reaction mixture (Table 1, entries 9–12). Other types of electrodes were also examined. The experimental results indicated that the Pt/Pt electrode was the best electrode couple in this reaction (Table 1, entries 13–15). In addition, when the reaction was performed under air atmosphere instead of oxygen atmosphere, the reaction yield was sharply decreased from 84% to 25%, which implied that the oxygen atmosphere was crucial to this transformation (Table 1, entry 16). After investigation, the

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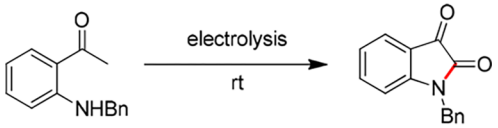
Table 1. Optimization of the Reaction Conditions[a]



1a 2a

entry	electrode	solvent	electrolyte	current density (mA/cm^2)	yield[b] (%)
1	Pt/Pt	MeOH	KI	8.9	67
2	Pt/Pt	MeOH	Me_4NI	8.9	51
3	Pt/Pt	MeOH	Et_4NI	8.9	62
4	**Pt/Pt**	**MeOH**	***n*-Bu$_4$NI**	8.9	**84**
5	Pt/Pt	MeOH	NaBr	8.9	trace
6	Pt/Pt	MeOH	$LiClO_4$	8.9	trace
7	Pt/Pt	MeOH	*n*-Bu$_4$NI	4.4	65
8	Pt/Pt	MeOH	*n*-Bu$_4$NI	13.3	74
9	Pt/Pt	EtOH	*n*-Bu$_4$NI	8.9	trace
10	Pt/Pt	DMSO	*n*-Bu$_4$NI	8.9	trace
11	Pt/Pt	CH_3CN	*n*-Bu$_4$NI	8.9	trace
12	Pt/Pt	CH_2Cl_2	*n*-Bu$_4$NI	8.9	trace
13	C/Pt	MeOH	*n*-Bu$_4$NI	8.9	79
14	Pt/C	MeOH	*n*-Bu$_4$NI	8.9	55
15	Pt/Cu	MeOH	*n*-Bu$_4$NI	8.9	71
16[c]	Pt/Pt	MeOH	*n*-Bu$_4$NI	8.9	25
17[d]	Pt/Pt	MeOH	*n*-Bu$_4$NI	0	n. d.

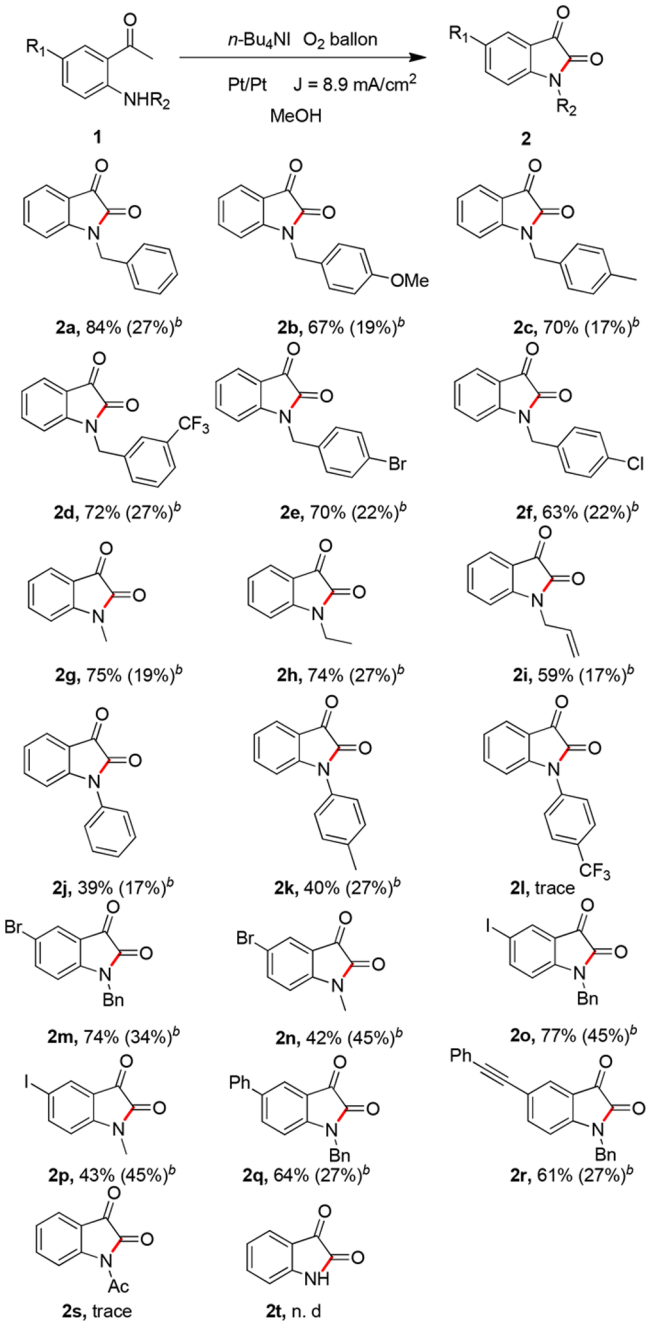
[a]Reaction conditions: **1a** (0.5 mmol), electrolyte (1 mmol), O_2 ballon, solvent (10 mL); the electrolysis was conducted at a constant current (8.9 mA/cm^2) in an undivided cell, room temperature. [b]The isolated yields after column chromatograpy. [c]Under air. [d]Stirring for 24 h at room temperature. n. d. = not detected.

optimal reaction conditions were summarized as follows: 2′-aminoacetophenones (0.5 mmol), *n*-Bu$_4$NI (1 mmol), MeOH (10 mL), and O_2 (ballon) in an undivided cell equipped with two platinum-plate electrodes. The reaction was conducted with a constant current density of 8.9 mA/cm^2 at room temperature (Table 1, entry 4).

It was worth noting that under the standard reaction conditions without pass electricity, no desired product was detected by TLC and the ^{1}H NMR after stirring for 24 h (Table 1, entry 17). This result suggested that the reaction driving force should be the employment of electric energy.

With the optimized conditions in hand, the scope of this reaction was investigated and the results were showed in Table 2. To our delight, compounds **1a**−**1r** with various substitutions on both the aryl ring and the nitrogen atom can be employed as the reaction substrates to perform this transformation smoothly with the consumption of 9.0−23.9 F charge, affording the desired products **2a**−**2r** in moderate to good yields, as shown in Table 2. On the other hand, various *N*-alkyl substituted isatins without substitution on the aromatic ring were synthesized in 59−84% yields (**2a**−**2i**). Afterward, the 2′-aminoacetophenones with different *N*-phenyl substituents on the nitrogen atom could also be examined in this reaction. The corresponding products can be obtained in spite of relatively lower yields (**2j**−**2l**), perhaps due to the low nucleophilicity of nitrogen atom. Moreover, it was found that the bromo/iodine-substituted 2′-aminoacetophenone derivatives were compatible with the standard reaction conditions to give isatins with moderate yields (**2m**−**2p**). To our satisfaction, when R_1 was the phenyl or the phenylacetylene substituent, the reaction can be still carried out well. The corresponding products can be

Table 2. Electrochemical Synthesis of Various Isatins[a]



[a]Reaction conditions: Table 1, entry 4. The isolated yields after column chromatograpy. n. d. = not detected. [b]The values in the parentheses were the current efficiency.

obtained in the yields of 64% and 61% (**2q** and **2r**), respectively. However, the 2′-aminoacetophenone bearing either electron withdrawing group or no substituent on the nitrogen of the amino group failed to afford the desired products (**2s** and **2t**). It should be mentioned that the reaction between methyl ketones and iodine in the alcohol solvents could provide corresponding carboxylic esters with a loss of one carbon atom.[20] This was also observed in our reactions, which resulted in moderate yields of the desired products. In addition, the reaction current efficiency was listed in the parentheses of the Table 2, which represented a mild and green method for

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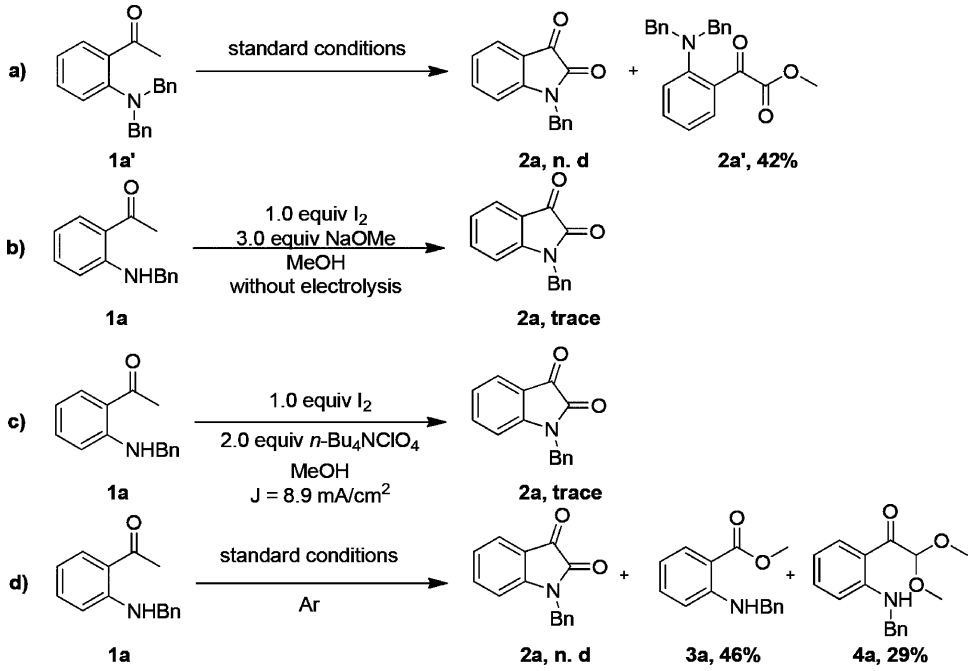
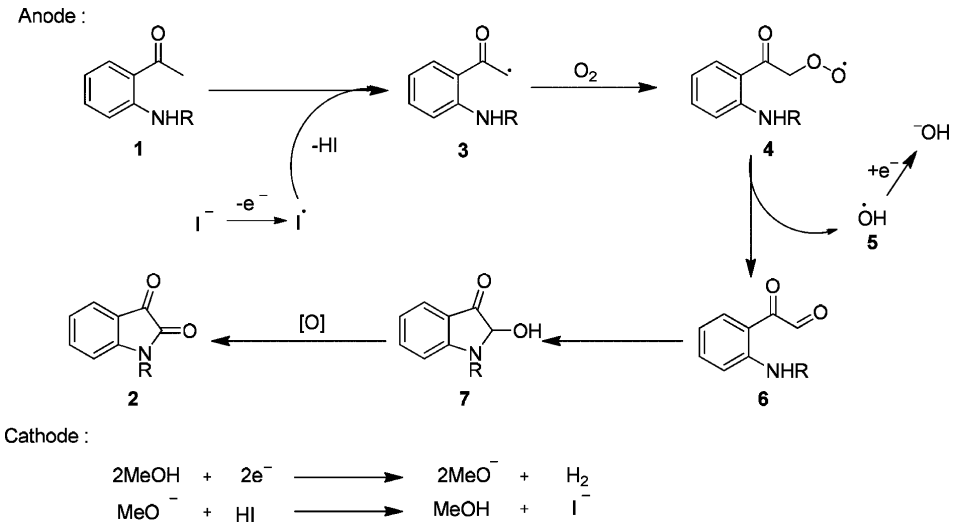
Scheme 1. Control Experiments for the Reaction



Scheme 2. Proposed Reaction Mechanism



the synthesis of isatins, although the current efficiency was relatively low.

To gain insight into the reaction mechanism, some control experiments were carried out (Scheme 1). First, substrate **1a**′ was subjected to standard conditions to understand the role of the amine group in the reaction mechanism. No desired product **2a** was observed, but **2a**′ was isolated, which was identical to our previous reports.[15] This result not only suggested that the secondary amine was necessary for this transformation, but also implied that 2-(2-(dibenzylamino)-phenyl)-2-oxoacetaldehyde may be the intermediate in this reaction (Scheme 1a). Subsequently, when 1.0 equiv of molecular iodine was employed as an oxidant in the presence of sodium methoxide (3.0 equiv) without electrolysis, a trace amount of the desired product was detected and the substrate **1a** was recovered (Scheme 1b). When the reaction was electrolyzed in the presence of 1.0 equiv of molecular iodine and 2.0 equiv of n-Bu_4NClO_4, trace amount of product **2a** and 1-(2-(benzylamino)-5-iodophenyl)ethanone (**1o**) were found (Scheme 1c). The substrate **1a** could also be oxidized by the overstoichiometric amounts of charge under the condition (1.1 V vs Ag/AgCl) and a trace amount of benzaldehyde was also detected. These results indicated that molecular iodine (I_2) or hypoiodite was not the active species in the initial step (from species **1** to **3** in Scheme 2). The reaction should be initiated by an iodine radical generated on the anode surface. Moreover, when the reaction was electrolyzed under argon atmosphere instead of oxygen atmosphere, no desired product was observed. In contrast, methyl 2-(benzylamino)benzoate (**3a**) and 1-(2-(benzylamino)phenyl)-2,2-dimethoxyethanone (**4a**) were obtained with the yields of 46% and 29%, respectively, under this condition (Scheme 1d). These results further indicated that the oxygen atmosphere promoted this transformation (from species **3** to **4** in Scheme 2) and inhabited the

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radical coupling between species **3** and iodine radial at the same time.

To further understand this reaction, electron paramagnetic resonance (EPR) experiments were performed to detect the possible free radicals involved in the reaction process. As shown in Figure 1, a complicated spectra **a** was obtained in the

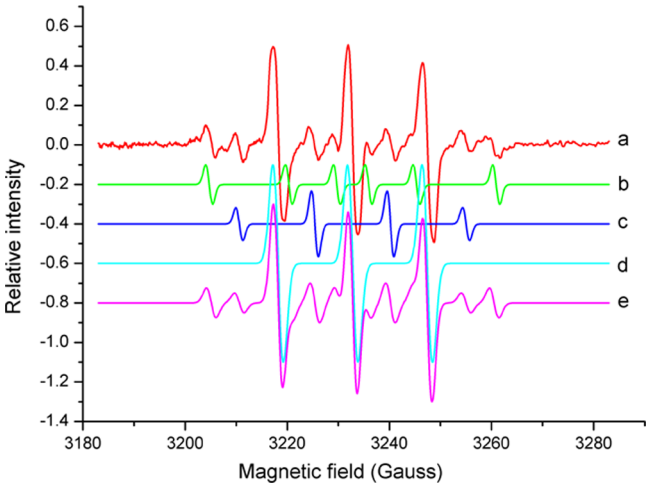

Figure 1. EPR spectra (X band, 9.7 GHz, room temperature) for reaction mixtures in the presence of the radical trapper DMPO and their simulations (**b**–**e**). (a) Spectrum **a** was the experimental spectrum. (b) Simulation of (2-NHBn)PhCOCH$_2$-DMPO. (c) Simulation of DMPO-OH. (d) Simulation of DMPOX. (e) Overlapping of spectra **b**, **c**, and **d** with an intensity ratio of 3:2:10 led to the complicated **e**, which was consistent with the experimental result **a**.

presence of the radical trapper 5,5-dimethyl-1-proline-*N*-oxide (DMPO). Three signals were identified by the characteristic hyperfine constants for nitrogen and β-proton.[21] One was assigned to be (2-NHBn)PhCOCH$_2$-DMPO with the A_{14N} = 15.2 G and A_{1H} = 25 G. The hyperfine constant of β-proton was a little higher than that of the saturated carbon center, perhaps due to the effect of the nitrogen group. Another signal can be ascribed to DMPO-OH and the hyperfine constants for nitrogen and proton were $A_{14N} = A_{1H}$ = 14.8 G. The last signal was found to be the oxidized DMPO with an A_{14N} = 14.6 G for the nitrogen atom, which was possibly oxidized by oxidizing substances generated under our reaction conditions. Spectra **b**, **c**, and **d** were their corresponding simulations ((2-NHBn)-PhCOCH$_2$-DMPO, DMPO-OH and DMPOX), respectively. When we overlapped the spectra **b**, **c**, and **d** with an intensity ratio of 3:2:10, the complicated spectra **e** were obtained, which was consistent with the experimental result **a**. On the other hand, only weak background signal was observed in the absence of 1-(2-(benzylamino)phenyl)ethanone (**1a**). Therefore, these results further provided evidence for a radical process in the reaction.

Base on the results mentioned above and the previous reports, a plausible mechanism was proposed for this electrocatalytic C–H/N–H cross coupling reaction (Scheme 2). First, an iodine free radical generated on the platinum anode surface via an electrochemical oxidation subsequently reacts with substrate **1** to produce intermediate **3**, accompanied by the loss of molecular hydrogen iodide. Perhaps due to the low concentration of radical intermediate **3** and iodine radical, this radical intermediate **3** is more easily trapped by oxygen molecule to form intermediate **4**[22] than the radical/radical coupling. However, the intermediate **4** is unstable and easily loses hydroxy radical **5**[23] to generate corresponding intermediate **6** under our reaction conditions. The leaving hydroxy radical **5** can be easily reduced in the cathode due to its high redox potential.[24] Afterward, the intramolecular nucleophilic addition of intermediate **6** occurs, in which the amine group attacks the aldehyde group to give the intermediate **7**. Finally, the intermediate **7** is further oxidized to afford the desired product **2**. This oxidation can occur on the anode surface or can be conducted by molecular I_2 and CH_3OI generated in the reaction. On the cathode surface, MeOH is reduced to generate the methoxide anion and hydrogen gas, which can further react with hydrogen iodide to regenerate iodide anion to complete the catalytic cycle.

In conclusion, we developed a mild electrochemically catalyzed approach to synthesize various isatins in moderate to good yields. The reaction was initiated by the iodine radical via an anodic oxidation, and subsequently induced C–O and C–N bond formation. This green process features the employment of electric energy as driving force, high atom economy, and no additional conducting salts. In addition, the reaction intermediates were detected by EPR and a probably radical reaction mechanism was proposed.

EXPERIMENTAL SECTION

General Information. All products were characterized by ^{1}H NMR and ^{13}C{^{1}H}NMR, using TMS as an internal reference (^{1}H NMR: 400 MHz, ^{13}C{^{1}H}NMR: 100 MHz). HRMS (ESI) data were recorded on a Q-TOF Premier. Commercial reagent and compound were used without purification unless otherwise indicated. Substrates **1a**–**1i** and **1s** were prepared according to the literature procedures.[10b] Substrates **1j**–**1k**[25] and **1m**–**1r**[26,10b] as well as **1a**′[27] were synthesized according to the literature procedures.

Representative Procedures for the Synthesis of Isatins. An undivided cell was equipped with a magnet stirrer, platinum plate (1.5 × 1.5 cm^2) electrode, as the working electrode and counter electrode. In the electrolytic cell, a mixture of 2′-aminoacetophenones (0.5 mmol), *n*-Bu$_4$NI (1 mmol, 369.4 mg), O_2 (balloon), and MeOH (10 mL) was allowed to stir and electrolyze at constant current conditions (8.9 mA/cm^2) under room temperature until the reaction finished (TLC analysis). Then the solvent was removed with a rotary evaporator and the residue was purified by column chromatography on silica gel to afford the desired product. The product was dried under high vacuum for at least 0.5 h before it was weighed and characterized by NMR spectroscopy.

EPR Measurements and Simulations for the Capture of Radicals. An undivided cell was equipped with a magnet stirrer, two platinum electrodes (1.5 × 1.5 cm^2) as both the working electrode and the counter electrode, respectively. A mixture of 1-(2-(benzylamino)-phenyl)ethanone (**1a**) (0.5 mmol, 112.5 mg), *n*-Bu$_4$NI (1 mmol, 369.4 mg), O_2 (balloon), and MeOH (10 mL) was stirred and electrolyzed at constant current conditions (8.9 mA/cm^2) under room temperature for 1 h. A 0.05 mL reaction solution was taken out into a small tube and mixed well with 0.03 mL of DMPO aqueous solution. Then the mixture was quick-frozen with liquid nitrogen and measured by EPR at room temperature. EPR simulation was performed with EasySpin software package in Mathlab.[28] The simulation parameters were microwave frequency 9.072 GHz, line width 1.1 G, g-2.00515 (without calibration). The hyperfine constants were shown in the main text.

*1-Benzylindoline-2,3-dione (**2a**).*[10c] The title compound was prepared according to the general working procedure (5 h, 14.9 F) and purified by column chromatography (petroleum ether/ethyl acetate = 10:1) to give the product as a red solid: 84% yield, (100.0 mg); ^{1}H NMR (CDCl$_3$, 400 MHz, ppm): δ = 7.61 (d, J = 7.1 Hz, 1H), 7.48 (t, J = 7.4 Hz, 1H), 7.34–7.27 (m, 5H), 7.09 (t, J = 7.2 Hz, 1H), 6.78 (d, J = 7.5 Hz, 1H), 4.93 (s, 2H); ^{13}C{^{1}H}NMR (CDCl$_3$, 100

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MHz, ppm): δ = 183.3, 158.3, 150.7, 138.4, 134.5, 129.1, 128.2, 127.4, 125.4, 123.9, 117.7, 111.0, 44.1.

*1-(4-Methoxybenzyl)indoline-2,3-dione (**2b**).*[10b] The title compound was prepared according to the general working procedure (7 h, 20.9 F) and purified by column chromatography (petroleum ether/ethyl acetate = 10:1) to give the product as a red solid: 67% yield, (89.8 mg); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ = 7.61−7.59 (m, 1H), 7.48 (td, *J* = 7.8 Hz, *J* = 1.4 Hz,1H), 7.29−7.26 (m, 2H), 7.08 (td, *J* = 7.6 Hz, *J* = 0.76 Hz,1H), 6.89−6.85 (m, 2H), 6.80 (d, *J* = 8.0 Hz, 1H), 4.87 (s, 2H), 3.79 (s, 3H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz, ppm): δ = 183.4, 159.5, 158.2, 150.8, 138.3, 128.9, 126.5, 125.4, 123.8, 117.7, 114.4, 111.0, 55.3, 43.6.

*1-(4-Methylbenzyl)indoline-2,3-dione (**2c**).*[30] The title compound was prepared according to the general working procedure (8 h, 23.9 F) and purified by column chromatography (petroleum ether/ethyl acetate = 10:1) to give the product as a red solid: 70% yield, (90.1 mg); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ = 7.60 (d, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 7.8 Hz, 2H), 7.15 (d, *J* = 7.8 Hz, 2H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 1H); 4.89 (s, 2H), 2.33 (s, 3H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz, ppm): δ = 183.4, 158.3, 150.8, 138.3, 138.0, 131.4, 129.7, 127.5, 125.4, 123.8, 117.7, 110.0, 43.8, 21.1.

*1-(3-(Trifluoromethyl)benzyl)indoline-2,3-dione (**2d**).* The title compound was prepared according to the general working procedure (5 h, 14.9 F) and purified by column chromatography (petroleum ether/ethyl acetate = 10:1) to give the product as a red solid: 72% yield (110.2 mg), mp = 168−170 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ = 7.65 (d, *J* = 7.4 Hz, 1H), 7.59 (d, *J* = 8.7 Hz, 2H), 7.55−7.47 (m, 3H), 7.14 (t, *J* = 7.5 Hz, 1H), 6.76 (d, *J* = 8.0 Hz, 1H), 4.99 (s, 2H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz, ppm): δ = 182.8, 158.3, 150.3, 138.5, 135.7, 131.5 (q, *J* = 32.2 Hz), 130.7, 129.7, 125.7, 125.2 (q, *J* = 3.7 Hz), 124.2, 124.18 (q, *J* = 3.8 Hz), 123.8 (q, *J* = 270.7 Hz), 117.7, 110.7, 43.6; HRMS calcd. $[C_{16}H_{10}F_3NO_2 + Na]^+$: 328.0561, found: 328.0563.

*1-(4-Bromobenzyl)indoline-2,3-dione (**2e**).*[29] The title compound was prepared according to the general working procedure (6 h, 17.9 F) and purified by column chromatography (petroleum ether/ethyl acetate = 10:1) to give the product as a red solid: 70% yield, (110.1 mg); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ = 7.63 (d, *J* = 7.4 Hz, 1H), 7.52−7.47 (m, 3H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.12 (t, *J* = 7.6 Hz, 1H), 6.74 (d, *J* = 7.9 Hz, 1H), 4.89 (s, 2H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz, ppm): δ = 183.0, 158.2, 150.4, 138.4, 133.6, 132.2, 129.1, 125.6, 124.1, 122.2, 117.7, 110.8, 43.5.

*1-(4-Chlorobenzyl)indoline-2,3-dione (**2f**).*[10b] The title compound was prepared according to the general working procedure (6 h, 17.9 F) and purified by column chromatography (petroleum ether/ethyl acetate = 10:1) to give the product as a red solid: 63% yield, (85.8 mg); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ = 7.63 (d, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 7.9 Hz, 1H), 7.34−7.29 (m, 4H), 7.12 (t, *J* = 7.5 Hz, 1H), 6.75 (d, *J* = 7.9 Hz, 1H), 4.90 (s, 2H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz, ppm): δ = 183.0, 158.2, 150.4, 138.4, 134.1, 133.0, 129.3, 128.8, 125.6, 124.1, 117.7, 110.8, 43.4.

*1-Methylindole-2,3-dione (**2g**).*[10c] The title compound was prepared according to the general working procedure (7 h, 20.9 F) and purified by column chromatography (petroleum ether/ethyl acetate = 6:1) to give the product as a red solid: 75% yield, (60.2 mg); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ = 7.64−7.60 (m, 2H), 7.14 (t, *J* = 7.6 Hz, 1H), 6.91 (d, *J* = 7.9 Hz, 1H), 3.26 (s, 3H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz, ppm): δ = 183.4, 158.3, 151.5, 138.4, 125.4, 123.9, 117.4, 109.9, 26.3.

*1-Ethylindoline-2,3-dione (**2h**).*[10c] The title compound was prepared according to the general working procedure (5 h, 14.9 F) and purified by column chromatography (petroleum ether/ethyl acetate = 6:1) to give the product as a red solid: 74% yield, (64.7 mg); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ = 7.62−7.58 (m, 2H), 7.12 (t, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 3.82−3.77 (m, 2H), 1.32 (td, *J* = 7.2 Hz, *J* = 1.5 Hz, 3H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz, ppm): δ = 183.7, 157.9, 150.7, 138.4, 125.5, 123.6, 117.6, 110.0, 35.0, 12.5.

*1-Allylindoline-2,3-dione (**2i**).*[10c] The title compound was prepared according to the general working procedure (8 h, 23.9 F) and purified by column chromatography (petroleum ether/ethyl acetate = 10:1) to give the product as a red solid: 59% yield, (55.2 mg); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ = 7.63−7.56 (m, 2H), 7.13 (t, *J* = 7.5 Hz, 1H), 6.90 (d, *J* = 7.9 Hz, 1H), 5.81−5.90 (m, 1H), 5.39−5.25 (m, 2H), 4.38 (d, *J* = 5.2 Hz, 1H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz, ppm): δ = 183.3, 157.9, 150.8, 138.3, 130.3, 125.4, 123.8, 118.7, 117.5, 110.9, 42.5.

*1-Phenylindoline-2,3-dione (**2j**).*[10c] The title compound was prepared according to the general working procedure (8 h, 23.9 F) and purified by column chromatography (petroleum ether/ethyl acetate = 10:1) to give the product as a red solid: 39% yield, (43.8 mg); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ = 7.64−7.62 (m, 1H), 7.51−7.45 (m, 3H), 7.41−7.34 (m, 3H), 7.13−7.09 (m, 1H), 6.83 (d, *J* = 8.0 Hz, 1H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz, ppm): δ = 182.9, 157.3, 151.7, 138.4, 132.9, 130.0, 128.9, 126.0, 125.7, 124.3, 117.5, 111.3.

*1-(p-Tolyl)indoline-2,3-dione (**2k**).*[10c] The title compound was prepared according to the general working procedure (5 h, 14.9 F) and purified by column chromatography (petroleum ether/ethyl acetate = 10:1) to give the product as a red solid: 40% yield, (47.4 mg); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ = 7.61 (d, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.9 Hz, 1H), 7.28 (d, *J* = 8.1 Hz, 2H), 7.23−7.19 (m, 2H), 7.09 (t, *J* = 7.5 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 2.36 (s, 3H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz, ppm): δ = 182.1, 156.4, 150.9, 138.0, 137.3, 129.5, 129.1, 124.8, 124.5, 123.2, 116.4, 110.2, 20.2.

*1-Benzyl-5-bromoindoline-2,3-dione (**2m**).*[10c] The title compound was prepared according to the general working procedure (4 h, 11.9 F) and purified by column chromatography (petroleum ether/ethyl acetate = 10:1) to give the product as a red solid: 74% yield, (116.1 mg); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ = 7.72 (s, 1H), 7.59 (dd, *J* = 8.4 Hz, *J* = 1.9 Hz, 1H), 7.38−7.30 (m, 5H), 6.68 (d, *J* = 8.4 Hz, 1H), 4.93 (s, 2H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz, ppm): δ = 182.1, 157.5, 149.4, 140.5, 134.0, 129.2, 128.4, 128.2, 127.4, 118.8, 116.8, 112.7, 44.2.

*5-Bromo-1-methylindoline-2,3-dione (**2n**).*[10b] The title compound was prepared according to the general working procedure (3 h, 9.0 F) and purified by column chromatography (petroleum ether/ethyl acetate = 10:1) to give the product as a red solid: 42% yield, (50.2 mg); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ = 7.67−7.63 (m, 2H), 6.75 (d, *J* = 8.3 Hz, 1H), 3.18 (s, 3H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz, ppm): δ = 181.1, 156.5, 149.1, 139.6, 127.1, 117.6, 115.6, 110.6, 25.3.

*1-Benzyl-5-iodoindoline-2,3-dione (**2o**).*[10c] The title compound was prepared according to the general working procedure (3 h, 9.0 F) and purified by column chromatography (petroleum ether/ethyl acetate = 6:1) to give the product as a red solid: 77% yield, (139.9 mg); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ = 7.83 (s, 1H), 7.77 (d, *J* = 8.3 Hz,1H), 7.38−7.30 (m, 5H), 6.57 (d, *J* = 8.3 Hz, 1H), 4.92 (s, 2H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz, ppm): δ = 181.9, 157.2, 150.0, 146.3, 134.0, 133.9, 129.2, 128.4, 127.4, 119.2, 113.2, 86.3, 44.1.

*5-Iodo-1-methylindoline-2,3-dione (**2p**).*[10b] The title compound was prepared according to the general working procedure (3 h, 9.0 F) and purified by column chromatography (petroleum ether/ethyl acetate = 6:1) to give the product as a red solid: 43% yield, (62.3 mg); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ = 7.88−7.92 (m, 2H), 6.72 (d, *J* = 8.2 Hz, 1H), 3.25 (s, 3H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz, ppm): δ = 182.0, 157.2, 150.7, 146.4, 133.7, 119.0, 112.1, 86.1, 26.3.

*1-Benzyl-5-phenylindoline-2,3-dione (**2q**).*[10c] The title compound was prepared according to the general working procedure (5 h, 14.9 F) and purified by column chromatography (petroleum ether/ethyl acetate = 10:1) to give the product as a red solid: 64% yield, (100.0 mg); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ = 7.85 (d, *J* = 1.7 Hz, 1H), 7.70 (dd, *J* = 8.2 Hz, *J* = 2.0 Hz,1H), 7.50−7.42 (m, 5H), 7.38−7.37 (m, 5H), 6.85 (d, *J* = 8.2 Hz, 1H), 4.97 (s, 2H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz, ppm): δ = 183.4, 158.4, 149.7, 138.9, 137.5, 136.8, 134.5, 129.1, 128.2, 127.9, 127.5, 127.1, 126.6, 124.0, 118.1, 111.4, 44.2.

*1-Benzyl-5-(phenylethynyl)indoline-2,3-dione (**2r**).* The title compound was prepared according to the general working procedure (5 h, 14.9 F) and purified by column chromatography (petroleum ether/

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ethyl acetate = 10:1) to give the product as a red solid: 61% yield, (103.6 mg), mp = 180−182 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ = 7.69 (d, J = 1.6 Hz, 1H), 7.55 (dd, J = 8.2 Hz, J = 1.7 Hz,1H), 7.43−7.41 (m, 2H), 7.30−7.25 (m, 8H), 6.70 (d, J = 8.2 Hz, 1H), 4.88 (s, 2H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz, ppm): δ = 182.6, 158.1, 149.8, 141.1, 134.2, 131.6, 129.2, 128.7, 128.5, 128.3, 128.3, 127.4, 122.5, 119.4, 117.7, 111.1, 90.5, 87.2, 44.2; HRMS calcd. $[C_{23}H_{15}NO_2 + H]^+$: 338.1181, found: 338.1176.

*Methyl-2-(2-(dibenzylamino)phenyl)-2-oxoacetate(**2a′**).* The title compound was prepared according to the general working procedure (2.5 h, 7.5 F) and purified by column chromatography (petroleum ether/ethyl acetate = 20:1) to give the product as a yellow oil: 42% yield, (75.1 mg); ^{13}C{^{1}H}NMR ($CDCl_3$, 400 MHz, ppm): δ = 7.65 (d, J = 7.7 Hz, 1H), 7.39 (t, J = 7.7 Hz,1H), 7.21−7.17 (m, 6H), 7.09 (t, J = 7.5 Hz, 1H), 6.98 (d, J = 6.2 Hz, 4H), 6.88 (d, J = 8.1 Hz, 1H), 4.03 (s, 4H), 3.79 (s, 3H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz, ppm): δ = 188.6, 165.0, 152.9, 136.1, 134.0, 131.5, 129.4, 129.2, 128.3, 127.6, 123.0, 122.5, 57.6, 52.7; HRMS calcd. $[C_{23}H_{21}NO_3 + H]^+$: 360.1600, found: 360.1597.

*Methyl-2-(benzylamino)benzoate(**3a**).* The title compound was prepared according to the general working procedure (5 h, 14.9 F) and purified by column chromatography (petroleum ether/ethyl acetate = 30:1) to give the product as a yellow oil: 46% yield, (55.1 mg). ^{1}H NMR (CD_3COCD_3, 400 MHz, ppm): δ = 8.23 (s, 1H), 7.88 (dd, J = 8.0 Hz, J = 1.6 Hz, 1H), 7.41−7.32 (m, 5H), 7.30−7.25 (m, 1H), 6.73 (d, J = 8.4 Hz, 1H), 6.61−6.57 (m, 1H), 4.51 (d, J = 5.7 Hz, 2H), 3.83 (s, 3H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz, ppm): δ = 168.1, 149.9, 137.8, 133.6, 130.6, 127.6, 126.1, 126.0, 113.8, 110.6, 109.1, 50.5, 45.9; HRMS calcd. $[C_{15}H_{15}NO_2 + H]^+$: 242.1181, found: 242.1182.

*1-(2-(Benzylamino)phenyl)-2,2-dimethoxyethanone(**4a**).* The title compound was prepared according to the general working procedure (5 h, 14.9 F) and purified by column chromatography (petroleum ether/ethyl acetate = 20:1) to give the product as a yellow oil: 29% yield, (41.1 mg). ^{1}H NMR (CD_3COCD_3, 400 MHz, ppm): δ = 9.22 (s, 1H), 8.13 (dd, J = 8.2 Hz, J = 1.3 Hz, 1H), 7.40−7.33 (m, 5H), 7.31−7.25 (m, 1H), 6.77 (d, J = 8.6 Hz, 1H), 6.61−6.57 (m, 1H), 5.16 (s, 1H), 4.53 (d, J = 5.7 Hz, 2H), 3.46 (s, 6H); ^{13}C{^{1}H}NMR ($CDCl_3$, 100 MHz, ppm): δ = 194.9, 152.0, 138.3, 135.7, 132.6, 128.7, 127.3, 127.1, 114.6, 114.5, 112.2, 102.8, 54.3, 46.8; HRMS calcd. $[C_{17}H_{19}NO_3 + Na]^+$: 308.1263, found: 308.1256.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00635.

^{1}H NMR and ^{13}C NMR spectra for all the products (PDF)

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Notes

The authors declare no competing financial interest.

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