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Efficient one-step synthesis of pyrrolo[3,4-*c*]quinoline-1,3-dione derivatives by organocatalytic cascade reactions of isatins and β-ketoamides†

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We describe an efficient one-step synthesis of pyrrolo[3,4-*c*]quinolinedione derivatives using ethylenediamine diacetate (EDDA)-catalyzed cascade reactions of isatins and β-ketoamides. It is the first direct conversion of isatins to pyrrolo[3,4-*c*]quinolinedione derivatives *via* C–N bond cleavage and isatin ring expansion. Furthermore, this reaction provides a one-step synthetic route for the production of biologically interesting complex molecules that are generally prepared using multi-step reactions.

Pyrrolo[3,4-*c*]quinoline-1,3-dione moieties (**1**) exhibit a broad spectrum of biologically and pharmacologically important activities (Fig. 1).[1] For instance, compound **2** is a potent inhibitor of caspase-3 (IC_{50} = 3 nM),[2] which plays a key role in apoptosis.[3] Caspases are attractive targets for therapeutic intervention in cardiovascular, neurodegenerative, infectious and metabolic disorders.[4] In particular, caspase-3 inhibitors have been described as promising cardioprotectants,[5] hepatoprotectants,[6] and neuroprotectants.[7] Furthermore, compound **3** has been previously shown to have inhibitory activity against HCV polymerase in a cell based HCV replication assay with an IC_{50} of <50 μM, and is currently used to treat and prevent HCV infection.[8] Recently, alpkinidine (**4**), which bears a pyrrolo[3,4-*c*]-quinolinone nucleus, was isolated from *Xestospongia* cf. *carbonaria* and *X.* cf. *exigua*,[9] and found to be solid tumor selective in a disk diffusion soft agar colony assay against murine cell lines.[9] Subsequently, it was reported to show potent therapeutic efficacy *in vivo* in HCT-116-bearing mice.[10]

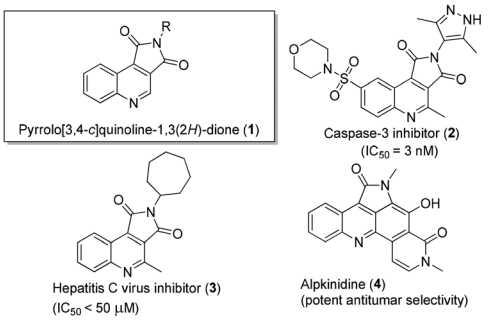
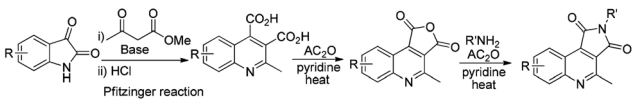
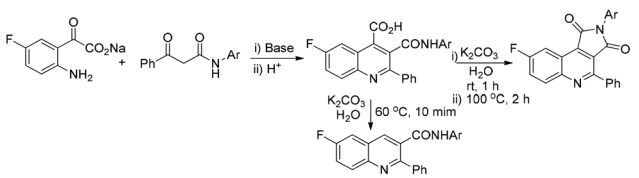


Fig. 1 Pyrrolo[3,4-*c*]quinoline structure **1** and biologically active molecules **2–4** bearing its skeleton.



Scheme 1 General and typical methods for the synthesis of pyrrolo[3,4-*c*]-quinoline-1,3-diones.



Scheme 2 Another synthetic approach for pyrrolo[3,4-*c*]quinoline-1,3-diones.

Given the importance of these valuable biological and pharmacological activities, several synthetic methods have been reported for the production of pyrrolo[3,4-*c*]quinoline-1,3-dione derivatives.[11] Of these methods, multi-step reactions using the Pfitzinger reaction as a key step from isatins are shown in Scheme 1.[11c,d,g,h,l] However, these procedures are limited by their durations, complexities, the harsh reaction conditions required and their low yields.[11c,d,g,h,l]

Recently, a facile procedure was described for the 2-step syntheses of novel pyrrolo[3,4-*c*]quinolinedione derivatives *via* the cyclocondensation of 2-amino-5-fluorophenyl glyoxylic acid with β-ketoamides (Scheme 2).[12] However, this reaction

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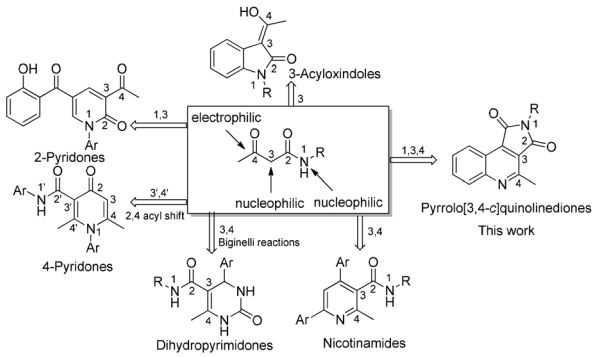
†Electronic supplementary information (ESI) available: Depiction of ^{1}H, ^{13}C NMR and HRMS spectra for all products **7–48**, and CIF data for **39**. CCDC 934811. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c3ob40791h



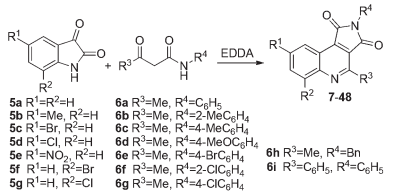
Scheme 3 Three reaction sites (N1, C3 and C4) of β-ketoamides to give biologically interesting heterocycles.

depends on temperature, and undergoes decarboxylation at high temperature to afford other quinoline-3-carboxamide derivatives.

Although these known methods have been widely used for the synthesis of pyrrolo[3,4-*c*]quinolinedione derivatives, there is a need for a simple, cost effective, environmentally benign method with wide applicability that is capable of producing more elaborate substitution patterns. This has prompted a search for a new method of preparing a variety of pyrrolo[3,4-*c*]-quinolinedione derivatives using a one-step reaction. We considered the utilization of isatins[13] and β-ketoamides as starting materials and reagents because they are widely used for the synthesis of a variety of heterocyclic and fused heterocyclic compounds. In particular, several important methods of synthesizing biologically active heterocycles such as 2-pyridones,[14] 4-pyridones,[15] 3-acyloxindoles,[16] dihydropyrimidones,[17] and nicotinamides[18] starting from β-ketoamides have already been reported, which involve the two nucleophilic sites N1 and C3 or one electrophilic site C4 (Scheme 3). However, no one-step synthesis of pyrrolo[3,4-*c*]quinolinedione derivatives from β-ketoamides has been described to date.

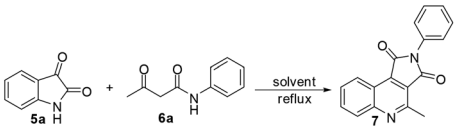
Recently, we have reported on new methodologies for synthesizing a variety of benzopyrans and polycycles by organocatalytic reactions of 1,3-dicarbonyls or resorcinols with α,β-unsaturated aldehydes.[19] We describe herein ethylenediamine diacetate (EDDA)-catalyzed cascade reactions for the one-step syntheses of pyrrolo[3,4-*c*]quinolinedione derivatives starting from different isatins and β-ketoamides in good yields (Scheme 4).

To afford pyrrolo[3,4-*c*]quinolinedione **7**, we first reacted isatin (**5a**) with 3-oxo-*N*-phenylbutanamide (**6a**) in the presence of a number of Lewis acids (10 mol%) or Brønsted acids



Scheme 4

Table 1 Reactions of isatin (**5a**) with 3-oxo-*N*-phenylbutanamide (**6a**) using a number of catalysts



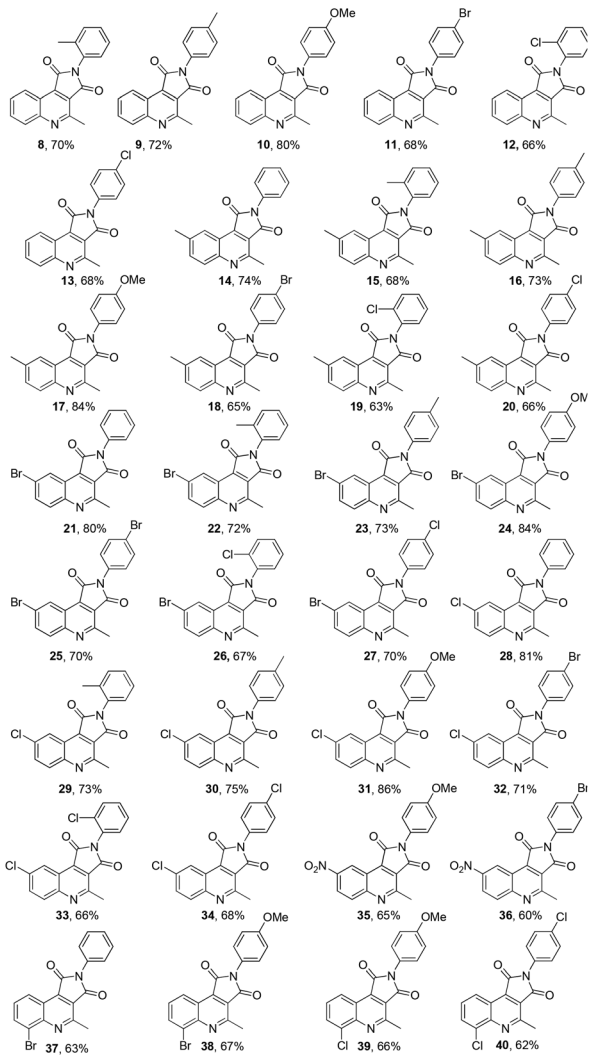
Entry	Catalysts	Solvent	Temp.	Time (h)	Yield (%)
1	$MgBr_2$	Toluene	Reflux	16	Trace
2	$FeCl_3$	Toluene	Reflux	16	Trace
3	$InCl_3$	Toluene	Reflux	16	Trace
4	$CuSO_4$	Toluene	Reflux	16	35
5	$CaCl_2$	Toluene	Reflux	12	55
6	$Ru(PPh_3)_3Cl_2$	Toluene	Reflux	12	25
7	$Yb(OTf)_3$	Toluene	Reflux	12	44
8	$ZnCl_2$	Toluene	Reflux	12	16
9	$BF_3{\cdot}Et_2$	Toluene	Reflux	12	15
10	AcOH	Toluene	Reflux	12	71
11	TFA	Toluene	Reflux	12	10
12	TEA	Toluene	Reflux	12	10
13	L-Proline	Toluene	Reflux	8	70
14	PPTS	Toluene	Reflux	8	65
15	Pyr·HCl	Toluene	Reflux	8	69
16	[DPMA][OTf]	Toluene	Reflux	8	68
17	EDDA	Toluene	Reflux	6	80
18	EDDA	CH_2Cl_2	40 °C	16	72
19	EDDA	$CHCl_3$	60 °C	16	69
20	EDDA	Benzene	80 °C	10	73
21	EDDA	Acetonitrile	80 °C	16	65
22	EDDA	Methanol	60 °C	8	58
23	EDDA	DMF	100 °C	8	30

(10 mol%) as catalysts in toluene under reflux (Table 1). When $MgBr_2$, $FeCl_3$, and $InCl_3$ as Lewis acid catalysts were refluxed in toluene for 16 h, a trace amount of products was produced (entries 1–3). The use of 10 mol% of other Lewis acid catalysts, namely $CuSO_4$, $CaCl_2$, $Ru(PPh_3)_3Cl_2$, $Yb(OTf)_3$, $ZnCl_2$, or $BF_3{\cdot}OEt_2$, under reflux for 12 h provided **7** in 15–55% yield (entries 4–9). Using acetic acid, **7** was obtained in 71% yield (entry 10), whereas reaction in the presence of trifluoroacetic acid (TFA) (10 mol%) gave **7** in low yield (10%) (entry 11). Using 10 mol% of triethylamine (TEA) as a Brønsted base, **7** was produced in only 10% yield (entry 12). Using 10 mol% of Brønsted acids and bases as bifunctional catalysts, the desired product was produced in increased yield. For example, reactions with L-proline and several salts, namely pyridinium *p*-toluenesulfonate (PPTS), pyridine hydrochloride (Pyr·HCl), or diphenylmethanaminium trifluoromethanesulfonate ([DPMA]-[OTf]), gave **7** in 70, 65, 69, and 68% yield, respectively (entries 13–16). Importantly, the use of 10 mol% of ethylenediamine diacetate (EDDA) as a catalyst improved yields. These reactions were solvent dependent and the best yield (80%) was obtained in toluene under reflux for 6 h. The structure of **7** was determined by ^{1}H NMR and by comparison with previously reported data for pyrrolo[3,4-*c*]quinolinedione.[20,12*b*]

To prepare pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione derivatives with a variety of different substituents on the benzene ring of the quinoline nucleus, several isatins bearing an electron-donating or -withdrawing group on the benzene ring were

reacted with a number of β-ketoamides under optimized reaction conditions (10 mol% of EDDA, toluene, reflux 6 h). To investigate the influences of substituents on reactivities of β-ketoamides, the effects of a number of *N*-aryl-3-oxobutanamides (**6b–6g**) bearing electron-donating or -withdrawing groups on the benzene ring were also examined. Results are summarized in Table 2. Reactions between isatin and 3-oxo-*N*-*o*-tolylbutanamide (**6b**), 3-oxo-*N*-*p*-tolylbutanamide (**6c**), or *N*-(4-methoxyphenyl)-3-oxobutanamide (**6d**), which all possess an electron-donating group on the benzene ring, afforded products **8–10** in 70, 72, and 80% yield, respectively, whereas those with *N*-(4-bromophenyl)-3-oxobutanamide (**6e**), *N*-(2-chlorophenyl)-3-oxobutanamide (**6f**), or *N*-(4-chlorophenyl)-3-oxobutanamide (**6g**), possessing electron-withdrawing groups, provided **11–13** in 68, 66, and 68% yield, respectively. Treatment of 5-methylisatin (**5b**) with 3-oxo-*N*-phenylbutanamide (**6a**) or several *N*-aryl-3-oxobutanamides (**6b–6g**) produced compounds **14–20** in 63–84% yield. Using 5-bromoisatin (**5c**), 5-chloroisatin (**5d**), and 5-nitroisatin (**5e**), the desired products **21–36** were also produced in 60–86% yield. Reactions between 7-bromoisatin (**5f**) or 7-chloroisatin (**5g**) and 3-oxo-*N*-phenylbutanamide (**6a**) or *N*-aryl-3-oxobutanamides (**6d** and **6g**) were also successful. When 7-bromoisatin (**5f**) was treated with 3-oxo-*N*-phenylbutanamide (**6a**) or *N*-(4-methoxyphenyl)-3-oxobutanamide (**6d**), products **37** and **38** were produced in 63 and 67% yield, respectively. Using 7-chloroisatin (**5g**) and *N*-(4-methoxyphenyl)-3-oxobutanamide (**6d**) or *N*-(4-chlorophenyl)-3-oxobutanamide (**6g**), compounds **39** and **40** were obtained in 66 and 62%, respectively. These results show that isatins with substituents at the 5-position on the benzene ring provide products in somewhat higher yields than isatins substituted at the 7-position. Reactions of *N*-aryl-3-oxobutanamides possessing an electron-donating group on the *N*-phenyl ring afford products in better yields than their counterparts with an electron-withdrawing group. The structures of the synthesized compounds **8–40** were unambiguously confirmed by X-ray diffraction analysis of compound **39**[21] (Fig. 2).

Table 2 A variety of pyrrolo[3,4-*c*]quinolinediones **8–40** synthesized by EDDA-catalyzed cascade reactions



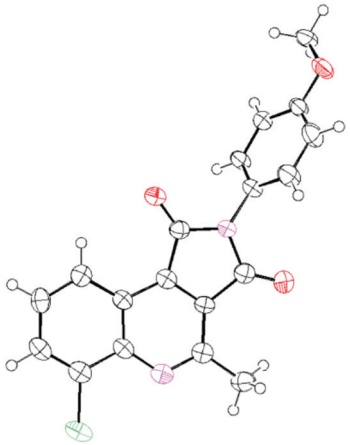
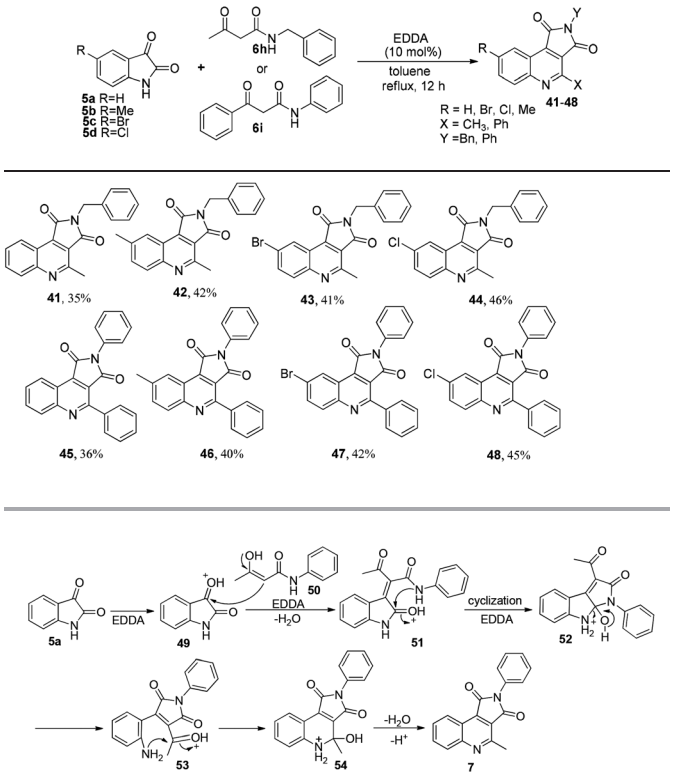


Fig. 2 X-ray structure of compound **39**.

In order to examine the utilities of these reactions, further reactions between isatins and *N*-benzyl-3-oxobutanamide (**6h**) and 3-oxo-*N*,3-diphenylpropanamide (**6i**) were investigated. Results are presented in Table 3. Reactions between isatin (**5a**), 5-methylisatin (**5b**), 5-bromoisatin (**5c**), or 5-chloroisatin (**5d**) and *N*-benzyl-3-oxobutanamide (**6h**) in the presence of 10 mol% of EDDA in refluxing toluene for 12 h provided the desired products **41–44** in 35–46% yield, whereas reactions between these and 3-oxo-*N*,3-diphenylpropanamide (**6i**) afforded products **45–48** in 36–45% yield.

A proposed mechanism of the EDDA-catalyzed cascade reaction for **7** through Knoevenagel type condensation and cyclization is depicted in Scheme 5.[22] We suppose that the carbonyl group of isatin (**5a**) is protonated by EDDA to give intermediate **49**, which facilitates a nucleophilic attack of the enol form **50** of β-ketoamide (**6a**) followed by dehydration and proton transfer to give **51**. Intermediate **51** then undergoes intramolecular cyclization by N1 nucleophilic attack of the β-ketoamide group followed by proton transfer to form intermediate **52**, and ring-opening of intermediate **52** followed by proton transfer gives

Table 3 Synthesis of other pyrrolo[3,4-*c*]quinolinedione derivatives **41–48**



Scheme 5 Proposed mechanism of the formation of **7** *via* cascade reactions.

the free aromatic amine **53**. Subsequently, the NH_2 group of **53** attacks a carbonyl group by intramolecular cyclization to form intermediate **54**, which on elimination of water and deprotonation results in **7**.

Conclusions

In summary, an efficient and facile one-step synthesis of pyrrolo[3,4-*c*]quinolinedione derivatives has been developed using ethylenediamine diacetate (EDDA)-catalyzed cascade reactions of isatins and β-ketoamides. Using this methodology, a variety of pyrrolo[3,4-*c*]quinolinediones have been synthesized. This methodology has the advantages of mild reaction conditions, inexpensive non-metal catalyst, and straightforward. In particular, this reaction solves the problems posed by the need for multi-step reactions to synthesize pyrrolo[3,4-*c*]quinolinedione derivatives.

Experimental section

General experimental details

All experiments were carried out under a nitrogen atmosphere. Merck pre-coated silica gel plates (Art. 5554) with a fluorescent indicator were used for analytical TLC. Flash column chromatography was performed using silica gel 9385 (Merck). ^{1}H and ^{13}C NMR spectra were recorded at 25 °C on Bruker Avance DPX 300 MHz, Varian VNS 300 MHz, or Varian VNS-600 MHz spectrometers in $CDCl_3$, DMSO-d_6 or CD_2Cl_2 as the solvent. IR spectra were recorded on a Jasco FTIR 5300 spectrophotometer. All melting points were obtained on a Fisher-Johns melting point apparatus and are uncorrected. HRMS was carried out at the Korea Basic Science Institute.

General procedure for the synthesis of pyrrolo[3,4-*c*]quinoline-1,3-dione derivatives: 7–48. To a solution of isatins **5** (1.0 mmol) in toluene (8 mL) was added β-ketoamides (1.1 mmol) and ethylenediamine diacetate (18 mg, 0.1 mmol) at room temperature. The reaction mixture was refluxed for 6–12 h. After completion of the reaction as indicated by TLC (hexane–EtOAc, 6 : 1, v/v), the solvent was evaporated, and the residue was purified by flash column chromatography on silica gel using hexane–EtOAc (4 : 1, v/v) to give 1*H*-pyrrolo[3,4-*c*]-quinoline-1,3(2*H*)-dione derivatives **7–48.**

*4-Methyl-2-phenyl-1*H*-pyrrolo[3,4-c]quinoline-1,3(2*H*)-dione (**7**).*[12b,20] Brown solid; yield 230 mg; 80%; mp 163–164 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.83 (dd, J = 8.1, 0.6 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 7.89 (td, J = 8.7, 1.5 Hz, 1H), 7.71 (td, J = 8.1, 0.9 Hz, 1H), 7.55–7.52 (m, 2H), 7.47–7.41 (m, 3H), 3.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.41, 167.20, 155.30, 151.60, 135.67, 132.90, 131.23, 129.26, 129.22, 129.14, 128.35, 126.66, 125.00, 121.56, 120.67, 22.21; IR (KBr): 3064, 2924, 1718, 1597, 1499, 1377, 1113, 871, 776, 691, 629, 577, 509, cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{18}H_{12}N_2O_2$: 288.0899, Found: 288.0898.

*4-Methyl-2-(*o*-tolyl)-1*H*-pyrrolo[3,4-c]quinoline-1,3(2*H*)-dione (**8**).*[20a,23a,b] Brown solid; yield 211 mg; 70%; mp 198–199 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.77 (d, J = 8.4 Hz, 1H), 8.10 (d, J = 8.4 Hz, 1H), 7.86–7.81 (m, 1H), 7.66 (dd, J = 8.4, 7.2 Hz, 1H), 7.34–7.25 (m, 3H), 7.17 (d, J = 8.4 Hz, 1H), 3.03 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.45, 167.20, 155.28, 151.54, 136.59, 135.94, 132.90, 131.22, 130.10, 129.63, 129.19, 129.10, 128.76, 126.95, 125.03, 121.85, 120.73, 22.18, 18.08; IR (KBr): 3063, 2926, 1718, 1626, 1497, 1377, 1115, 871, 769, 632, 583, 514 cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{19}H_{14}N_2O_2$: 302.1055, Found: 302.1051.

*4-Methyl-2-(*p*-tolyl)-1*H*-pyrrolo[3,4-c]quinoline-1,3(2*H*)-dione (**9**).*[20a,23c] Brown solid; yield 218 mg; 72%; mp 194–195 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.83 (d, J = 7.8 Hz, 1H), 8.14 (d, J = 8.7 Hz, 1H), 7.88 (t, J = 7.8 Hz, 1H), 7.71 (dd, J = 7.8, 7.5 Hz, 1H), 7.32 (brs, 4H), 3.07 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.57, 167.34, 155.26, 151.58, 138.45, 135.72, 132.85, 129.88, 129.24, 129.08, 128.50, 126.52, 125.02, 121.61, 120.68, 22.23, 21.24; IR (KBr): 3063, 2924, 1720, 1628, 1515, 1386, 1119, 873, 817, 777, 641, 557, 508 cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{19}H_{14}N_2O_2$: 302.1055, Found: 302.1055.

*2-(4-Methoxyphenyl)-4-methyl-1*H*-pyrrolo[3,4-c]quinoline-1,3-(2*H*)-dione (**10**).*[20a] Brown solid; yield 254 mg; 80%; mp 231–232 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.81 (d, J = 8.4 Hz, 1H), 8.15 (d, J = 8.7 Hz, 1H), 7.87 (dd, J = 8.1, 7.2 Hz, 1H), 7.70 (dd, J = 7.8, 7.5 Hz, 1H), 7.34 (d, J = 8.7 Hz, 2H), 7.02 (d, J = 9.0 Hz, 2H), 3.84 (s, 3H), 3.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.61, 167.38, 159.39, 155.20, 151.37, 135.76, 132.90, 129.10, 128.00, 124.99, 123.72, 121.59, 120.65, 114.53, 55.50, 22.10; IR (KBr): 2986, 2840, 1711, 1514, 1395, 1260, 1175, 1119,

1094, 1032, 739 cm^{-1}; HRMS (EI^+): *m/z*: calcd for $C_{19}H_{14}N_2O_3$: 318.1004, Found: 318.1003.

*2-(4-Bromophenyl)-4-methyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3-(2*H*)-dione* (**11**). Brown solid; yield 249 mg; 68%; mp 226–227 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.83 (d, J = 8.4 Hz, 1H), 8.16 (d, J = 8.7 Hz, 1H), 7.91 (td, J = 8.4, 1.5 Hz, 1H), 7.73 (td, J = 8.1, 0.9 Hz, 1H), 7.65 (d, J = 8.7 Hz, 2H), 7.36 (d, J = 8.7 Hz, 2H), 3.85 (s, 3H), 3.12 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.01, 166.83, 155.31, 151.59, 135.67, 133.11, 132.41, 130.34, 129.31, 129.28, 128.02, 124.98, 122.13, 121.47, 120.65, 22.17; IR (KBr): 3098, 2925, 2856, 1719, 1625, 1491, 1392, 1116, 824, 805, 773, 639, 589 cm^{-1}; HRMS (EI^+): *m/z*: calcd for $C_{18}H_{11}BrN_2O_2$: 366.0004, Found: 366.0000.

*2-(2-Chlorophenyl)-4-methyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3-(2*H*)-dione* (**12**).[20a] Brown solid; yield 213 mg; 66%; mp 155–156 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.86 (d, J = 8.1 Hz, 1H), 8.24 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 7.2, 6.9 Hz, 1H), 7.76 (d, J = 7.8, 7.5 Hz, 1H), 7.61–7.58 (m, 1H), 7.49–7.44 (m, 2H), 7.40–7.34 (m, 1H), 3.13 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.75, 166.54, 155.42, 151.67, 135.94, 133.33, 133.03, 130.90, 130.76, 130.51, 129.28, 129.23, 129.21, 127.82, 125.11, 121.86, 120.78, 22.23; IR (KBr): 3071, 2924, 1715, 1594, 1540, 1374, 1059, 1033, 763, 592, 538 cm^{-1}; HRMS (EI^+): *m/z*: calcd for $C_{18}H_{11}ClN_2O_2$: 322.0509, Found: 322.0511.

*2-(4-Chlorophenyl)-4-methyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3-(2*H*)-dione* (**13**). Brown solid; yield 219 mg; 68%; mp 224–225 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.81 (d, J = 7.8 Hz, 1H), 8.14 (d, J = 8.7 Hz, 1H), 7.89 (dd, J = 8.4, 6.9 Hz, 1H), 7.71 (dd, J = 8.1, 7.2 Hz, 1H), 7.49 (d, J = 8.7 Hz, 2H), 7.42 (d, J = 8.7 Hz, 2H), 3.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.12, 166.92, 155.28, 151.67, 135.52, 134.08, 133.02, 129.75, 129.42, 129.09, 127.74, 124.93, 121.40, 120.58, 116.34, 22.25; IR (KBr): 3064, 2925, 2855, 1722, 1625, 1495, 1387, 1117, 1089, 806, 771, 637, 588, 502 cm^{-1}; HRMS (EI^+): *m/z*: calcd for $C_{18}H_{11}ClN_2O_2$: 322.0509, Found: 322.0507.

*4,8-Dimethyl-2-phenyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione* (**14**).[12b] Brown solid; yield 224 mg; 74%; mp 194–195 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.02 (d, J = 8.7 Hz, 1H), 7.70 (dd, J = 8.7, 1.8 Hz, 1H), 7.55–7.50 (m, 2H), 7.47–7.39 (m, 3H), 3.04 (s, 3H), 2.58 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.49, 167.34, 154.17, 150.37, 139.74, 135.32, 134.73, 131.31, 129.17, 128.84, 128.25, 126.62, 123.54, 121.44, 120.75, 22.03, 21.88; IR (KBr): 3061, 2960, 2922, 1719, 1600, 1498, 1375, 1103, 825, 754, 686, 624, 580 cm^{-1}; HRMS (EI^+): *m/z*: calcd for $C_{19}H_{14}N_2O_2$: 302.1055, Found: 302.1057.

*4,8-Dimethyl-2-(*o*-tolyl)-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione* (**15**). Brown solid; yield 215 mg; 68%; mp 213–214 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.97 (d, J = 8.7 Hz, 1H), 7.65 (dd, J = 8.7, 1.5 Hz, 1H), 7.31–7.26 (m, 3H), 7.16 (d, J = 7.8 Hz, 1H), 2.99 (s, 3H), 2.51 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.56, 167.35, 154.14, 150.32, 139.67, 136.57, 135.30, 134.99, 131.17, 130.17, 129.54, 128.76, 126.90, 123.54, 121.74, 120.80, 22.00, 21.84, 18.06; IR (KBr): 3051, 2923, 1714, 1603, 1497, 1377, 1102, 834, 750, 631, 589 cm^{-1}; HRMS (EI^+): *m/z*: calcd for $C_{20}H_{16}N_2O_2$: 316.1212, Found: 316.1209.

*4,8-Dimethyl-2-(*p*-tolyl)-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione* (**16**). Brown solid; yield 231 mg; 73%; mp 197–198 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.01 (d, J = 8.7 Hz, 1H), 7.70 (d, J = 8.7 Hz, 1H), 7.32 (brs, 4H), 3.04 (s, 3H), 2.58 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.66, 167.49, 154.15, 150.37, 139.65, 138.32, 135.26, 134.78, 129.82, 128.83, 128.60, 126.47, 123.55, 121.50, 120.76, 22.04, 21.87, 21.23; IR (KBr): 3043, 2921, 2860, 1716, 1604, 1513, 1376, 1124, 1088, 1023, 812, 745, 657, 596, 552, 508 cm^{-1}; HRMS (EI^+): *m/z*: calcd for $C_{20}H_{16}N_2O_2$: 316.1212, Found: 316.1212.

*2-(4-Methoxyphenyl)-4,8-dimethyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione* (**17**). Brown solid; yield 279 mg; 84%; mp 194–195 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 (s, 1H), 7.99 (d, J = 8.7 Hz, 1H), 7.68 (dd, J = 8.7, 1.8 Hz, 1H), 7.34 (d, J = 9.0 Hz, 2H), 7.02 (d, J = 9.0 Hz, 2H), 3.84 (s, 3H), 3.01 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.76, 167.57, 159.31, 154.09, 150.30, 139.65, 135.24, 134.74, 128.79, 127.98, 123.86, 123.51, 121.45, 120.71, 114.49, 55.50, 22.00, 21.86; IR (KBr): 2925, 2842, 1715, 1514, 1394, 1249, 1174, 1126, 1032, 821, 560 cm^{-1}; HRMS (EI^+): *m/z*: calcd for $C_{20}H_{16}N_2O_3$: 332.1161, Found: 332.1162.

*2-(4-Bromophenyl)-4,8-dimethyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3-(2*H*)-dione* (**18**). Brown solid; yield 247 mg; 65%; mp 227–228 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.06 (d, J = 8.7 Hz, 1H), 7.74 (dd, J = 8.7, 1.8 Hz, 1H), 7.65 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 8.7 Hz, 2H), 3.06 (s, 3H), 2.60 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.09, 166.96, 154.14, 150.38, 139.91, 135.46, 134.55, 132.33, 130.34, 128.87, 127.95, 123.44, 121.98, 121.25, 120.64, 22.03, 21.88; IR (KBr): 3010, 2919, 2854, 1723, 1604, 1495, 1382, 1121, 1080, 1012, 813, 778, 748, 644, 590, 501 cm^{-1}; HRMS (EI^+): *m/z*: calcd for $C_{19}H_{13}BrN_2O_2$: 380.0160, Found: 380.0160.

*2-(2-Chlorophenyl)-4,8-dimethyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3-(2*H*)-dione* (**19**). Brown solid; yield 212 mg; 63%; mp 231–232 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.02 (d, J = 8.4 Hz, 1H), 7.70 (d, J = 8.7 Hz, 1H), 7.59–7.56 (m, 1H), 7.44–7.39 (m, 3H), 3.04 (s, 3H), 2.57 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.86, 166.67, 154.22, 150.44, 139.72, 135.35, 134.83, 133.22, 130.79, 130.72, 130.42, 129.21, 128.86, 127.76, 123.55, 121.64, 120.75, 22.07, 21.88; IR (KBr): 3209, 3017, 2923, 1721, 1597, 1484, 1379, 1100, 1064, 834, 755, 695, 588 cm^{-1}; HRMS (EI^+): *m/z*: calcd for $C_{19}H_{13}ClN_2O_2$: 336.0666, Found: 336.0665.

*2-(4-Chlorophenyl)-4,8-dimethyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3-(2*H*)-dione* (**20**). Brown solid; yield 222 mg; 66%; mp 235–236 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.52 (s, 1H), 7.99 (d, J = 9.0 Hz, 1H), 7.69 (dd, J = 8.7, 1.8 Hz, 1H), 7.48 (d, J = 8.7 Hz, 2H), 7.41 (d, J = 9.0 Hz, 2H), 3.01 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.15, 167.02, 154.11, 150.39, 139.86, 135.41, 134.47, 133.93, 129.78, 129.35, 128.87, 127.67, 123.40, 121.21, 120.59, 22.05, 21.88; IR (KBr): 2967, 2925, 1721, 1607, 1497, 1384, 1277, 1191, 1121, 1091, 1019, 817, 748, 597, 535, 506 cm^{-1}; HRMS (EI^+): *m/z*: calcd for $C_{19}H_{13}ClN_2O_2$: 336.0666, Found: 336.0664.

*8-Bromo-4-methyl-2-phenyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione* (**21**).[12b] Brown solid; yield 293 mg; 80%; mp 187–188 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.98 (d, J = 2.1 Hz, 1H), 8.00 (d,

J = 9.0 Hz, 1H), 7.93 (dd, *J* = 9.3, 2.1 Hz, 1H), 7.55–7.50 (m, 2H), 7.45–7.43 (m, 3H), 3.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.98, 166.69, 155.74, 150.02, 136.39, 134.58, 131.04, 130.74, 129.24, 128.45, 127.08, 126.54, 123.80, 122.14, 121.47, 22.20; IR (KBr): 3063, 2924, 1717, 1592, 1498, 1388, 1129, 830, 745, 680, 579 cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{18}H_{11}BrN_2O_2$: 366.0004, Found: 366.0001.

*8-Bromo-4-methyl-2-(*o*-tolyl)-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**22**).* Brown solid; yield 274 mg; 72%; mp 209–210 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.92 (d, *J* = 2.1 Hz, 1H), 7.95 (d, *J* = 9.0 Hz, 1H), 7.88 (dd, *J* = 9.0, 1.2 Hz, 1H), 7.34–7.25 (m, 3H), 7.15 (d, *J* = 7.5 Hz, 1H), 3.00 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.07, 166.71, 155.74, 150.05, 136.52, 136.36, 134.83, 131.26, 130.73, 129.91, 129.71, 128.68, 127.10, 126.98, 123.73, 122.44, 121.55, 22.20, 18.07; IR (KBr): 3076, 3021, 2969, 1714, 1590, 1495, 1375, 1123, 837, 753, 674, 581 cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{19}H_{13}BrN_2O_2$: 380.0160, Found: 380.0159.

*8-Bromo-4-methyl-2-(*p*-tolyl)-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**23**).* Brown solid; yield 277 mg; 73%; mp 253–254 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.99 (d, *J* = 2.1 Hz, 1H), 7.99 (d, *J* = 9.0 Hz, 1H), 7.93 (dd, *J* = 9.3, 1.5 Hz, 1H), 7.31 (brs, 4H), 3.05 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.18, 166.86, 155.73, 150.10, 138.55, 136.30, 134.62, 130.79, 129.89, 128.35, 127.10, 126.41, 123.70, 122.20, 121.50, 22.24, 21.24; IR (KBr): 3047, 2924, 1723, 1594, 1515, 1376, 1130, 1090, 890, 838, 749, 675, 563, 503 cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{19}H_{13}BrN_2O_2$: 380.0160, Found: 380.0158.

*8-Bromo-2-(4-methoxyphenyl)-4-methyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**24**).* Brown solid; yield 333 mg; 84%; mp 251–252 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.00 (d, *J* = 2.1 Hz, 1H), 8.02 (d, *J* = 9.0 Hz, 1H), 7.94 (dd, *J* = 9.3, 2.1 Hz, 1H), 7.34 (d, *J* = 9.3 Hz, 2H), 7.03 (d, *J* = 9.0 Hz, 2H), 3.85 (s, 3H), 3.06 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.49, 167.18, 159.84, 155.97, 150.27, 136.62, 135.07, 130.97, 128.17, 127.43, 124.03, 122.57, 121.85, 114.89, 55.77, 22.30; IR (KBr): 2924, 2842, 1714, 1517, 1396, 1253, 1143, 1095, 1036, 824, 569 cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{19}H_{13}BrN_2O_3$: 396.0110, Found: 396.0110.

*8-Bromo-2-(4-bromophenyl)-4-methyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**25**).* Brown solid; yield 311 mg; 70%; mp 244–245 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.04 (d, *J* = 2.1 Hz, 1H), 8.22 (d, *J* = 9.0 Hz, 1H), 8.02 (dd, *J* = 9.0, 2.1 Hz, 1H), 7.67 (d, *J* = 4.5 Hz, 2H), 7.35 (d, *J* = 4.8 Hz, 2H), 3.14 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6) δ 165.30, 165.13, 154.27, 148.72, 134.77, 133.39, 130.90, 129.85, 129.42, 127.25, 125.47, 122.04, 121.13, 120.50, 120.14, 20.80; IR (KBr): 3082, 2924, 2855, 1721, 1590, 1493, 1393, 1125, 1072, 1007, 831, 809, 773, 685, 586 cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{18}H_{10}Br_2N_2O_2$: 443.9109, Found: 443.9111.

*8-Bromo-2-(2-chlorophenyl)-4-methyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**26**).* Brown solid; yield 268 mg; 67%; mp 213–214 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.98 (d, *J* = 2.1 Hz, 1H), 8.01 (d, *J* = 9.0 Hz, 1H), 7.95 (d, *J* = 9.3, 2.1 Hz, 1H), 7.61–7.58 (m, 1H), 7.50–7.41 (m, 2H), 7.39–7.35 (m, 1H), 3.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.39, 166.06, 155.84, 150.17, 136.48, 134.74, 133.19, 131.01, 130.80, 130.65, 130.52, 128.95, 127.86, 127.15, 123.83, 122.38, 121.54, 22.27; IR (KBr): 3072, 2925, 2855, 1720, 1589, 1484, 1382, 1148, 1097, 825, 756, 672, 625, 581, 509 cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{18}H_{10}BrClN_2O_2$: 399.9614, Found: 399.9613.

*8-Bromo-2-(4-chlorophenyl)-4-methyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**27**).* Brown solid; yield 280 mg; 70%; mp 245–246 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.98 (d, *J* = 1.8 Hz, 1H), 8.00 (d, *J* = 9.3 Hz, 1H), 7.94 (dd, *J* = 9.0, 2.1 Hz, 1H), 7.50 (d, *J* = 8.7 Hz, 2H), 7.41 (d, *J* = 8.7 Hz, 2H), 3.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.74, 166.47, 155.75, 150.16, 136.54, 134.48, 134.23, 130.84, 129.57, 129.48, 127.66, 127.05, 123.95, 122.02, 121.43, 22.26; IR (KBr): 3094, 2927, 1725, 1594, 1498, 1389, 1141, 1089, 887, 831, 812, 780, 750, 672, 594, 550, 508 cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{18}H_{10}BrClN_2O_2$: 399.9614, Found: 399.9612.

*8-Chloro-4-methyl-2-phenyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**28**).* Brown solid; yield 261 mg; 81%; mp 181–182 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.80 (d, *J* = 2.1 Hz, 1H), 8.07 (d, *J* = 9.3 Hz, 1H), 7.80 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.55–7.50 (m, 2H), 7.45–7.42 (m, 3H), 3.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.01, 166.70, 155.57, 149.84, 135.51, 134.74, 133.86, 131.04, 130.69, 129.25, 128.45, 126.55, 123.71, 122.20, 121.05, 22.14; IR (KBr): 3062, 2924, 1723, 1596, 1499, 1383, 1134, 1103, 830, 747, 683, 624, 581 cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{18}H_{11}ClN_2O_2$: 322.0509, Found: 322.0508.

*8-Chloro-4-methyl-2-(*o*-tolyl)-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**29**).* Brown solid; yield 245 mg; 73%; mp 197–198 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.72 (d, *J* = 2.1 Hz, 1H), 8.01 (d, *J* = 9.3 Hz, 1H), 7.73 (dd, *J* = 9.0, 2.1 Hz, 1H), 7.33–7.24 (m, 3H), 7.15 (d, *J* = 7.5 Hz, 1H), 3.00 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.08, 166.70, 155.55, 149.83, 136.50, 135.41, 134.95, 133.79, 131.24, 130.66, 129.91, 129.69, 128.67, 126.97, 123.71, 122.47, 121.08, 22.13, 18.06; IR (KBr): 3077, 3022, 2970, 1715, 1593, 1496, 1374, 1124, 839, 754, 695, 631, 582 cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{19}H_{13}ClN_2O_2$: 336.0666, Found: 336.0664.

*8-Chloro-4-methyl-2-(*p*-tolyl)-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**30**).* Brown solid; yield 252 mg; 75%; mp 244–245 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.81 (d, *J* = 1.8 Hz, 1H), 8.06 (d, *J* = 8.7 Hz, 1H), 7.82–7.78 (m, 1H), 7.31 (brs, 4H), 3.06 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.21, 166.89, 155.56, 149.91, 138.56, 135.42, 134.79, 133.78, 130.74, 129.90, 128.35, 126.42, 123.75, 122.27, 121.08, 22.18, 21.24; IR (KBr): 3086, 3045, 2925, 1723, 1595, 1514, 1376, 1136, 1087, 839, 790, 748, 695, 576, 504 cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{19}H_{13}ClN_2O_2$: 336.0666, Found: 336.0664.

*8-Chloro-2-(4-methoxyphenyl)-4-methyl-1*H*-pyrrolo[3,4-*c*]-quinoline-1,3(2*H*)-dione (**31**).* Brown solid; yield 303 mg; 86%; mp 213–214 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.79 (d, *J* = 2.1 Hz, 1H), 8.07 (d, *J* = 9.0 Hz, 1H), 7.80 (dd, *J* = 9.3, 2.4 Hz, 1H), 7.33 (d, *J* = 9.0 Hz, 2H), 7.02 (d, *J* = 9.0 Hz, 2H), 3.85 (s, 3H), 3.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.29, 166.96, 159.47, 155.52, 149.76, 135.48, 134.85, 133.84, 130.63, 127.94, 123.73, 123.56, 122.26, 121.08, 114.56, 55.52, 22.09; IR (KBr): 2968, 2841, 1712, 1517, 1397, 1254, 1144, 1093, 1036, 820,

518 cm^{-1}; HRMS (EI^+): *m*/*z*: calcd for $C_{19}H_{13}ClN_2O_3$: 352.0615, Found: 352.0612.

*2-(4-Bromophenyl)-8-chloro-4-methyl-1*H-*pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**32**).* Brown solid; yield 284 mg; 71%; mp 259–260 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.81 (d, J = 2.4 Hz, 1H), 8.11 (d, J = 9.0 Hz, 1H), 7.83 (dd, J = 9.3, 2.4 Hz, 1H), 7.65 (d, J = 8.7 Hz, 2H), 7.35 (d, J = 8.7 Hz, 2H), 3.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.62, 166.36, 155.57, 149.76, 145.43, 135.80, 134.16, 132.47, 130.63, 130.09, 127.94, 123.73, 122.28, 122.14, 121.07, 22.08; IR (KBr): 3084, 2924, 2855, 1713, 1596, 1497, 1374, 1129, 1074, 1008, 831, 812, 776, 700, 587 cm^{-1}; HRMS (EI^+): *m*/*z*: calcd for $C_{18}H_{10}BrClN_2O_2$: 399.9614, Found: 399.9618.

*8-Chloro-2-(2-chlorophenyl)-4-methyl-1*H-*pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**33**).* Brown solid; yield 235 mg; 66%; mp 200–201 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.80 (d, J = 2.1 Hz, 1H), 8.08 (d, J = 9.0 Hz, 1H), 7.82 (d, J = 9.0, 2.4 Hz, 1H), 7.61–7.58 (m, 1H), 7.49–7.41 (m, 2H), 7.38–7.34 (m, 1H), 3.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.43, 166.09, 155.68, 150.01, 135.54, 134.90, 133.94, 133.20, 131.00, 130.77, 130.66, 130.52, 128.96, 127.86, 123.79, 122.44, 121.12, 22.23; IR (KBr): 3208, 3074, 2964, 1720, 1592, 1484, 1377, 1149, 1096, 826, 756, 688, 583 cm^{-1}; HRMS (EI^+): *m*/*z*: calcd for $C_{18}H_{10}Cl_2N_2O_2$: 356.0119, Found: 356.0119.

*8-Chloro-2-(4-chlorophenyl)-4-methyl-1*H-*pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**34**).* Brown solid; yield 242 mg; 68%; mp 241–242 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.75 (d, J = 1.8 Hz, 1H), 8.05 (d, J = 9.0 Hz, 1H), 7.79 (dd, J = 9.0, 2.1 Hz, 1H), 7.49 (d, J = 8.7 Hz, 2H), 7.40 (d, J = 8.7 Hz, 2H), 3.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.74, 166.45, 155.56, 149.95, 135.61, 134.54, 134.18, 133.95, 130.79, 129.54, 129.45, 127.64, 123.62, 122.02, 120.93, 22.20; IR (KBr): 3085, 2926, 2856, 1721, 1593, 1497, 1394, 1264, 1237, 1129, 1091, 887, 810, 777, 748, 703, 647, 590, 559, 503 cm^{-1}; HRMS (EI^+): *m*/*z*: calcd for $C_{18}H_{10}Cl_2N_2O_2$: 356.0119, Found: 356.0118.

*2-(4-Methoxyphenyl)-4-methyl-8-nitro-1*H-*pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**35**).* Brown solid; yield 236 mg; 65%; mp 211–212 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.69 (d, J = 2.4 Hz, 1H), 8.62 (d, J = 9.3, 2.4 Hz, 1H), 8.27 (d, J = 9.3 Hz, 1H), 7.34 (d, J = 9.0 Hz, 2H), 7.03 (d, J = 9.0 Hz, 2H), 3.85 (s, 3H), 3.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.79, 166.36, 159.61, 159.29, 152.84, 147.05, 137.48, 131.13, 127.86, 125.94, 123.28, 121.80, 119.48, 114.63, 55.54, 22.62; IR (KBr): 3091, 2924, 2844, 1723, 1622, 1513, 1394, 1343, 1256, 1119, 1095, 1033, 919, 824, 789, 750, 679 cm^{-1}; HRMS (EI^+): *m*/*z*: calcd for $C_{19}H_{13}N_3O_5$: 363.0855, Found: 363.0855.

*2-(4-Bromophenyl)-4-methyl-8-nitro-1*H-*pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**36**).* Brown solid; yield 247 mg; 60%; mp 217–218 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.71 (d, J = 2.4 Hz, 1H), 8.64 (dd, J = 9.3, 2.4 Hz, 1H), 8.30 (d, J = 9.6 Hz, 1H), 7.67 (d, J = 9.0 Hz, 2H), 7.37 (d, J = 8.7 Hz, 2H), 3.14 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.16, 165.79, 159.35, 152.95, 147.22, 137.36, 132.56, 131.26, 129.91, 127.84, 126.16, 123.16, 122.51, 121.74, 119.45, 22.66; IR (KBr): 3086, 2923, 2853, 1729, 1632, 1537, 1495, 1382, 1348, 1076, 1014, 814, 750, 644, 589, 502 cm^{-1}; HRMS (EI^+): *m*/*z*: calcd for $C_{18}H_{10}BrN_3O_4$: 410.9855, Found: 410.9855.

*6-Bromo-4-methyl-2-phenyl-1*H-*pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**37**).* Brown solid; yield 231 mg; 63%; mp 200–202 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.84 (dd, J = 8.1, 0.9 Hz, 1H), 8.22 (dd, J = 7.5, 1.2 Hz, 1H), 7.58–7.51 (m, 3H), 7.46–7.42 (m, 3H), 3.14 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.94, 166.65, 156.36, 148.37, 136.33, 136.13, 131.15, 129.40, 129.26, 128.47, 126.64, 125.04, 124.73, 122.38, 122.00, 22.56; IR (KBr): 3075, 2923, 2853, 1721, 1596, 1498, 1378, 1106, 890, 788, 756, 700, 631, 587 cm^{-1}; HRMS (EI^+): *m*/*z*: calcd for $C_{18}H_{11}BrN_2O_2$: 366.0004, Found: 366.0002.

*6-Bromo-2-(4-methoxyphenyl)-4-methyl-1*H-*pyrrolo[3,4-*c*]-quinoline-1,3(2*H*)-dione (**38**).* Brown solid; yield 265 mg; 67%; mp 198–199 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.77 (d, J = 8.4 Hz, 1H), 8.17 (d, J = 7.2 Hz, 1H), 7.50 (dd, J = 8.7, 7.8 Hz, 1H), 7.34 (d, J = 8.7 Hz, 2H), 7.02 (d, J = 9.0 Hz, 2H), 3.85 (s, 3H), 3.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.20, 166.87, 159.47, 156.26, 148.20, 136.21, 136.06, 129.30, 127.99, 124.93, 124.70, 123.62, 122.36, 121.89, 114.56, 55.52, 22.54; IR (KBr): 2976, 2841, 1716, 1512, 1386, 1259, 1168, 1122, 1096, 828, 786, 740, 573 cm^{-1}; HRMS (EI^+): *m*/*z*: calcd for $C_{19}H_{13}BrN_2O_3$: 396.0110, Found: 396.0113.

*6-Chloro-2-(4-methoxyphenyl)-4-methyl-1*H-*pyrrolo[3,4-*c*]-quinoline-1,3(2*H*)-dione (**39**).* Brown solid; yield 232 mg; 66%; mp 218–219 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.73 (d, J = 8.1 Hz, 1H), 7.95 (d, J = 6.6 Hz, 1H), 7.58 (dd, J = 8.1, 7.8 Hz, 1H), 7.34 (d, J = 8.7 Hz, 2H), 7.02 (d, J = 9.0 Hz, 2H), 3.84 (s, 3H), 3.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.21, 166.93, 159.47, 156.09, 147.44, 136.01, 133.71, 132.63, 128.88, 127.98, 123.97, 123.60, 122.36, 121.96, 114.56, 55.52, 22.54; IR (KBr): 2979, 2846, 1715, 1513, 1388, 1249, 1107, 1013, 900, 829, 792, 703, 573, 531 cm^{-1}; HRMS (EI^+): *m*/*z*: calcd for $C_{19}H_{13}ClN_2O_3$: 352.0615, Found: 352.0612.

*6-Chloro-2-(4-chlorophenyl)-4-methyl-1*H-*pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**40**).* Brown solid; yield 221 mg; 62%; mp 266–267 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.81 (d, J = 4.2 Hz, 1H), 8.05 (d, J = 3.9 Hz, 1H), 7.69 (dd, J = 4.2, 3.9 Hz, 1H), 7.56 (d, J = 4.2 Hz, 2H), 7.47 (d, J = 4.2 Hz, 2H), 3.13 (s, 3H); ^{13}C NMR (150 MHz, CD_2Cl_2) δ 167.08, 166.89, 156.44, 148.00, 136.43, 134.48, 134.23, 133.21, 130.35, 129.74, 129.48, 128.35, 124.33, 122.81, 122.44, 22.65; IR (KBr): 3099, 2970, 2928, 1718, 1620, 1494, 1386, 1172, 1096, 1013, 902, 824, 788, 758, 675, 596, 504 cm^{-1}; HRMS (EI^+): *m*/*z*: calcd for $C_{18}H_{10}Cl_2N_2O_2$: 356.0119, Found: 356.0122.

*2-Benzyl-4-methyl-1*H-*pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**41**).* Brown solid; yield 106 mg; 35%; mp 206–207 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.78 (d, J = 8.1 Hz, 1H), 8.14 (dd, J = 8.7 Hz, 1H), 7.89–7.83 (m, 1H), 7.69 (dd, J = 8.1, 7.2 Hz, 1H), 7.47–7.44 (m, 2H), 7.35–7.27 (m, 3H), 4.87 (s, 2H), 3.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.03, 167.82, 158.94, 154.92, 136.29, 135.95, 132.93, 129.06, 128.77, 128.67, 128.03, 124.89, 121.98, 120.64, 41.76, 29.67, 21.86; IR (KBr): 3063, 2924, 2854, 1710, 1625, 1432, 1391, 1339, 1112, 1075, 775, 704, 631, 549, 502 cm^{-1}; HRMS (EI^+): *m*/*z*: calcd for $C_{19}H_{14}N_2O_2$: 302.1055, Found: 302.1054.

*2-Benzyl-4,8-dimethyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**42**).* Brown solid; yield 133 mg; 42%; mp 183–184 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.48 (s, 1H), 7.92 (d, J = 8.7 Hz, 1H), 7.61 (d, J = 8.7 Hz, 1H), 7.40 (d, J = 7.8 Hz, 2H), 7.29–7.21 (m, 3H), 4.81 (s, 2H), 2.94 (s, 3H), 2.51 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.26, 168.17, 153.84, 150.19, 139.53, 136.08, 135.20, 128.76, 128.69, 127.98, 123.41, 121.85, 120.70, 41.69, 21.82; IR (KBr): 3034, 2938, 1710, 1598, 1396, 1344, 1109, 1070, 933, 832, 753, 702, 629, 508 cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{20}H_{16}N_2O_2$: 316.1212, Found: 316.1209.

*2-Benzyl-8-bromo-4-methyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**43**).* Brown solid; yield 156 mg; 41%; mp 192–193 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.93 (d, J = 1.8 Hz, 1H), 7.95 (d, J = 9.0 Hz, 1H), 7.88 (dd, J = 9.0, 2.1 Hz, 1H), 7.44 (d, J = 6.9 Hz, 2H), 7.35–7.27 (m, 3H), 4.86 (s, 2H), 3.00 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.74, 167.49, 155.41, 149.86, 136.25, 135.82, 135.03, 130.61, 128.81, 128.75, 128.12, 126.98, 123.60, 122.56, 121.43, 41.86, 22.03; IR (KBr): 3078, 2922, 2850, 1708, 1587, 1390, 1334, 1072, 924, 838, 750, 699, 625, 556 cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{19}H_{13}BrN_2O_2$: 380.0160, Found: 380.0158.

*2-Benzyl-8-chloro-4-methyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**44**).* Brown solid; yield 155 mg; 46%; mp 190–191 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.77 (d, J = 1.8 Hz, 1H), 8.07 (d, J = 9.3 Hz, 1H), 7.78 (dd, J = 9.3, 2.4 Hz, 1H), 7.45 (d, J = 7.5 Hz, 2H), 7.35–7.27 (m, 3H), 4.87 (s, 2H), 3.03 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.82, 167.59, 155.46, 149.54, 136.02, 135.78, 135.71, 134.20, 130.55, 129.05, 128.98, 128.36, 123.93, 122.97, 121.35, 42.17, 22.07; IR (KBr): 3074, 2925, 2854, 1711, 1497, 1394, 1335, 1079, 925, 838, 749, 696, 625, 563, 501 cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{19}H_{13}ClN_2O_2$: 336.0666, Found: 336.0663.

*2,4-Diphenyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**45**).* Brown solid; yield 126 mg; 36%; mp 246–247 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.98 (dd, J = 8.4 Hz, 1H), 8.28 (d, J = 8.4 Hz, 1H), 8.01–7.98 (m, 2H), 7.93 (td, J = 8.4, 1.5 Hz, 1H), 7.76 (td, J = 8.1, 0.9 Hz, 1H), 7.53–7.51 (m, 4H), 7.48–7.38 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.00, 166.49, 155.43, 151.85, 137.09, 136.60, 133.10, 131.38, 130.21, 130.18, 130.04, 129.72, 129.14, 128.32, 128.08, 126.77, 125.10, 120.87, 120.74; IR (KBr): 3060, 1721, 1593, 1501, 1382, 1116, 779, 744, 687 cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{23}H_{14}N_2O_2$: 350.1055, Found: 350.1057.

*8-Methyl-2,4-diphenyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**46**).* Brown solid; yield 146 mg; 40%; mp 256–257 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.74 (s, 1H), 8.17 (d, J = 8.7 Hz, 1H), 7.98–7.95 (m, 2H), 7.77 (dd, J = 8.7, 1.8 Hz, 1H), 7.55–7.41 (m, 8H), 2.63 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.21, 166.64, 154.42, 150.68, 140.50, 136.66, 136.04, 135.62, 131.34, 130.08, 129.88, 129.81, 129.11, 128.26, 128.06, 126.72, 123.59, 120.96, 120.60, 22.04; IR (KBr): 3061, 2924, 1720, 1595, 1496, 1377, 1135, 1108, 831, 753, 694, 624, 506 cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{24}H_{16}N_2O_2$: 364.1212, Found: 364.1215.

*8-Bromo-2,4-diphenyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**47**).* Brown solid; yield 180 mg; 42%; mp 241–242 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.13 (s, 1H), 8.12 (d, J = 9.0 Hz, 1H), 7.99–7.97 (m, 3H), 7.53–7.49 (m, 5H), 7.45–7.43 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.51, 166.11, 155.64, 150.22, 136.70, 136.08, 135.94, 131.55, 130.99, 130.29, 130.09, 129.18, 128.44, 128.13, 127.14, 126.60, 124.51, 121.54, 121.23; IR (KBr): 3062, 2926, 1721, 1585, 1497, 1381, 1143, 1108, 970, 832, 744, 685, 625, 540 cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{23}H_{13}BrN_2O_2$: 428.0160, Found: 428.0163.

*8-Chloro-2,4-diphenyl-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**48**).* Brown solid; yield 173 mg; 45%; mp 229–230 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.96 (d, J = 2.4 Hz, 1H), 8.21 (d, J = 9.0 Hz, 1H), 7.99–7.96 (m, 2H), 7.86 (dd, J = 9.3, 2.4 Hz, 1H), 7.54–7.47 (m, 5H), 7.45–7.42 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.55, 166.16, 155.53, 150.08, 136.15, 136.10, 134.19, 131.55, 131.02, 130.27, 130.11, 129.19, 128.96, 128.46, 128.14, 126.63, 123.79, 121.13, 121.18; IR (KBr): 3060, 2925, 1721, 1592, 1497, 1381, 1144, 1108, 973, 831, 746, 686, 625, 541 cm^{-1}; HRMS (EI$^+$): *m*/*z*: calcd for $C_{23}H_{13}ClN_2O_2$: 384.0666, Found: 384.0664.

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