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Synthesis of *N*-Arylisatins by the Reaction of Arynes with Methyl 2-Oxo-2-(arylamino)acetates

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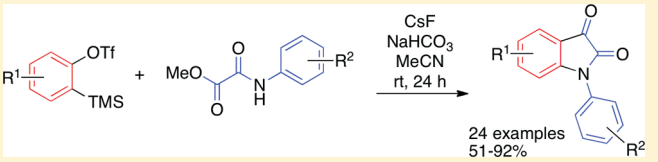
Supporting Information

ABSTRACT: N-Arylisatins are efficiently prepared by the reaction of 2-oxo-2-(arylamino)acetates and arynes under mild reaction conditions



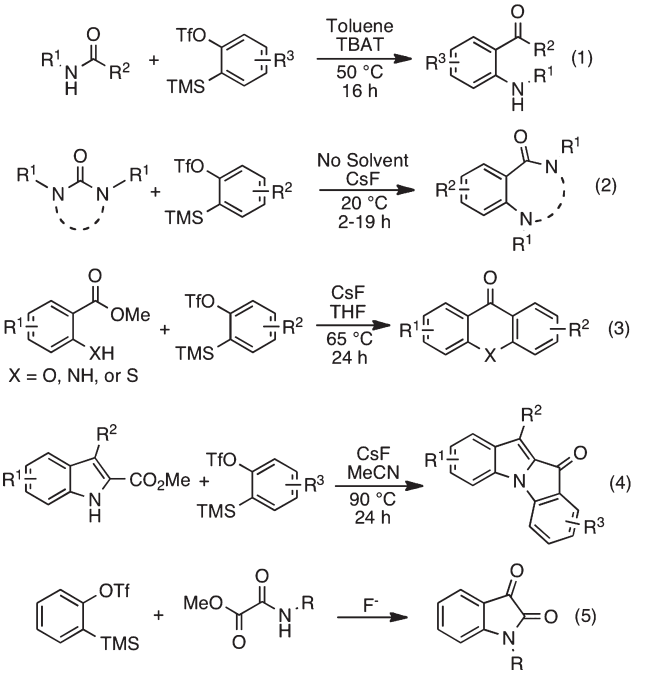
INTRODUCTION

Isatins are highly sought after compounds because of their biological and medicinal activities.[1] They exhibit a broad array of biologically important properties, including antifungal,[2] antiviral,[3] anti-HIV,[4] anti-AIDS,[4] antiprotozoal,[5] anticancer,[1b] antitumor,[6] and antileukemia properties.[7]

N-Arylisatins remain underexplored, however, in part because of their limited synthetic accessibility. There are only a few methods currently available for synthesizing *N*-arylisatins, and most suffer from poor yields and limited diversification. For example, a newer method involves reacting N−H isatins with aryl boronic acids and copper reagents.[8] However, yields are low and only *para*- or *meta*-substituted aryl boronic acids seem to react well. A slightly older method utilizes *N*,*N*-diarylamines and oxalyl chlorides.[9] A disadvantage of this method is not only the poor yields but also the fact that only symmetrical *N*,*N*-diarylamines can be utilized, for the most part.[10] Because isatins have exhibited impressive biological properties and convenient methods for synthesizing *N*-arylisatins are lacking, our group decided to examine an aryne-based method for producing them.

Aryne methodologies have recently proven valuable in the synthesis of a large number of heteroatom-containing structures.[11] Mechanistically, many of these methodologies are initiated by nucleophilic attack of a heteroatom, usually oxygen or nitrogen, onto the transient aryne intermediate. In fact, our group has shown that a variety of heteroatoms can undergo this process, including sulfonamides and anilines.[12] Shortly thereafter, we published the insertion reaction of arynes into the nitrogen−carbon bond of *N*-aryltrifuoroacetamides and *N*-arylsulfinamides.[13] Later on, Greaney et al. extended this methodology by demonstrating that arynes can undergo the same insertion with simple carboxamides (eq 1).[14] These reactions presumably involve a charged four-membered ring intermediate, which will be further highlighted herein. A similar mechanism has been proposed for the reaction of ureas and arynes (eq 2).[15]

In recent years, our group has published related methodologies where nucleophilic heteroatoms attack benzyne. For example, the reaction of arynes and *ortho*-heteroatom-substituted benzoates afford medicinally relevant acridones, xanthones, and thioxanthones (eq 3).[16] Also, in 2009, it was shown that methyl-2-indolecarboxylates react with arynes in a similar way to form indoloindolones (eq 4).[17] The success of the aforementioned reactions led us to explore the possibility of reacting *N*-substituted methyl oxamates with arynes (eq 5).



RESULTS AND DISCUSSION

Initial experiments suggested that the reaction of this parent system (R = Ph) worked; however, further optimization of the reaction conditions was needed in order to improve the yield.

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Table 1. Reaction of Various Methyl 2-Oxo-2-(arylamino)acetates with 2-(Trimethylsilyl)phenyl Trifluoromethanesulfonate[a]

entry	substrate	R =	product	% yield[b]
1	**1a**	H	**1aa**	78
2	**2a**	4-Me	**2aa**	82
3	**3a**	4-OPh	**3aa**	82
4	**4a**	4-F	**4aa**	90
5	**5a**	4-Cl	**5aa**	64
6	**6a**	4-Br	**6aa**	65
7	**7a**	4-I	**7aa**	72
8	**8a**	4-NO_2	-	-[c]
9	**9a**	4-CN	**9aa**	62
10	**10a**	4-CO_2Et	**10aa**	68
11	**11a**	4-CF_3	**11aa**	51
12	**12a**	3-CF_3	**12aa**	55
13	**13a**	2-*t*-Bu	**13aa**	82
14	**14a**	2-Ph	**14aa**	80
15	**15a**	2,5-$(OMe)_2$	**15aa**	75
16	**16a**	2,4,6-Me_3	**16aa**	67
17	**17a**	2,3-$(CH)_4$-	**17aa**	88
18	**18a**	2-I	**18aa**	84 (58)[d]

[a] Reaction conditions: 0.50 mmol of amide, 1.0 mmol of benzyne, 3.0 mmol of CsF, 1.0 mmol of $NaHCO_3$, MeCN (5 mL) at rt for 1 d. [b] Isolated Yield. [c] A complicated mixture was observed on TLC [d] 4.1 mmol scale reaction of amide. Only 1.5 equiv of the benzyne precursor were employed.

HPLC yield analysis was employed in order to conveniently observe the affects imparted by a variety of bases, solvents, times, temperatures, and the stoichiometry of the process. A direct relationship between the yield of *N*-phenylisatin and the amount of the benzyne precursor used (1.5−3.0 equiv) was observed. Out of cost concerns, 2.0 equiv of the benzyne precursor was chosen as an upper limit. $NaHCO_3$ was identified as the most effective base in this reaction. Ambient temperatures were optimal, as higher temperatures seemed to promote unwanted, unidentified side reactions. Acetonitrile was the best solvent for the ambient temperature employed, presumably due to its favorable solubility of CsF relative to other typical solvents used in benzyne chemistry, such as THF, DME, and toluene. For the parent system, optimal conditions were obtained when 2 equiv of the benzyne precursor, 2 equiv of $NaHCO_3$, 6 equiv of CsF, and MeCN (0.1 M) were employed under ambient temperatures for 24 h (Table 1, entry 1).

With optimal conditions in hand, the scope and limitations of this reaction were explored (Table 1). The effect imparted by electronically diverse substituents was studied by substituting at the *para* position of the methyl 2-oxo-2-(phenylamino)acetate, thus avoiding steric effects (entries 1−11). Compared to the parent substrate (**1a**), it was observed that electron-rich substituents seem to promote this reaction to a small extent (entries 2 and 3), whereas electron-poor substituents seem to lower the yield of this reaction (entries 8−11). Unfortunately, a complicated mixure was observed for the reaction of a substrate containing a nitro substituent (**8a**, entry 8). However, this came as no surprise, since this problem has been observed previously.[17] It is likely that the nitro moeity itself is reacting with benzyne. On the other hand, we were pleased to see that this reaction is little affected by *ortho* substitution (entries 13−18). For example, good yields were obtained when even bulky substituents, such as a *tert*-butyl group (entry 13) or an iodide (entry 18), were placed *ortho* to the reacting nitrogen atom. Furthermore, a 67% yield was obtained for substrate **16a**, where both *ortho* positions were substituted with methyl groups. Attempts were made to scale up the preparation of product **18aa** using only 1.5 equiv of the

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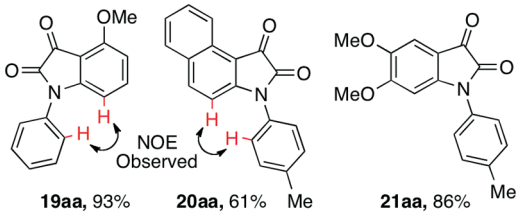
benzyne precursor (as opposed to 2.0 equiv). However, as expected, a lower yield of 58% was obtained.

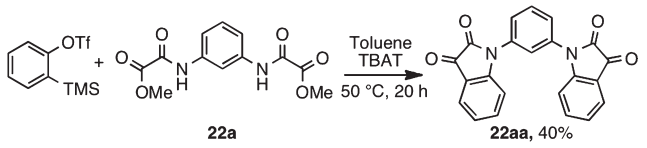
The scope and limitations of this reaction were further explored by examining other benzyne precursors (Figure 1). Unsymmetrical benzyne precursors were tested in order to observe the regioselectivity of the reaction. In fact, an excellent yield of a single regioisomer (**19aa**) was isolated from the reaction of **2a** with 2-methoxy-6-(trimethylsilyl)phenyl trifluoromethanesulfonate. Likewise, although in a lower yield, **20aa** was isolated as a single regioisomer from the reaction of **2a** with 2-(trimethylsilyl)naphthalen-1-yl trifluoromethanesulfonate. In addition to the unsymmetrical benzyne precursors, a symmetrical dimethoxybenzyne precursor was allowed to react with **2a**, producing **21aa** in an excellent 86% yield.



19aa, 93% **20aa**, 61% **21aa**, 86%

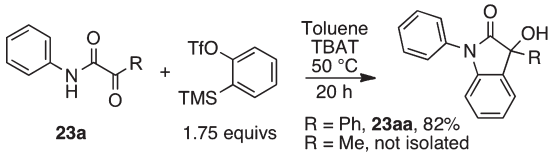
Figure 1. Products using other benzyne precursors.

Scheme 1. Double Annulation



22a **22aa**, 40%

Scheme 2. Reaction of 2-Oxo-*N*,2-diphenylacetamide with 2-(Trimethylsilyl)phenyl Trifluoromethanesulfonate



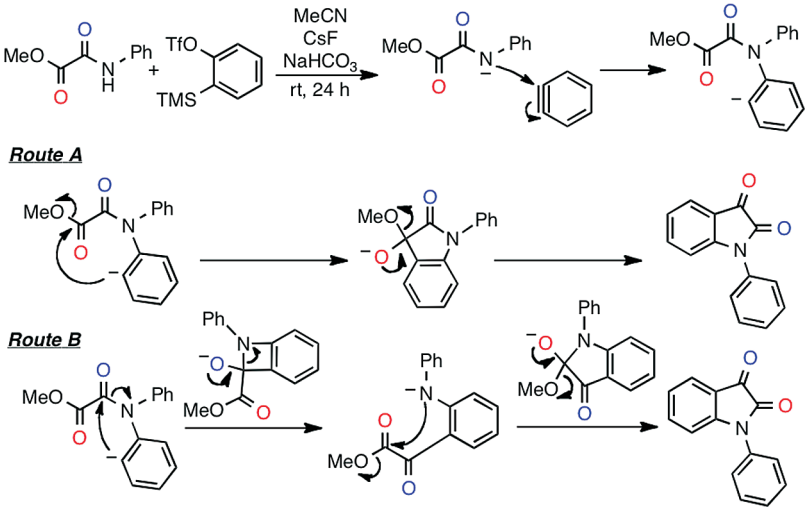
23a 1.75 equivs R = Ph, **23aa**, 82%
R = Me, not isolated

Our process was also carried out using a substrate bearing two amide groups (Scheme 1). Using our optimized conditions with twice the amount of benzyne precursor, a low yield of the desired *bis*-isatin **22aa** was isolated (33%). On the other hand, using reaction conditions similar to those of Greeney (eq 1), an increased yield of 40% was obtained.

Other substrates have also been examined for compatibility in this annulation reaction. In most cases, however, significant limitations have been observed. For example, *N*-alkylamides do not work. Significant amounts of starting material and minimal amounts of the desired products were observed by GC−MS analysis. Further attempts to optimize this reaction failed. Another disappointing observation was that the corresponding *p*-tolylsulfonamide (*p*-TolSO_2NHCOCO_2Me) did not react favorably. Only the *N*-arylation product was isolated, as noted previously by our group for other *N*-arylsulfonamides.[18] Lastly, in an attempt to form a six-membered ring hetero cycle using our methodology, methyl 2,2-dimethyl-3-oxo-3-(phenylamino)propanoate was synthesized and subjected to our reaction conditions. However, none of the desired product was formed, even after screening a variety of reaction conditions. Finally, it should be mentioned that various heteroaromatic substrates, including substrates with a pyridine or an isoxazole ring, proved to be problematic and complicated product mixtures were observed upon TLC analysis.

On the other hand, it was pleasing to see that a ketone, as opposed to the methyl ester, underwent the annulation reaction to afford a 3-hydroxyoxindole, an emerging new scaffold for drug discovery, which possesses potential anticancer properties, in addition to other favorable properties (Scheme 2).[19] Initial experiments with the ketone 2-oxo-*N*,2-diphenylacetamide provided only poor yields using our earlier optimized conditions. However, again using 2.3 equiv of TBAT and toluene at 50 °C, the desired 3-hydroxyindole (**23aa**, R = Ph) was obtained in a good yield when 1.75 equiv of the benzyne precursor was used. However, when R = Me, a complicated mixture was observed on TLC analysis and the desired product was not isolated.

Scheme 3. Possible Mechanisms



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It is believed that two mechanisms are possible for this process, routes A and B in Scheme 3. Both suggested routes share a common first step, nucleophilic attack by nitrogen on the benzyne, resulting in an aryl carbanion. From there, at least two possibilities exist with regard to how the desired isatin is formed. Route A suggests that the aryl carbanion attacks the distant ester carbonyl and displaces a methoxy group. This type of mechanism has also been suggested in our earlier work (see eqs 3 and 4). On the other hand, Greaney's work (eq 1) suggests another possibility, route B. This route involves attack of the aryl carbanion onto the nearest carbonyl group, the amide carbonyl, forming a strained four-membered ring intermediate, which then fragments into a structure where the nitrogen can now attack the ester carbonyl. Both routes eventually lead to the desired isatin. However, the carbonyl groups end up in different places depending on the route. Further efforts are underway in order to shed light on this process.

CONCLUSION

In conclusion, *N*-arylisatins appear to possess a number of highly desirable biological properties but have proven difficult to access synthetically. Our group has developed a convenient and efficient methodology for synthesizing a diverse array of functionally substituted *N*-arylisatins under mild reaction conditions. The necessary starting materials are easily prepared in high yields by reacting anilines with methyl 2-chloro-2-oxoacetate. The methodology proceeds efficiently under mild reaction conditions and tolerates a broad range of functionally diverse substituents, with respect to both electronic and steric effects. In addition, a 3-hydroxyoxindole, another medicinally relevant scaffold, has been synthesized using a slightly modified version of Greaney's amide insertion conditions and 2-oxo-*N*,2-diphenylacetamide. Two mechanistic possibilities appear to exist for this process, and further studies are underway to distinguish which is more likely.

EXPERIMENTAL SECTION

General. The ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz or 400 and 100 MHz, respectively. Thin layer chromatography was performed using commercially prepared 60-mesh silica gel plates, and visualization was effected with short wavelength UV light (254 nm). All melting points are uncorrected. All reagents were used directly as obtained commercially.

Typical Experimental Procedure for Starting Materials 1a−18a and 22a. To a cold solution (0 °C) of the desired amine (10.0 mmol) and triethylamine (**1a**−**18a**: 12 mmol, 1.67 mL; **22a**: 24.0 mmol, 3.35 mL) in anhydrous dichloromethane (50 mL) was added methyl 2-chloro-2-oxoacetate (**1a**−**18a**: 10.5 mmol, 0.967 mL; **22a**: 21.0 mmol, 1.933 mL) dropwise. The ice bath was removed, and the resulting mixture was allowed to stir overnight before it was quenched with HCl (1 N) and extracted with ethyl acetate. The combined organic layers were washed with saturated $NaHCO_3$ and finally water before being dried with anhydrous $MgSO_4$ and concentrated in vacuo. The crude product was purified by washing with Et_2O/Hex (1:1), acetone, or dichloromethane until most of the color disappeared. In some cases, the solids were recrystallized from toluene. The solids obtained were finally dried under vacuum.

Methyl 2-Oxo-2-(phenylamino)acetate (1a). The product was isolated as a white solid: mp = 112−114 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.83 (s, 1 H), 7.61 (d, J = 8.2 Hz, 2 H), 7.35 (t, J = 7.8 Hz, 2 H), 7.16 (t, J = 7.4 Hz, 1 H), 3.94 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.7, 153.8, 136.4, 129.5, 125.8, 120.1, 54.3; HRMS (EI) calcd for $[M + H]^+$ ($M = C_9H_9NO_3$) 180.0689, found 180.0680.

Methyl 2-Oxo-2-(*p*-tolylamino)acetate (2a). The product was isolated as a white solid: mp = 148−150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (s, 1 H), 7.52 (d, J = 8.3 Hz, 2 H), 7.14 (d, J = 8.2 Hz, 2 H), 3.92 (s, 3 H), 2.31 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 153.6, 135.4, 133.8, 129.8, 119.9, 54.1, 21.1; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{10}H_{11}NO_3$) 194.0812, found 194.0809.

Methyl 2-Oxo-2-[(4-phenoxyphenyl)amino]acetate (3a). The product was isolated as a tan solid: mp =97−99 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (s, 1 H), 7.63 (d, J = 8.9 Hz, 2 H), 7.73 (t, J = 7.9 Hz, 2 H), 7.10 (t, J = 7.4 Hz, 1 H), 7.10−6.99 (m, 4 H), 3.93 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 157.1, 154.7, 153.7, 131.7, 129.9, 123.5, 121.7, 119.5, 118.9, 54.1; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{15}H_{13}NO_4$) 272.0917, found 272.0916.

Methyl 2-[(4-Fluorophenyl)amino]-2-oxoacetate (4a). The product was isolated as a white solid: mp = 154−156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1 H), 7.65−7.61 (m, 2 H), 7.07 (t, J = 8.6 Hz, 2 H), 3.97 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$, extra peaks due to C−F coupling) δ 163.3, 161.5, 161.4, 158.9, 153.7, 132.48, 132.45, 121.84, 121.76, 117.6, 116.3, 116.1, 54.3; HRMS (EI) calcd for $[M + H]^+$ ($M = C_9H_8FNO_3$) 198.0561, found 198.0558.

Methyl 2-[(4-Chlorophenyl)amino]-2-oxoacetate (5a). The product was isolated as a white solid: mp = 166−168 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1 H), 7.61 (d, J = 8.8 Hz, 2 H), 7.34 (d, J = 8.7 Hz, 2 H), 3.97 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 153.7, 134.9, 130.9, 129.5, 121.2, 54.4; HRMS (EI) calcd for $[M + H]^+$ ($M = C_9H_8ClNO_3$) 214.0265, found 214.0264.

Methyl 2-[(4-Bromophenyl)amino]-2-oxoacetate (6a). The product was isolated as a white solid: mp = 170−172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (s, 1 H), 7.56 (d, J = 8.9 Hz, 2 H), 7.49 (d, J = 8.8 Hz, 2 H), 3.97 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 153.7, 135.4, 132.5, 121.5, 118.6, 54.4; HRMS (EI) calcd for $[M + H]^+$ ($M = C_9H_8BrNO_3$) 257.9760, found 257.9759.

Methyl 2-[(4-Iodophenyl)amino]-2-oxoacetate (7a). The product was isolated as a tan solid: mp = 172−174 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1 H), 7.69 (d, J = 8.8 Hz, 2 H), 7.43 (d, J = 8.8 Hz, 2 H), 3.98 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 153.7, 138.4, 136.1, 121.8, 89.5, 54.4; HRMS (EI) calcd for $[M + H]^+$ ($M = C_9H_8INO_3$) 305.9622, found 305.9623.

Methyl 2-[(4-Nitrophenyl)amino]-2-oxoacetate (8a). The product was isolated as a yellow solid: mp =230−233 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1 H), 8.29 (d, J = 9.0 Hz, 2 H), 7.84 (d, J = 9.2 Hz, 2 H), 4.01 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.4, 155.8, 143.7, 143.3, 124.7, 120.4, 53.4; HRMS (EI) calcd for $[M + H]^+$ ($M = C_9H_8N_2O_5$) 225.0506, found 225.0504.

Methyl 2-[(4-Cyanophenyl)amino]-2-oxoacetate (9a). The product was isolated as a tan solid: mp =210−212 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (s, 1 H), 7.80 (d, J = 8.8 Hz, 2 H), 7.69 (d, J = 8.8 Hz, 2 H), 4.01 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 154.0, 140.2, 133.7, 120.1, 118.6, 109.0, 54.6; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{10}H_8N_2O_3$) 205.0608, found 205.0607.

Ethyl 4-(2-Methoxy-2-oxoacetamido)benzoate (10a). The product was isolated as a pale yellow solid: mp = 147−149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.19 (s, 1 H), 8.01 (d, J = 8.7 Hz, 2 H), 7.73 (d, J = 8.7 Hz, 2 H), 4.33 (q, J = 7.1 Hz, 2 H), 3.91 (s, 3 H), 1.35 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 161.1, 154.0, 140.3, 130.9, 127.3, 119.4, 61.1, 54.2, 14.4; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{12}H_{13}NO_5$) 252.0866, found 252.0868.

Methyl 2-Oxo-2-[(4-(trifluoromethyl)phenyl)amino]acetate (11a). The product was isolated as a white solid: mp = 154−156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (s, 1 H), 7.87 (d, J = 8.0 Hz, 2 H), 7.66 (d, J = 7.8 Hz, 2 H), 4.01 (s, 3 H); ^{13}C NMR (75 MHz, DMSO-d_6, extra peaks due to C−F coupling) δ 160.6, 155.6, 141.1, 126.1, 126.03, 125.98,

125.93, 125.0, 124.6, 122.4, 120.5, 53.3; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{10}H_8F_3NO_3$) 248.0556, found 248.0527.

Methyl 2-Oxo-2-[(3-(trifluoromethyl)phenyl)amino]acetate (12a). The product was isolated as a white solid: mp = 112−115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.19 (s, 1 H), 7.93−7.89 (m, 2 H), 7.48 (t, J = 7.9 Hz, 1 H), 7.42 (d, J = 7.7 Hz, 1 H), 3.94 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$, extra peaks due to C−F coupling) δ 161.3, 154.1, 137.0, 131.8, 131.5, 130.0, 125.1, 123.2, 122.4, 122.3, 122.2, 116.95, 116.91, 116.87, 116.8, 54.4; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{10}H_8F_3NO_3$) 248.0556, found 248.0530.

Methyl 2-[(2-(*tert*-Butyl)phenyl)amino]-2-oxoacetate (13a). The product was isolated as a tan solid: mp = 57−61 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.17 (s, 1 H), 7.89 (dd, J = 1.2, 8.0 Hz, 1 H), 7.35 (dd, J = 1.3, 7.9 Hz, 1 H), 7.19 (td, J = 1.3, 7.9 Hz, 1 H), 7.11 (td, J = 1.3, 7.8 Hz, 1 H), 3.89 (s, 3 H), 1.39 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 153.3, 140.9, 133.8, 126.9, 126.5, 126.2, 124.5, 53.9, 34.2, 30.5; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{13}H_{17}NO_3$) 236.1281, found 236.1288.

Methyl 2-[(1,1′-Biphenyl)-2-ylamino]-2-oxoacetate (14a). The product was isolated as a white solid: mp = 85−88 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1 H), 8.44 (d, J = 8.15 Hz, 1 H), 7.46 (t, J = 7.3 Hz, 2 H), 7.41−7.32 (m, 4 H), 7.24 (d, J = 6.3 Hz, 1 H), 7.18 (t, J = 7.2 Hz, 1 H), 3.76 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 153.0, 136.8, 133.0, 132.3, 129.9, 128.8, 128.7, 128.2, 127.9, 125.0, 120.2, 53.4; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{15}H_{13}NO_3$) 256.0968, found 256.0972.

Methyl 2-[(2,5-Dimethoxyphenyl)amino]-2-oxoacetate (15a). The product was isolated as a white solid: mp = 105−107 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.36 (s, 1 H), 8.00 (d, J = 2.9 Hz, 1 H), 6.73 (d, J = 8.9 Hz, 1 H), 6.55 (dd, J = 2.9, 9.0 Hz, 1 H), 3.88 (s, 3 H), 3.78 (s, 3 H), 3.70 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 153.5, 153.3, 142.6, 126.4, 110., 109.6, 106.2, 56.1, 55.6, 53.8; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{11}H_{13}NO_5$) 240.0866, found 240.0866.

Methyl 2-(Mesitylamino)-2-oxoacetate (16a). The product was isolated as a white solid: mp = 99−101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1 H), 6.87 (s, 2 H), 3.90 (s, 3 H), 2.24 (s, 3 H) 2.15 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 154.5, 137.5, 134.6, 129.4, 128.9, 53.6, 20.8, 18.2; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{12}H_{15}NO_3$) 222.1125, found 222.1122.

Methyl 2-(Naphthalen-1-ylamino)-2-oxoacetate (17a). The product was isolated as a white solid: mp = 112−114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.41 (s, 1 H), 8.12 (d, J = 7.5 Hz, 1 H), 7.86−7.84 (m, 2 H), 7.72 (d, J = 8.2 Hz, 1 H), 7.56−7.46 (m, 3 H), 3.98 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 154.2, 134.0, 130.7, 129.0, 126.8, 126.6, 126.4, 126.2, 125.8, 120.1, 119.7, 54.3; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{13}H_{11}NO_3$) 230.0812, found 230.0810.

Methyl 2-[(2-Iodophenyl)amino]-2-oxoacetate (18a). The product was isolated as a light brown solid: mp = 116−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.29 (s, 1 H), 8.28 (d, J = 8.0 Hz, 1 H), 7.78 (d, J = 7.6 Hz, 1 H), 7.35 (t, J = 7.4 Hz, 1 H), 6.88 (t, J = 7.1 Hz, 1 H), 3.96 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.1, 153.7, 139.2, 137.0, 129.5, 127.2, 121.5, 89.8, 54.3; HRMS (EI) calcd for $[M + H]^+$ ($M = C_9H_8INO_3$) 305.9622, found 305.9629.

Dimethyl 2,2′-[1,3-Phenylenebis(azanediyl)]bis(2-oxoacetate) (22a). The product was isolated as a white solid: mp = 186−191 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.85 (s, 2 H), 8.21 (s, 1 H), 7.47 (d, J = 7.2 Hz, 2 H), 7.31 (t, J = 7.8 Hz, 1 H), 3.83 (s, 6 H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.7, 156.1, 138.4, 129.7, 117.8, 113.5, 53.83; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{12}H_{12}N_2O_6$) 281.0768, found 281.0771.

Experimental Procedure for 2-Oxo-*N*,2-diphenylacetamide (23a). To a cold solution (0 °C) of 2-oxo-2-phenylacetic acid (11 mmol, 1.65 g) in anhydrous dichloromethane (25 mL) was added oxalyl chrolide (12 mmol, 1.03 mL) followed by anhydrous DMF (1.3 mmol, 0.1 mL) via syringe in a dropwise fashion (Caution! The addition of DMF can initiate an extremely rapid release of gas if added too quickly.) The mixture was allowed to stir in an ice bath until bubbling ceased. At this point, the entire reaction mixture was slowly cannulated over to a cold solution (0 °C) of aniline (10.0 mmol, 0.91 mL) and triethylamine (15 mmol, 2.1 mL) in anhydrous dichloromethane (25 mL). The ice bath was removed, and the resulting mixture was allowed to stir overnight before it was quenched with HCl (1 N) and extracted with ethyl acetate. The combined organic layers were washed with saturated $NaHCO_3$ and then water before being dried with anhydrous $MgSO_4$ and concentrated in vacuo. The crude product was purified via flash chromatography using gradient solvent mixtures of ethyl acetate/hexanes. Isolated was a yellow solid: mp = 64−66 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.00 (s, 1 H), 8.42 (d, J = 7.2 Hz, 2 H), 7.74−7.64 (m, 3 H), 7.52 (t, J = 7.6 Hz, 2 H), 7.41 (t, J = 7.9 Hz, 2 H), 7.21 (t, J = 7.4 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.6, 159.1, 136.8, 134.8, 133.2, 131.6, 129.4, 128.7, 125.5, 120.1; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{14}H_{11}NO_2$) 226.0863, found 226.0861.

Typical Procedure for Synthesis of the Isatin Derivatives 1aa−21aa. To a dry 5 dram vial containing a solution of the amide (0.5 mmol) and the aryne precursor (1.0 mmol) in MeCN (5 mL, anhydrous) was added $NaHCO_3$ (1.0 mmol) and CsF (3.0 mmol). The vial was sealed and allowed to stir for 24 h at rt. The reaction mixture was then filtered through a plug of silica gel using ethyl acetate, concentrated *in vacuo*, and purified by flash chromatography using gradient solvent combinations of ethyl acetate/hexanes or dichloromethane/hexanes.

1-Phenylindoline-2,3-dione (1aa). The product was isolated as an orange solid (96.3 mg, 78%): mp = 136−139 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (ddd, J = 0.6, 1.3, 7.5 Hz, 1 H), 7.60−7.41 (m, 6 H), 7.18 (td, J = 0.8, 7.6 Hz, 1 H), 6.91 (d, J = 8.1 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.1, 157.5, 151.9, 138.5, 133.4, 130.2, 129.0, 126.2, 125.8, 124.5, 117.7, 111.5; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{14}H_9NO_2$) 224.0706, found 224.0707.

1-*p*-Tolylindoline-2,3-dione (2aa). The product was isolated as a red-orange solid (97.2 mg, 82%): mp = 137−139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 7.5 Hz, 1 H), 7.66 (t, J = 7.3 Hz, 1 H), 7.49 (d, J = 8.2 Hz, 2 H), 7.42 (d, J = 8.3 Hz, 2 H), 7.30 (d, J = 7.5 Hz, 1 H), 7.00 (d, J = 8.1 Hz, 1 H), 2.56 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.2, 157.6, 152.0, 139.1, 138.5, 130.7, 130.3, 126.0, 125.6, 124.3, 117.6, 111.4, 21.4; HRMS (EI) calcd for $C_{15}H_{11}NO_2$ 237.0790, found 237.0791.

1-(4-Phenoxyphenyl)indoline-2,3-dione (3aa). The product was isolated as a yellow-orange solid (129.2 mg, 82%): mp = 145−148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 7.4 Hz, 1 H), 7.54 (t, J = 7.8 Hz, 1 H), 7.40−7.34 (m, 4 H), 7.18−7.11 (m, 4 H), 7.07 (d, J = 8.2 Hz, 2 H), 6.88 (d, J = 7.97 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.0, 157.9, 157.6, 156.2, 151.8, 138.5, 130.1, 127.7, 127.4, 125.6, 124.4, 124.3, 119.8, 119.5, 117.5, 111.3; HRMS (EI) calcd for $C_{20}H_{13}NO_3$ 315.0895, found 315.0899.

1-(4-Fluorophenyl)indoline-2,3-dione (4aa). The product was isolated as a bright orange solid (108.5 mg, 90%): mp = 235−237 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 7.5 Hz, 1 H), 7.57 (t, J = 7.8 Hz, 1 H), 7.44−7.40 (m, 2 H), 7.29−7.24 (m, 2 H), 7.20 (t, J = 7.6 Hz, 1 H), 6.86 (d, J = 8.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, extra peaks due to C−F coupling) δ 182.8, 163.7, 161.2, 157.6, 151.7, 138.6, 129.0, 128.9, 128.3, 128.2, 125.9, 124.7, 117.7, 117.4, 117.2, 111.3; HRMS (EI) calcd for $C_{14}H_8FNO_2$ 241.0539, found 241.0539.

1-(4-Chlorophenyl)indoline-2,3-dione (5aa). The product was isolated as an orange solid (82.2 mg, 64%): mp = 194−197 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 7.5 Hz, 1 H), 7.59−7.53 (m, 3 H), 7.39 (d, J = 8.6 Hz, 2 H), 7.20 (t, J = 7.6 Hz, 1 H), 6.90 (d, J = 6.9 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.6, 157.4, 151.3, 138.6, 134.7, 131.5, 130.4, 127.5, 126.0, 124.7, 117.7, 111.3; HRMS (EI) calcd for $C_{14}H_8ClNO_2$ 257.0244, found 257.0248.

1-(4-Bromophenyl)indoline-2,3-dione (6aa). The product was isolated as a light orange solid (97.8 mg, 65%): mp = 178−180 °C; ^{1}H

NMR (400 MHz, $CDCl_3$) δ 7.69−7.66 (m, 3 H), 7.56 (t, J = 7.8 hz, 1 H), 7.32 (d, J = 8.5 Hz, 2 H), 7.20 (t, J = 7.5 Hz, 1 H), 6.90 (d, J = 8.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.5, 157.2, 151.1, 138.6, 133.3, 132.0, 127.7, 125.9, 124.7, 122.6, 117.6, 111.3; HRMS (EI) calcd for $C_{14}H_8BrNO_2$ 300.9738, found 300.9742.

1-(4-Iodophenyl)indoline-2,3-dione (7aa). The product was isolated as an orange solid (125.6 mg, 72%): mp = 198−201 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.5 Hz, 2 H), 7.69 (d, J = 7.51 Hz, 1 H), 7.56 (t, J = 7.8 Hz, 1 H), 7.21−7.17 (m, 3 H), 6.90 (d, J = 8.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.5, 157.2, 151.1, 139.3, 138.6, 132.7, 127.8, 126.0, 124.8, 117.6, 111.3, 94.1; HRMS (EI) calcd for $C_{14}H_8INO_2$ 348.9600, found 348.9601.

4-(2,3-Dioxoindolin-1-yl)benzonitrile (9aa). The product was isolated as a light orange solid (77.2 mg, 62%): mp = 282−284 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.3 Hz, 2 H), 7.714−7.705 (m, 3 H), 7.64 (t, J = 7.8 Hz, 1 H), 7.23 (t, J = 7.51 Hz, 1 H), 6.99 (d, J = 7.9 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.9, 157.2, 150.0, 137.9, 137.6, 133.8, 127.0, 124.9, 124.1, 118.4, 117.9, 110.9, 110.5; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{15}H_8N_2O_2$) 249.0659, found 249.0656.

Ethyl 4-(2,3-Dioxoindolin-1-yl)benzoate (10aa). The product was isolated as a light orange solid (100.3 mg, 68%): mp = 127−129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.6 Hz, 2 H), 7.70 (d, J = 7.5 Hz, 1 H), 7.59−7.52 (m, 3 H), 7.20 (t, J = 7.5 Hz, 1 H), 6.97 (d, J = 8.1 Hz, 1 H), 4.40 (q, J = 7.1 Hz, 2 H), 1.41 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.3, 165.6, 157.1, 150.9, 138.6, 136.9, 131.3, 130.6, 126.0, 125.5, 124.8, 117.7, 111.4, 61.5, 14.5; HRMS (EI) calcd for $C_{17}H_{13}NO_4$ 295.0839, found 295.0845.

1-[4-(Trifluoromethyl)phenyl]indoline-2,3-dione (11aa). The product was isolated as a bright orange solid (74.2 mg, 51%): mp = 177−181 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.4 Hz, 2 H), 7.73 (d, J = 6.9 Hz, 1 H), 7.62−7.59 (m, 3 H), 7.23 (t, J = 7.5 Hz, 1 H), 6.98 (d, J = 8.1 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, extra peaks due to C−F coupling) δ 182.2, 157.2, 150.8, 138.7, 136.2, 131.0, 130.6, 128.9, 127.33, 127.29, 127.26, 127.22, 126.3, 126.1, 125.1, 125.0, 122.4, 117.7, 111.3; HRMS (EI) calcd for $C_{15}H_8F_3NO_2$ 291.0507, found 291.0509.

1-[3-(Trifluoromethyl)phenyl]indoline-2,3-dione (12aa). The product was isolated as a yellow-orange solid (80.0 mg, 55%): mp = 124−127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74−7.65 (m, 5 H), 7.60 (td, J = 1.2, 8.0 Hz, 1 H), 7.23 (t, J = 7.6 Hz, 1 H), 6.92 (d, J = 8.1 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, extra peaks due to C−F coupling) δ 182.3, 157.3, 150.9, 138.7, 133.7, 130.9, 129.6, 126.1, 125.74, 125.70, 125.0, 123.04, 123.00, 117.7, 111.2; HRMS (EI) calcd for $C_{15}H_8F_3NO_2$ 291.0507, found 291.0507.

1-(2-*tert*-Butylphenyl)indoline-2,3-dione (13aa). The product was isolated as a light orange solid (114.4 mg, 82%): mp = 109−113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (t, J = 7.9 Hz, 2 H), 7.51 (td, J = 1.1, 7.8 Hz, 1 H), 7.44 (t, J = 7.7 Hz, 1 H), 7.34 (td, J = 1.3, 7.5 Hz, 1 H), 7.14 (t, J = 7.5 Hz, 1 H), 7.05 (dd, J = 1.4, 7.8 Hz, 1 H), 6.42 (d, J = 8.0 Hz, 1 H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.4, 159.2, 154.1, 149.6, 138.7, 131.7, 130.5, 130.2, 129.4, 128.4, 125.4, 124.2, 11.8, 112.7, 35.8, 31.9; HRMS (EI) calcd for $C_{18}H_{17}NO_2$ 279.1259, found 279.1265.

1-[(1,1′-Biphenyl)-2-yl]indoline-2,3-dione (14aa). The product was isolated as a red solid (119.6 mg, 80%): mp = 157−162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56−7.53 (m, 4 H), 7.40−7.36 (m, 2 H), 7.26−7.23 (m, 5 H), 7.03 (t, J = 7.3 Hz, 1 H), 6.48 (d, J = 7.5 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.8, 158.0, 152.2, 141.1, 138.3, 138.2, 131.7, 130.6, 130.1, 129.3, 128.74, 128.69, 128.2, 128.1, 125.4, 124.1, 117.2, 111.6; HRMS (EI) calcd for $C_{20}H_{13}NO_2$ 299.0946, found 299.0946.

1-(2,4-Dimethoxyphenyl)indoline-2,3-dione (15aa). The product was isolated as an orange solid (106.2 mg, 75%): mp = 114−117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, J = 0.7, 7.5 Hz, 1 H), 7.49 (t, J = 1.4, 7.9 Hz, 1 H), 7.11 (td, J = 0.73, 7.5 Hz, 1 H), 7.02−6.96 (m, 2 H), 6.86 (d, J = 2.6 Hz, 1 H), 6.59 (d, J = 8.0 Hz, 1 H), 3.77 (s, 3 H), 3.73 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.1, 157.7, 154.0, 152.2, 149.3, 138.4, 125.3, 124.0, 121.6, 117.6, 116.0, 114.7, 113.7, 111.8, 56.4, 56.0; HRMS (EI) calcd for $C_{16}H_{13}NO_4$ 283.0845, found 283.0839.

1-Mesitylindoline-2,3-dione (16aa). The product was isolated as a yellow-orange solid (88.8 mg, 67%): mp = 164−168 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 7.2 Hz, 1 H), 7.51 (t, J = 7.7 Hz, 1 H), 7.16 (t, J = 7.5 Hz, 1 H), 7.03 (s, 2 H), 6.44 (d, J = 7.8 Hz, 1 H), 2.35 (s, 3 H), 2.14 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.2, 157.5, 151.7, 139.8, 138.8, 136.3, 129.9, 128.0, 125.8, 124.3, 117.7, 111.2, 21.3, 18.1; HRMS (EI) calcd for $C_{17}H_{15}NO_2$ 265.1100, found 265.1103.

1-(Naphthalen-1-yl)indoline-2,3-dione (17aa). The product was isolated as an orange solid (120.2 mg, 88%): mp = 130−133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.2 Hz, 1 H), 7.98 (d, J = 8.2 Hz, 1 H), 7.75 (d, J = 7.3 Hz, 1 H), 7.70 (t, J = 8.4 Hz, 1 H), 7.64−7.49 (m, 4 H) 7.45 (td, J = 1.1, 7.9 Hz, 1 H), 7.17 (t, J = 7.5 Hz, 1 H), 6.44 (d, J = 8.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.1, 158.2, 152.8, 138.8, 135.0, 130.4, 129.5, 129.0, 127.6, 127.1, 126.2, 126.0, 125.7, 124.4, 122.6, 117.6, 112.0; HRMS (EI) calcd for $C_{18}H_{11}NO_2$ 273.0790, found 273.0786.

1-(2-Iodophenyl)indoline-2,3-dione (18aa). The product was isolated as a ruby red solid (156.2 mg, 84%): mp = 173−176 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 7.9 Hz, 1 H), 7.70 (d, J = 7.4 Hz, 1 H), 7.53−7.51 (m, 2 H), 7.36 (d, J = 7.6 Hz, 1 H), 7.26−7.15 (m, 2 H), 6.49 (d, J = 8.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.6, 157.0, 151.3, 140.8, 138.7, 136.2, 131.5, 130.2, 129.7, 125.8, 124.5, 117.4, 111.8, 98.1; HRMS (EI) calcd for $[M + Na]^+$ ($M = C_{14}H_8INO_2$) 371.9492, found 371.9497.

4-Methoxy-1-phenylindoline-2,3-dione (19aa). The product was isolated as a dark orange solid (118.1 mg, 93%): mp = 198−202 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (t, J = 6.9 Hz, 2 H), 7.49−7.38 (m, 4 H), 6.66 (d, J = 8.6 Hz, 1 H), 6.42 (d, J = 7.9 Hz, 1 H), 4.00 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.5, 159.2, 157.9, 152.5, 140.4, 133.2, 130.0, 128.9, 126.5, 107.9, 106.1, 103.7, 56.6; HRMS (EI) calcd for $[M + Na]^+$ ($M = C_{15}H_{11}NO_3$) 254.0812, found 254.0812.

3-Phenyl-1*H*-benzo[*e*]indole-1,2(3*H*)-dione (20aa). The product was isolated as a dark red solid (87.9 mg, 61%): mp = 221−224 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, J = 8.4 Hz, 1 H), 8.06 (d, J = 8.8 Hz, 1 H), 7.79 (d, J = 8.1 Hz, 1 H), 7.69 (t, J = 7.6 Hz, 1 H), 7.45 (d, J = 7.4 Hz, 1 H), 7.38 (d, J = 8.0 Hz, 2 H), 7.32 (d, J = 8.0 Hz, 2 H), 7.08 (d, J = 8.7 Hz, 1 H), 2.46 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.3, 158.4, 155.4, 140.7, 139.2, 131.7, 130.9, 130.6, 130.4, 129.5, 129.3, 126.4, 126.0, 123.8, 111.6, 109.4, 21.6; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{19}H_{13}NO_2$) 288.1019, found 288.1012.

5,6-Dimethoxy-1-phenylindoline-2,3-dione (21aa). The product was isolated as a dark red solid (128.2 mg, 86%): mp =211−214 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, J = 8.4 Hz, 2 H), 7.26 (d, J = 8.0 Hz, 2 H), 7.15 (s, 2 H), 3.871 (s, 3 H), 3.867 (s, 3 H), 2.42 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.7, 158.8, 158.4, 150.0, 146.3, 138.9, 130.8, 130.4, 126.1, 109.2, 107.4, 95.4, 56.9, 56.7, 21.5; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{17}H_{15}NO_4$) 298.1074, found 298.1068.

Experimental Procedure for 1,1′-(1,3-Phenylene)*bis*-(indoline-2,3-dione) (22aa). To a dry 5 dram vial containing a solution of the amide (0.5 mmol) and the aryne precursor (1.75 mmol, 0.522 g) in anhydrous THF (5 mL) was added TBAT (2.33 mmol, 1.257 g). The vial was sealed, placed in an oil bath at 50 °C, and allowed to stir for 20 h. The reaction mixture was then filtered through a plug of silica gel using ethyl acetate, concentrated *in vacuo*, and purified by flash chromatography using gradient solvent combinations of ethyl acetate/hexanes. The product was isolated as a light orange solid (78.2 mg, 40%): mp = 328−331 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.82 (t, J = 7.9 Hz, 1 H), 7.69−7.60 (m, 7 H),

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7.22 (t, J = 7.5 Hz, 2 H), 7.00 (d, J = 7.8 Hz, 2 H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 187.7, 182.4, 157.4, 150.7, 137.9, 134.3, 130.8, 126.0, 124.8, 123.8, 117.8, 110.8; HRMS (EI) calcd for $[M + H]^+$ (M = $C_{22}H_{12}N_2O_4$) 369.0870, found 369.0869.

Experimental Procedure for 3-Hydroxy-1,3-diphenylindolin-2-one (23aa). To a dry 5 dram vial containing a solution of the amide (0.5 mmol) and the aryne precursor (0.875 mmol, 0.261 g) in THF (5 mL, anhydrous) was added TBAT (1.17 mmol, 0.629 g). The vial was sealed, placed in an oil bath at 50 °C, and allowed to stir for 20 h. The reaction mixture was then filtered through a plug of silica gel using ethyl acetate, concentrated *in vacuo*, and purified by flash chromatography using gradient solvent combinations of ethyl acetate/hexanes. The product was isolated as a white solid (132.8 mg, 82%): mp = 166−170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57−7.26 (m, 12 H), 7.12 (t, J = 7.5 Hz, 1 H), 6.90 (d, J = 7.9 Hz, 1 H), 3.82 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 143.5, 140.5, 134.1, 131.5, 129.9 (3 C), 128.9 (2 C), 128.53, 128.49, 126.6 (2 C), 125.5 (3 C), 124.2, 110.2, 78.3; HRMS (EI) calcd for $[M + Na]^+$ (M = $C_{20}H_{15}NO_2$) 324.0995, found 324.1002.

■ ASSOCIATED CONTENT

Supporting Information. Copies of NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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