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Article

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Formal [4 + 2] Annulation of Oxindole-Embedded *ortho*-Quinone Methides with 1,3-Dicarbonyls: Synthesis of Spiro[Chromen-4,3´-Oxindole] Scaffolds

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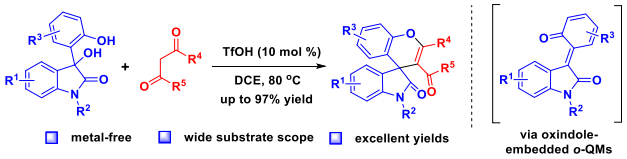
Graphic Abstract



Abstract: The oxindole-embedded *ortho*-quinone methides, *in situ* generated from oxindole-embedded *ortho*-hydroxybenzyl alcohols, were employed as reactive intermediates in formal [4 + 2] annulation with 1,3-dicarbonyls, providing an efficient access to spiro[chromen-4,3´-oxindole] scaffolds via a cascade conjugate addition/ketalization/dehydration process. This protocol featured metal-free conditions, wide substrate scope and excellent yields.

INTRODUCTION

Spirooxindoles and 4*H*-chromenes are privileged skeletons in an array of natural products and pharmaceutical agents (Figure 1).[1-2] Due to their structural complexities and diverse bioactivities, considerable efforts have been devoted to assembling these frameworks.[3-4] According to the

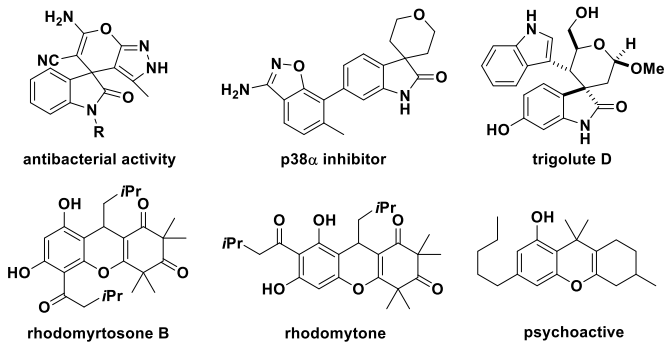
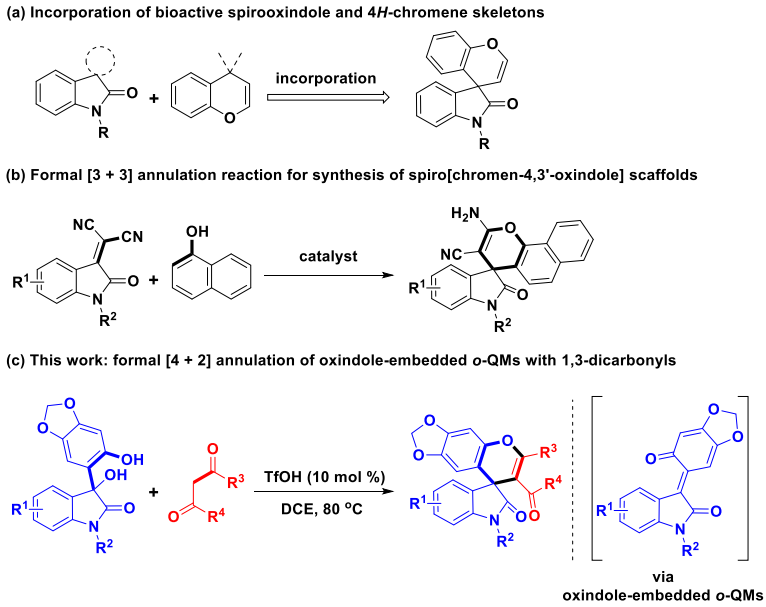


Figure 1. Natural products and bioactive compounds containing the spirooxindole or 4*H*-chromene core.

principle of superposition in drug discovery, incorporation of these two motifs would provide potential bioactivity from spiro[chromen-4,3´-oxindole] scaffolds (Scheme 1a). So far, although spirooxindoles have been successfully hybridized with various heterocyclic rings,[3] there are sporadic reports related to the synthesis of spiro[chromen-4,3´-oxindole] scaffolds. And the limited examples were realized by cascade [3 + 3] annulation-type reactions (Scheme 1b).[5] Therefore, it is appealing to develop new methods for efficient construction of these intriguing molecules.

Scheme 1. Synthesis of Spiro[Chromen-4,3´-Oxindole] Scaffolds.



ortho-Quinone methides (*o*-QMs) have emerged as highly reactive synthons for the synthesis of complex molecules and naturally occurring products, especially for chromanes and related analogues.[6] Owing to their inherent tendency of rearomatization, *o*-QMs have been commonly

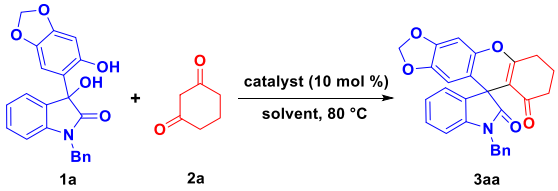
exploited as electron-deficient species to participate in conjugate addition[7] and [4 + n] cyclization reactions.[8-10] In spite of these significant progresses, to the best of our knowledge, there are no examples of *o*-QMs-involved reactions for one-pot assembly of spiro[chromen-4,3´-oxindole] scaffolds. In this context, we envisaged the introduction of an oxindole unit into the *o*-QMs would furnish a new class of oxindole-embedded *o*-QMs, which could undertake a formal [4 + 2] annulation with 1,3-dicarbonyls for rapid buildup of spiro[chromen-4,3´-oxindole] skeletons via a cascade conjugate addition/ketalization/dehydration sequence. As our continuing interest in the one-step assembly of molecular complexity,[11] herein, we reported a formal [4 + 2] annulation of *in situ* generated oxindole-embedded *o*-QMs with 1,3-dicarbonyls for one-pot synthesis of spiro[chromen-4,3´-oxindole] compounds (Scheme 1c). This reaction featured metal-free conditions, wide substrate scope and high yields.

RESULTS AND DISCUSSION

To test the feasibility of our proposal, we commenced our investigations with the reaction between oxindole-embedded *ortho*-hydroxybenzyl alcohol **1a** and 1,3-cyclohexanedione **2a** (Table 1). To our delight, the reaction proceeded smoothly and delivered the desired product **3aa** in 94% yield when 10 mol % of trifluoromethanesulfonic acid (TfOH) was used as the catalyst in DCE at 80 °C (Table 1, entry 1). Then a series of Brønsted acids were screened, such as *p*-toluenesulfonic acid monohydrate ($TsOH·H_2O$), methanesulfonic acid (MsOH) and trifluoroacetic acid (TFA). However, all of them led to inferior results (Table 1, entries 2-7). Afterwards, Lewis acids were evaluated and it was found that $Sc(OTf)_3$ also exhibited a high efficiency to furnish **3aa** in 93% yield (Table 1, entries 8 and 9). Subsequently, decreasing the catalyst loading to 5 mol % resulted in a diminished yield (Table 1, entry 10). Finally, the exploration of solvents such as THF, toluene and MeCN indicated that DCE was the best solvent (Table 1, entries 11-13). Consequently, TfOH was selected as the best catalyst to catalyze this reaction in DCE.

With the optimized conditions in hand, the substrate scope and generality of the developed formal [4 + 2] annulation were evaluated. At first, a wide range of oxindole-embedded *ortho*-hydroxybenzyl alcohols **1** bearing various substituents were subjected to the reactions with 1,3-cyclohexanedione **2a**, which proceeded efficiently and afforded the corresponding

Table 1. Optimization of the Reaction Conditions[a]



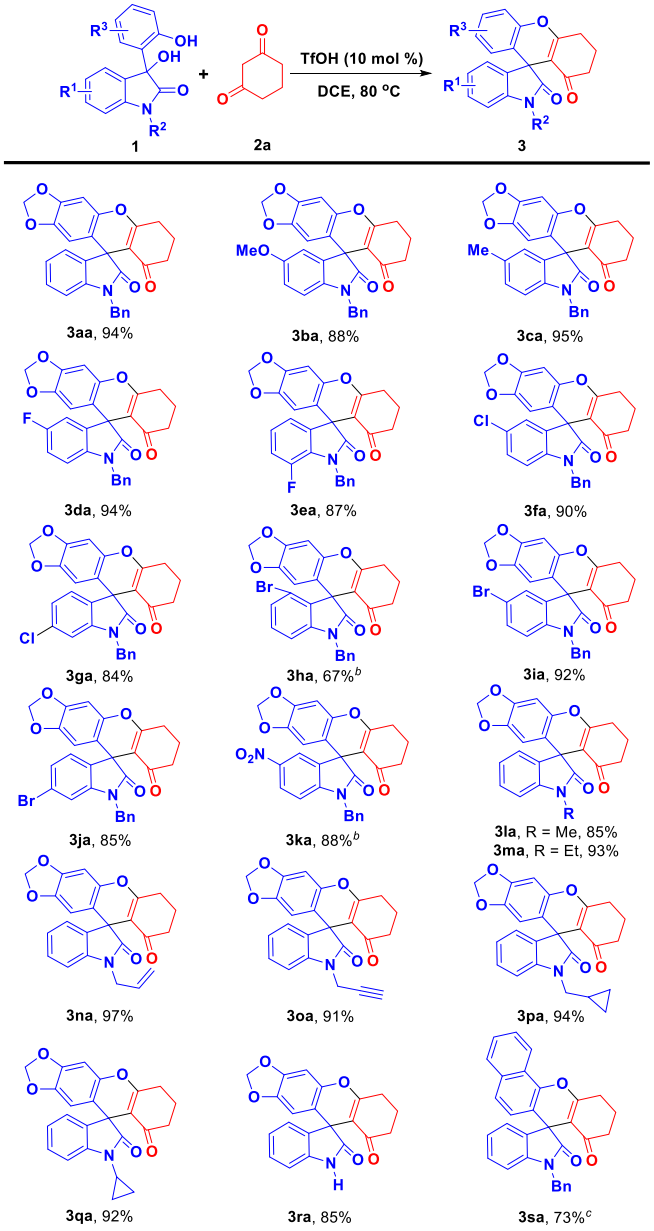
entry	catalyst	solvent	yield [b] (%)
1	TfOH	DCE	94
2	$TsOH·H_2O$	DCE	77
3	MsOH	DCE	72
4	TFA	DCE	26
5	(−)-CSA	DCE	33
6	$PhCO_2H$	DCE	14
7	HOAc	DCE	<10
8	$Sc(OTf)_3$	DCE	93
9	$Cu(OTf)_2$	DCE	86
10[c]	TfOH	DCE	85
11	TfOH	THF	78
12	TfOH	toluene	42
13	TfOH	MeCN	83

[a]Reaction conditions: **1a** (0.1 mmol), **2** (0.12 mmol) and catalyst (10 mol %) in solvent (1 mL) at 80 °C for 8 h. TfOH = trifluoromethanesulfonic acid, $TsOH·H_2O$ = *p*-toluenesulfonic acid monohydrate, MsOH = methanesulfonic acid, TFA = trifluoroacetic acid, (–)-CSA = (–)-10-camphorsulfonic acid. [b]Isolated yield after column chromatography. [c]Catalyst (5 mol %), 24 h.

spiro[chromen-4,3´-oxindole] products in good to excellent yields (Table 2). With respect to the R^1 groups, electron-donating methoxy and methyl groups were well tolerated and furnished the desired products **3ba** and **3ca** in 88% and 95% yields, respectively. Moreover, electron-withdrawing halogens (fluoro, chloro, and bromo) at different positions had negligible influence on the transformations, giving the expected products **3da-3ja** in 67-94% yields. It is noted that the decreased yield of **3ha** might be ascribed to the steric hindrance of in situ generated oxindole-embedded *o*-QM intermediate. Remarkably, the substrate incorporating the stronger electron-withdrawing nitro group was also an ideal candidate and delivered product **3ka** in 88% yield, which could hardly be realized in previously reported *o*-QMs-involved reactions. It was worth mentioning that the achievement of fluorine- and nitro-containing substrates indicated the great potential in the medicinal industry. With regard to the R^2 groups, in addition to methyl and ethyl groups, the allyl and propargyl substituents functioned efficiently, providing the desired products **3la-3oa** in 85-97% yields. Notably, the alcohols carrying highly strained cyclopropyl and cyclopropylmethyl groups also worked well and produced the products **3pa** and **3qa** in 94% and 92% yields, correspondingly. Moreover, the substrate without a protecting group was examined

and afforded product **3ra** in 85% yield. As to the R^3 group, satisfyingly, the oxindole-embedded *ortho*-naphthoquinone methide was tolerable and gave the corresponding product **3sa** in 73% yield.

Table 2. Substrate Scope of Oxindole-Embedded *ortho*-Hydroxybenzyl Alcohols 1[a]

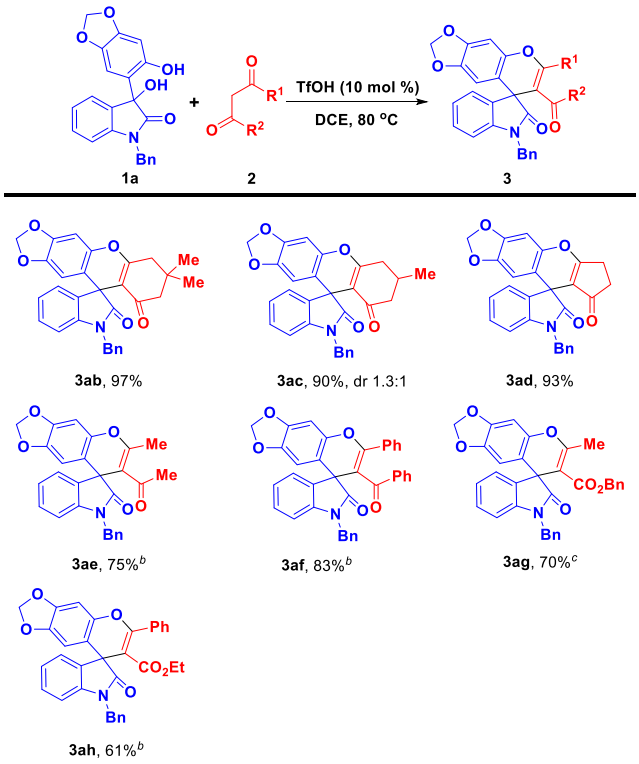


[a]Reaction conditions: **1** (0.1 mmol), **2a** (0.12 mmol) and TfOH (10 mol %) in DCE (1 mL) at 80 °C for 8 h. Isolated yield after column chromatography. [b]TfOH (20 mol %), 12 h. [c]24 h.

Next, the substrate scope of 1,3-dicarbonyls **2** was further examined, as shown in Table 3. Substituted 1,3-cyclohexanediones were fully compatible with the reaction conditions, yielding **3ab** and **3ac** in 97% and 90% yields, respectively. Notably, other 1,3-dicarbonyls such as

1,3-cyclopentanedione, 2,4-pentanedione and 1,3-diphenyl-1,3-propanedione are also good reaction partners for this reaction, delivering products **3ad-3af** in 75-93% yields. Gratifyingly, the employment of benzyl acetoacetate and ethyl benzoylacetate could proudce products **3ag** and **3ah** in moderate yields.

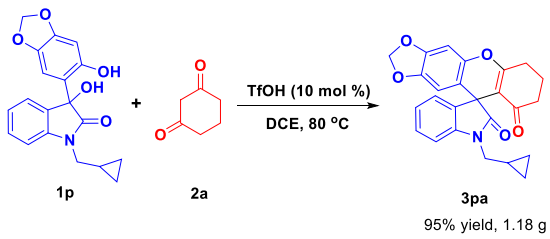
Table 3. Substrate Scope of 1,3-Dicarbonyls 2[a]



[a]Reaction conditions: **1a** (0.1 mmol), **2** (0.12 mmol) and TfOH (10 mol %) in DCE (1 mL) at 80 °C for 8 h. Isolated yield after column chromatography. [b]3 h. [c]TfOH (20 mol %).

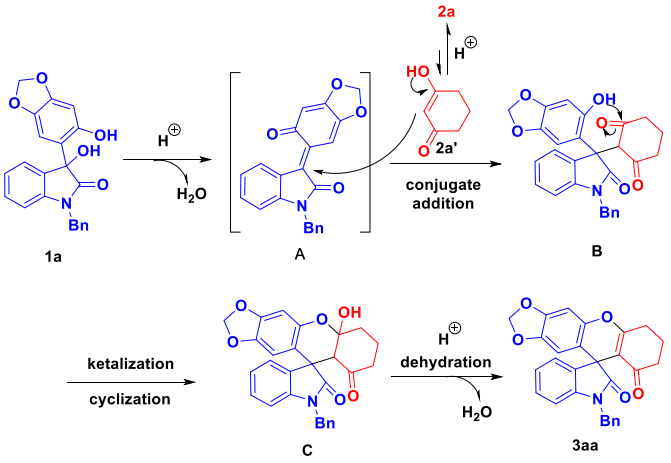
To substantiate the practicality of this protocol, the formal [4 + 2] annulation of **1p** with **2a** was performed on a gram scale, which reacted smoothly and gave spiro[chromen-4,3´-oxindole] **3pa** in 95% yield (Scheme 2).

Scheme 2. Gram-Scale Synthesis



On the basis of the above experimental results, a plausible mechanism was proposed, as shown in Scheme 3. Under the catalysis of Brønsted acid, the oxindole-embedded *o*-QM intermediate **A** is *in situ* generated via the dehydration of oxindole-embedded *ortho*-hydroxybenzyl alcohol **1a**. At the same time, 1,3-cyclohexanedione **2a** tautomerizes to the enol species **2a´**. Then the conjugate addition of **2a´** to intermediate **A** occurs and affords intermediate **B**, which subsequently undertakes the intramolecular ketalization to provide intermediate **C**. Finally, Brønsted acid-catalyzed dehydration of **C** gives the desired product **3aa**. Intriguingly, intermediates **A** and **C** have been isolated and characterized by NMR, which fully proves this hypothesis.

Scheme 3. Proposed Mechanism



CONCLUSION

In summary, the oxindole-embedded *o*-QMs, *in situ* generated from oxindole-embedded *ortho*-hydroxybenzyl alcohols, were designed as reactive intermediates in formal [4 + 2] annulation with 1,3-dicarbonyls, which offered an efficient route to pharmaceutically important spiro[chromen-4,3´-oxindole] scaffolds via a domino conjugate addition/ketalization/dehydration process. This method featured metal-free conditions, wide substrate scope and excellent yields, which exhibited promising prospects in organic synthesis and drug discovery.

Experimental Section

All commercially available reagents, unless otherwise indicated, were used without further purification. All solvents were purified and dried according to standard methods prior to use. Reactions were monitored by thin layer chromatography (TLC) with 0.2 mm silica gel-coated

HSGF 254 plates, visualized by UV light at 254 or 365 nm. Products were isolated and purified by column chromatography on 200-300 mesh silica gel. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker AMX 500 (500 MHz for ^{1}H NMR, 125 MHz for ^{13}C NMR and 470 MHz for ^{19}F NMR) spectrometer at room temperature. The chemical shifts (δ) were reported in ppm with respect to an internal standard, tetramethylsilane (0 ppm), and the solvent ($CDCl_3$, ^{1}H: δ = 7.26 ppm, ^{13}C: δ = 77.16 ppm). Coupling constants (*J*) are given in Hertz. Splitting patterns of apparent multiplets associated with an averaged coupling constants were designated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublets) and br (broadened). All ^{13}C spectra were recorded with broadband proton decoupling. HRMS were performed on a Waters XEVO QTOF mass spectrometer.

General Procedure for the Synthesis of Oxindole-Embedded *ortho*-Hydroxybenzyl Alcohols 1.[12]

A round-bottom flask was charged with isatin (1 mmol), phenol (3 mmol) and H_2O (6 mL). The reaction mixture was stirred vigorously at room temperature and monitored by TLC. After the consumption of isatin, the reaction mixture was extracted with ethyl acetate, and the combined organic layers were dried over anhydrous Na_2SO_4. The solvent was concentrated under reduced pressure, and the residue was purified by flash column chromatography (column chromatography eluent, petroleum ether/ EtOAc = 8:1) to afford products **1**. For the new compounds **1e**, **1g**, **1h**, **1j**, **1k**, **1m**, **1p** and **1q**, they have been characterized as follows.

General Procedure for Formal [4 + 2] Annulation of Oxindole-Embedded *ortho*-Hydroxybenzyl Alcohols 1 with 1,3-Dicarbonyls 2.

An oven-dried reaction tube was charged with oxindole-embedded *ortho*-hydroxybenzyl alcohols **1** (1.0 equiv, 0.1 mmol), 1,3-dicarbonyls **2** (1.2 equiv, 0.12 mmol), DCE (1 mL) and TfOH (10 mol %). The reaction mixture was stirred vigorously at 80 °C in oil bath for appropriate time and monitored by TLC. After the consumption of **1**, the reaction mixture was concentrated

under reduced pressure and then purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc) to afford products **3**.

General Procedure for Gram-Scale Synthesis of 3pa.

An oven-dried round-bottomed flask was charged with oxindole-embedded *ortho*-hydroxybenzyl alcohol **1p** (3.0 mmol, 1017 mg), 1,3-dicarbonyl **2a** (3.6 mmol, 403 mg), DCE (30 mL) and TfOH (0.3 mol, 45 mg). The reaction mixture was stirred vigorously at 80 °C in oil bath for 8 h, and monitored by TLC. After the consumption of **1p**, the reaction mixture was concentrated under reduced pressure and then purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc = 6:1) to afford product **3pa** as white solid in 95% yield (1180 mg).

1-benzyl-7-fluoro-3-hydroxy-3-(6-hydroxybenzo[d][1,3]dioxol-5-yl)indolin-2-one (1e). White solid; 358 mg, 91% yield; mp 124–126 °C; column chromatography eluent, petroleum ether/EtOAc = 8:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.87 (s, 1H), 7.29–7.20 (m, 6H), 7.11–6.98 (m, 2H), 6.50 (s, 1H), 6.25 (s, 1H), 5.85 (s, 2H), 4.99 (s, 2H), 4.87 (s, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 179.0, 151.7, 148.9, 147.8 (d, *J* = 244.6 Hz), 141.5, 136.0, 132.3, 129.0 (d, *J* = 8.8 Hz), 128.8 (2C), 127.8, 127.3 (2C), 124.8 (d, *J* = 6.3 Hz), 121.8, 118.5 (d, *J* = 19.4 Hz), 116.7, 106.5, 101.5 (comb, 2C), 79.1, 45.8 (d, *J* = 4.5 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ –132.6; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{17}FNO_5$ 394.1085; found 394.1086.

1-benzyl-6-chloro-3-hydroxy-3-(6-hydroxybenzo[d][1,3]dioxol-5-yl)indolin-2-one (1g). White solid; 364 mg, 89% yield; mp 120–122 °C; column chromatography eluent, petroleum ether/EtOAc = 8:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.87 (s, 1H), 7.38–7.22 (m, 6H), 7.12 (d, *J* = 7.7 Hz, 1H), 6.76 (s, 1H), 6.55 (s, 1H), 6.29 (s, 1H), 5.88 (s, 2H), 4.90 (d, *J* = 15.8 Hz, 1H), 4.79

(d, *J* = 15.8 Hz, 1H), 4.68 (s, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 179.2, 151.7, 149.0, 143.6, 141.6, 136.2, 134.3, 129.1 (2C), 128.1, 127.7, 127.1 (2C), 126.9, 123.9, 116.7, 110.8, 106.5, 101.7, 101.6, 78.7, 44.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{17}ClNO_5$ 410.0790; found 410.0795.

1-benzyl-4-bromo-3-hydroxy-3-(6-hydroxybenzo[d][1,3]dioxol-5-yl)indolin-2-one (1h). White solid; 408 mg, 90% yield; mp 129–131 °C; column chromatography eluent, petroleum ether/EtOAc = 8:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.78 (s, 1H), 7.28 (m, 4H), 7.22 (d, *J* = 7.3 Hz, 2H), 7.14 (t, *J* = 8.0 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 6.56 (s, 1H), 6.21 (s, 1H), 5.90 (s, 1H), 5.87 (s, 1H), 4.88 (d, *J* = 15.8 Hz, 1H), 4.82 (d, *J* = 15.8 Hz, 1H), 4.37 (s, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ177.8, 152.5, 149.2, 144.5, 141.4, 134.4, 131.7, 129.0 (2C), 128.0, 127.9, 127.7, 127.1 (2C), 120.8, 113.7, 109.2, 106.7, 101.6, 101.5, 80.5, 44.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{17}BrNO_5$ 454.0285; found 454.0283.

1-benzyl-6-bromo-3-hydroxy-3-(6-hydroxybenzo[d][1,3]dioxol-5-yl)indolin-2-one (1j). White solid; 381 mg, 84% yield; mp 116–118 °C; column chromatography eluent, petroleum ether/EtOAc = 8:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.99 (s, 1H), 7.32 (m, 5H), 7.24 (m, 2H), 6.93 (s, 1H), 6.62 (s, 1H), 6.27 (s, 1H), 5.90 (s, 1H), 5.89 (s, 1H), 4.91 (d, *J* = 15.8 Hz, 1H), 4.82 (d, *J* = 15.8 Hz, 1H), 4.44 (s, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 179.2, 152.0, 149.2, 143.7, 141.7, 134.2, 129.1 (2C), 128.2, 127.9, 127.4, 127.1 (2C), 126.9, 124.1, 116.9, 113.7, 106.6, 102.2, 101.6, 78.9, 44.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{17}BrNO_5$ 454.0285; found 454.0291.

1-benzyl-3-hydroxy-3-(6-hydroxybenzo[d][1,3]dioxol-5-yl)-5-nitroindolin-2-one (1k). Yellow solid; 365 mg, 87% yield; mp 140–142 °C; column chromatography eluent, petroleum ether/EtOAc = 8:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.23 (d, *J* = 8.7 Hz, 1H), 8.03 (s,

1H), 7.32 (m, 3H), 7.25 (m, 2H), 6.86 (d, *J* = 8.7 Hz, 1H), 6.56 (s, 1H), 6.42 (s, 1H), 5.92 (s, 2H), 5.00 (d, *J* = 15.8 Hz, 1H), 4.93 (d, *J* = 15.8 Hz, 1H), 4.46 (s, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 179.1, 150.9, 149.3, 144.3, 142.0, 133.8, 130.4, 130.3, 129.2, 128.4, 127.2, 127.1, 121.7, 116.3, 109.9, 106.2, 101.8, 101.7, 78.1, 44.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{17}N_2O_7$ 421.1030; found 421.1034.

1-ethyl-3-hydroxy-3-(6-hydroxybenzo[d][1,3]dioxol-5-yl)indolin-2-one (1m). White solid; 297 mg, 95% yield; mp 119–121 °C; column chromatography eluent, petroleum ether/EtOAc = 8:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.37 (s, 1H), 7.47 (d, *J* = 7.4 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 7.9 Hz, 1H), 6.55 (s, 1H), 6.25 (s, 1H), 5.86 (s, 1H), 5.84 (s, 1H), 4.63 (s, 1H), 3.73 (qq, *J* = 14.3, 7.2 Hz, 2H), 1.27 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 178.7, 152.3, 148.8, 142.2, 141.3, 130.4, 129.4, 126.2, 123.8, 117.1, 109.4, 106.8, 101.8, 101.4, 79.3, 35.2, 12.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{16}NO_5$ 314.1023; found 314.1026.

1-(cyclopropylmethyl)-3-hydroxy-3-(6-hydroxybenzo[d][1,3]dioxol-5-yl)indolin-2-one (1p). White solid; 305 mg, 90% yield; mp 108–110 °C; column chromatography eluent, petroleum ether/EtOAc = 8:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.38 (s, 1H), 7.48 (d, *J* = 7.4 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 6.98 (d, *J* = 7.9 Hz, 1H), 6.55 (s, 1H), 6.26 (s, 1H), 5.86 (s, 1H), 5.84 (s, 1H), 4.68 (s, 1H), 3.60 (dd, *J* = 14.5, 6.9 Hz, 1H), 3.52 (dd, *J* = 14.5, 7.0 Hz, 1H), 1.21–1.10 (m, 1H), 0.58–0.48 (m, 2H), 0.42–0.31 (m, 2H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 179.0, 152.3, 148.8, 142.8, 141.3, 130.3, 129.4, 126.1, 123.8, 117.1, 109.7, 106.7, 101.7, 101.4, 79.3, 44.8, 9.4, 4.0, 4.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{18}NO_5$ 340.1179; found 340.1180.

1-cyclopropyl-3-hydroxy-3-(6-hydroxybenzo[d][1,3]dioxol-5-yl)indolin-2-one (1q). White solid; 299 mg, 92% yield; mp 108–110 °C; column chromatography eluent, petroleum ether/EtOAc = 8:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.27 (s, 1H), 7.42 (m, 2H), 7.18 (m, 2H), 6.55 (s, 1H), 6.21 (s, 1H), 5.86 (s, 1H), 5.84 (s, 1H), 4.53 (s, 1H), 2.69–2.60 (m, 1H), 1.12–1.00 (m, 2H), 0.96–0.84 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 180.0, 152.2, 148.8, 143.6, 141.3, 130.4, 128.6, 125.9, 123.9, 117.2, 110.5, 106.8, 101.8, 101.4, 79.3, 22.5, 6.0, 6.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{16}NO_5$ 326.1023; found 326.1020.

1-benzyl-7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-dione (3aa). White solid; 42.4 mg, 94% yield; mp 237–239 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.4 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 7.4 Hz, 1H), 7.15–7.07 (m, 1H), 6.94–6.85 (m, 2H), 6.74 (d, *J* = 7.8 Hz, 1H), 6.59 (s, 1H), 6.00 (s, 1H), 5.86 (d, *J* = 1.2 Hz, 1H), 5.84 (d, *J* = 1.2 Hz, 1H), 5.09 (d, *J* = 15.7 Hz, 1H), 5.00 (d, *J* = 15.7 Hz, 1H), 2.83–2.67 (m, 2H), 2.48–2.29 (m, 2H), 2.17–2.08 (m, 1H), 2.07–1.96 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 195.8, 178.6, 167.9, 147.8, 145.3, 143.5, 142. 7, 136.5, 136.2, 128.8 (2C), 128.2, 127.6 (2C), 127.5, 123.0, 122.9, 114.0, 111.0, 109.3, 105.1, 101.7, 98.5, 48.7, 44.6, 36.9, 28.1, 20.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{28}H_{22}NO_5$ 452.1492; found 452.1497.

1-benzyl-5-methoxy-7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-dione (3ba). White solid; 42.3 mg, 88% yield; mp 261–263 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.3 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 7.4 Hz, 1H), 6.62 (m, 2H), 6.59 (s, 1H), 6.52–6.48 (m, 1H), 6.02 (s, 1H), 5.88 (d, *J* = 1.4 Hz, 1H), 5.86 (d, *J* = 1.4 Hz, 1H), 5.05 (d, *J* = 15.7 Hz, 1H), 4.99 (d, *J* = 15.7 Hz,

1H), 3.65 (s, 3H), 2.81–2.68 (m, 2H), 2.47–2.32 (m, 2H), 2.18–2.08 (m, 1H), 2.08–1.97 (m, 1H); ^{13}C NMR{^{1}H} (125 MHz, $CDCl_3$) δ 195.8, 178.3, 167.9, 156.2, 147.8, 145.3, 143.4, 137.8, 136.3, 136.2, 128.8 (2C), 127.6 (2C), 127.5, 113.9, 112.0, 110.9, 110.9, 109.6, 105.2, 101.7, 98.5, 55.6, 49.1, 44.7, 36.9, 28.1, 20.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{29}H_{24}NO_6$ 482.1598; found 482.1605.

1-benzyl-5-methyl-7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-dione (3ca). White solid; 44.2 mg, 95% yield; mp 250–252 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.5 Hz, 2H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 7.4 Hz, 1H), 6.90 (dd, *J* = 7.9, 0.8 Hz, 1H), 6.70 (d, *J* = 0.6 Hz, 1H), 6.62 (d, *J* = 7.9 Hz, 1H), 6.59 (s, 1H), 6.01 (s, 1H), 5.87 (d, *J* = 1.3 Hz, 1H), 5.86 (d, *J* = 1.3 Hz, 1H), 5.07 (d, *J* = 15.7 Hz, 1H), 4.99 (d, *J* = 15.7 Hz, 1H), 2.82–2.68 (m, 2H), 2.47–2.32 (m, 2H), 2.18 (s, 3H), 2.12 (dt, *J* = 17.6, 5.9 Hz, 1H), 2.09–1.99 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 195.9, 178.5, 167.8, 147.7, 145.2, 143.5, 140.3, 136.5, 136.3, 132.4, 128.7 (2C), 128.5, 127.6 (2C), 127.5, 123.9, 114.2, 111.1, 109.0, 105.3, 101.7, 98.4, 48.8, 44.7, 36.9, 28.1, 21.1, 20.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{29}H_{24}NO_5$ 466.1649; found 466.1657.

1-benzyl-5-fluoro-7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-dione (3da). White solid; 44.1 mg, 94% yield; mp 233–235 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.3 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 6.79 (td, *J* = 8.9, 2.6 Hz, 1H), 6.68–6.62 (m, 2H), 6.60 (s, 1H), 5.99 (s, 1H), 5.88 (d, *J* = 1.3 Hz, 1H), 5.87 (d, *J* = 1.3 Hz, 1H), 5.06 (d, *J* = 15.7 Hz, 1H), 4.99 (d, *J* = 15.7 Hz, 1H), 2.82–2.68 (m, 2H), 2.48–2.31 (m, 2H), 2.19–2.09 (m, 1H), 2.09–1.99 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 195.8, 178.3, 168.2, 159.5 (d, *J* = 239.6 Hz), 148.0,

145.4, 143.5, 138.6 (d, J = 1.9 Hz), 137.9 (d, *J* = 7.5 Hz), 135.9, 128.8 (2C), 127.7, 127.5 (2C), 114.4 (d, *J* = 23.4 Hz), 113.3, 111.2 (d, *J* = 24.8 Hz), 110.6, 109.8 (d, *J* = 8.0 Hz), 105.0, 101.8, 98.6, 49.1 (d, *J* = 1.6 Hz), 44. 8, 36.9, 28.1, 20.4; ^{19}F NMR (470 MHz, $CDCl_3$) δ -120.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{28}H_{21}FNO_5$ 470.1398; found 470.1403.

1-benzyl-7-fluoro-7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-di one (3ea). White solid; 40.8 mg, 87% yield; mp 256–258 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.4 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.27 (t, *J* = 7.4 Hz, 1H), 6.95–6.86 (m, 1H), 6.84 (td, *J* = 7.8, 4.6 Hz, 1H), 6.68 (d, *J* = 7.2 Hz, 1H), 6.58 (s, 1H), 5.92 (s, 1H), 5.86 (s, 1H), 5.84 (s, 1H), 5.22 (d, *J* = 15.3 Hz, 1H), 5.09 (d, *J* = 15.3 Hz, 1H), 2.82–2.65 (m, 2H), 2.47–2.27 (m, 2H), 2.12 (dt, *J* = 11.9, 5.6 Hz, 1H), 2.07–1.94 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 195.7, 178.2, 168.0, 147.9, 147.3 (d, *J* = 243.1 Hz), 145.3, 143.3, 139.3 (d, *J* = 2.9 Hz), 137.5, 129.3 (d, *J* = 8.6 Hz), 128.5 (2C), 127.8, 127.8, 127.5, 123.5 (d, *J* = 6.4 Hz), 119.0 (d, *J* = 2.9 Hz), 116.4 (d, *J* = 19.8 Hz), 113.5, 110.8, 104.9, 101.8, 98.5, 48.9 (d, *J* = 2.1 Hz), 46.0 (d, *J* = 4.4 Hz), 36.8, 28.1, 20.4; ^{19}F NMR (470 MHz, $CDCl_3$) δ -133.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{28}H_{21}FNO_5$ 470.1398; found 470.1401.

1-benzyl-5-chloro-7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-di one (3fa). White solid; 43.7 mg, 90% yield; mp 249–251 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.4 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.29 (t, *J* = 7.3 Hz, 1H), 7.07 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.87 (d, *J* = 2.0 Hz, 1H), 6.65 (d, *J* = 8.3 Hz, 1H), 6.60 (s, 1H), 5.97 (s, 1H), 5.89 (d, *J* = 0.9 Hz, 1H), 5.88 (s, 1H), 5.06 (d, *J* = 15.7 Hz, 1H), 4.99 (d, *J* = 15.7 Hz, 1H), 2.84–2.69 (m, 2H), 2.49–2.33 (m, 2H), 2.21–2.10 (m, 1H),

2.09–1.98 (m, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 195.8, 178.1, 168.2, 148.0, 145.4, 143.5, 141.3, 138.0, 135.7, 128.9 (2C), 128.2, 128.1, 127.7, 127.5 (2C), 123.6, 113.2, 110.5, 110.2, 104.9, 101.8, 98.6, 48.8, 44.8, 36.8, 28.1, 20.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{28}H_{21}ClNO_5$ 486.1103; found 486.1106.

1-benzyl-6-chloro-7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-dione (3ga). White solid; 40.8 mg, 84% yield; mp 253–255 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.4 Hz, 2H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 1H), 6.88 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.81 (d, *J* = 7.9 Hz, 1H), 6.74 (d, *J* = 1.8 Hz, 1H), 6.59 (s, 1H), 5.97 (s, 1H), 5.88 (d, *J* = 1.3 Hz, 1H), 5.86 (d, *J* = 1.3 Hz, 1H), 5.07 (d, *J* = 15.7 Hz, 1H), 4.94 (d, *J* = 15.7 Hz, 1H), 2.81–2.67 (m, 2H), 2.47–2.30 (m, 2H), 2.17–2.08 (m, 1H), 2.02 (ddq, *J* = 10.8, 8.3, 5.4 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 195.8, 178.4, 168.1, 148.0, 145.4, 143.9, 143.5, 135.6, 134.9, 133.8, 128.9 (2C), 127.8, 127.5 (2C), 124.0, 122.8, 113.3, 110.6, 109.8, 104.9, 101.8, 98.5, 48.4, 44.7, 36.9, 28.1, 20.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{28}H_{21}ClNO_5$ 486.1103; found 486.1103.

1-benzyl-4-bromo-7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-dione (3ha). White solid; 35.4 mg, 67% yield; mp 247–249 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.30 (t, *J* = 7.3 Hz, 1H), 7.02–6.96 (m, 2H), 6.70 (dd, *J* = 5.9, 2.7 Hz, 1H), 6.60 (s, 1H), 5.99 (s, 1H), 5.92–5.86 (m, 2H), 5.08 (d, *J* = 15.7 Hz, 1H), 4.99 (d, *J* = 15.7 Hz, 1H), 2.80–2.67 (m, 2H), 2.47–2.34 (m, 2H), 2.18–1.97 (m, 2H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 196.0, 177.9, 169.1, 148.1, 145.2, 144.7, 144.6, 135.8, 132.8, 129.7, 128.9 (2C), 127.7, 127.6 (2C),

126.7, 118.9, 111.4, 109.0, 108.4, 104.6, 101.8, 98.3, 50.3, 44.8, 36.8, 28.2, 20.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{28}H_{21}BrNO_5$ 530.0598; found 530.0599.

1-benzyl-5-bromo-7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-dione (3ia). White solid; 48.6 mg, 92% yield; mp 265–267 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 7.3 Hz, 2H), 7.38 (m, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.22 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.99 (d, *J* = 2.0 Hz, 1H), 6.60 (m, 2H), 5.97 (s, 1H), 5.89 (d, *J* = 1.3 Hz, 1H), 5.88 (d, *J* = 1.3 Hz, 1H), 5.05 (d, *J* = 15.7 Hz, 1H), 4.98 (d, *J* = 15.7 Hz, 1H), 2.84–2.67 (m, 2H), 2.50–2.32 (m, 2H), 2.21–2.09 (m, 1H), 2.10–1.99 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 195.8, 178.0, 168.2, 148.0, 145.4, 143.5, 141.8, 138.3, 135.7, 131.0, 128.9 (2C), 127.7, 127.5 (2C), 126.4, 115.6, 113.1, 110.7, 110.5, 105.0, 101.8, 98.6, 48.7, 44.7, 36.8, 28.1, 20.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{28}H_{21}BrNO_5$ 530.0598; found 530.0604.

1-benzyl-6-bromo-7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-dione (3ja). White solid; 45.0 mg, 85% yield; mp 272–274 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.2 Hz, 2H), 7.39 (m, 2H), 7.30 (t, *J* = 7.4 Hz, 1H), 7.04 (dd, *J* = 7.9, 1.7 Hz, 1H), 6.89 (d, *J* = 1.6 Hz, 1H), 6.76 (d, *J* = 7.9 Hz, 1H), 6.59 (s, 1H), 5.96 (s, 1H), 5.88 (d, *J* = 1.3 Hz, 1H), 5.86 (d, *J* = 1.3 Hz, 1H), 5.06 (d, *J* = 15.7 Hz, 1H), 4.94 (d, *J* = 15.7 Hz, 1H), 2.82–2.67 (m, 2H), 2.46–2.30 (m, 2H), 2.17–2.07 (m, 1H), 2.07–1.96 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 195.8, 178.3, 168.1, 148.0, 145.4, 144.1, 143.5, 135.6, 135.4, 128.9 (2C), 127.8, 127.5 (2C), 125.8, 124.4, 121.7, 113.2, 112.5, 110.6, 104.9, 101.8, 98.5, 48.4, 44.7, 36.8, 28.1, 20.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{28}H_{21}BrNO_5$ 530.0598; found 530.0597.

1-benzyl-5-nitro-7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-dione (3ka). Yellow solid; 43.6 mg, 88% yield; mp 292–294 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (dd, *J* = 8.7, 2.2 Hz, 1H), 7.79 (d, *J* = 2.2 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 1H), 6.83 (d, *J* = 8.7 Hz, 1H), 6.64 (s, 1H), 5.91 (s, 1H), 5.90 (s, 1H), 5.89 (s, 1H), 5.12 (d, *J* = 15.7 Hz, 1H), 5.05 (d, *J* = 15.7 Hz, 1H), 2.80 (t, *J* = 6.3 Hz, 2H), 2.47–2.34 (m, 2H), 2.23–2.03 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 196.1, 178.7, 168. 9, 148.5, 148.4, 145.6, 143.7, 143.6, 137.2, 135.0, 129.1 (2C), 128.1, 127.6 (2C), 125.5, 119.1, 112.2, 110.1, 108.8, 104.5, 102.0, 98.9, 48.6, 45.0, 36.7, 28.1, 20.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{28}H_{21}N_2O_7$ 497.1343; found 497.1355.

1-methyl-7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-dione (3la). White solid; 31.9 mg, 85% yield; mp 244–246 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (td, *J* = 7.7, 1.4 Hz, 1H), 6.94 (td, *J* = 7.4, 0.8 Hz, 1H), 6.92–6.88 (m, 2H), 6.58 (s, 1H), 6.02 (s, 1H), 5.85 (s, 2H), 3.35 (s, 3H), 2.78–2.66 (m, 2H), 2.42–2.26 (m, 2H), 2.15–2.06 (m, 1H), 2.05–1.96 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 195.8, 178.6, 167.8, 147.7, 145.2, 143.6, 143.6, 136.5, 128.4, 123.0, 122.9, 113.8, 111.2, 108.1, 105.2, 101.7, 98.4, 48.8, 36.9, 28.1, 26.8, 20.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{18}NO_5$ 376.1179; found 376.1188.

1-ethyl-7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-dione (3ma). White solid; 36.2 mg, 93% yield; mp 193–195 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (td, *J* = 7.5, 1.7 Hz, 1H), 6.96–6.87 (m, 3H), 6.57 (s, 1H), 6.02 (s, 1H), 5.85 (s, 2H), 3.94 (dq, *J* = 14.4, 7.2 Hz, 1H), 3.83 (dq, *J* = 14.3, 7.2

Hz, 1H), 2.80–2.66 (m, 2H), 2.43–2.26 (m, 2H), 2.15–2.06 (m, 1H), 2.05–1.94 (m, 1H), 1.40 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 195.8, 178.0, 167.7, 147.7, 145.2, 143.5, 142.6, 136.8, 128.3, 123.2, 122.6, 114.0, 111.2, 108.3, 105.1, 101.7, 98.4, 48.7, 36.9, 35.1, 28.1, 20.4, 12.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{20}NO_5$ 390.1336; found 390.1335.

1-allyl-7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-dione (3na). White solid; 38.9 mg, 97% yield; mp 192–194 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (td, *J* = 7.7, 1.4 Hz, 1H), 6.98–6.87 (m, 3H), 6.58 (s, 1H), 6.03 (s, 1H), 6.03–5.95 (m, 1H), 5.86 (s, 2H), 5.52 (dd, *J* = 17.2, 1.2 Hz, 1H), 5.31 (dd, *J* = 10.3, 1.1 Hz, 1H), 4.52 (ddt, *J* = 16.1, 4.8, 1.5 Hz, 1H), 4.41 (dd, *J* = 16.2, 5.7 Hz, 1H), 2.81–2.65 (m, 2H), 2.43–2.26 (m, 2H), 2.17–2.06 (m, 1H), 2.06–1.95 (m, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 195.8, 178.2, 167.8, 147.8, 145.3, 143.6, 142.7, 136.5, 131.8, 128.2, 123.1, 122.8, 118.0, 113.9, 111.1, 109.2, 105.2, 101.7, 98.5, 48.7, 43.1, 36.9, 28.1, 20.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{24}H_{20}NO_5$ 402.1336; found 402.1337.

1-(prop-2-yn-1-yl)-7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-dione (3oa). White solid; 36.3 mg, 91% yield; mp 211–213 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31–7.26 (m, 1H), 7.13 (d, *J* = 7.9 Hz, 1H), 6.98 (td, *J* = 7.5, 0.5 Hz, 1H), 6.92 (d, *J* = 7.4 Hz, 1H), 6.59 (d, *J* = 1.6 Hz, 1H), 6.09 (d, *J* = 1.6 Hz, 1H), 5.87 (d, *J* = 1.6 Hz, 2H), 4.92–4.79 (m, 1H), 4.51–4.38 (m, 1H), 2.81–2.67 (m, 2H), 2.46–2.27 (m, 3H), 2.11 (tt, *J* = 10.7, 5.3 Hz, 1H), 2.06–1.95 (m, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 195.9, 177.5, 167.9, 147.8, 145.31, 143.5, 141.6, 136.3, 128.3, 123.3, 123.1, 113.7, 110.9, 109.2, 105.2, 101.7, 98.4, 77.2, 72.4, 48.6, 36.8, 29.9, 28.1, 20.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{24}H_{18}NO_5$ 400.1179; found 400.1182.

1-(cyclopropylmethyl)-7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-dione (3pa). White solid; 39.0 mg, 94% yield; mp 184–186 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (td, *J* = 7.7, 1.6 Hz, 1H), 6.99 (d, *J* = 7.8 Hz, 1H), 6.95–6.86 (m, 2H), 6.57 (s, 1H), 6.10 (s, 1H), 5.86 (d, *J* = 1.2 Hz, 1H), 5.85 (d, *J* = 1.2 Hz, 1H), 3.73 (qd, *J* = 14.4, 6.8 Hz, 2H), 2.79–2.65 (m, 2H), 2.44–2.26 (m, 2H), 2.16–2.06 (m, 1H), 2.00 (dtt, *J* = 10.8, 8.2, 5.5 Hz, 1H), 1.38–1.28 (m, 1H), 0.67–0.54 (m, 2H), 0.51–0.38 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 195.7, 178.4, 167.7, 147.7, 145.2, 143.5, 143.1, 136.7, 128.2, 123.1, 122.6, 114.1, 111.1, 108.6, 105.1, 101.7, 98.4, 48. 7, 44.7, 36.8, 28.1, 20.4, 9.6, 4.0, 3.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{25}H_{22}NO_5$ 416.1492; found 416.1496.

1-cyclopropyl-7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-dione (3qa). White solid; 36.9 mg, 92% yield; mp 243–245 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.16 (d, *J* = 7.7 Hz, 1H), 6.93 (td, *J* = 7.4, 0.9 Hz, 1H), 6.86 (dd, *J* = 7.3, 0.8 Hz, 1H), 6.57 (s, 1H), 5.96 (s, 1H), 5.86 (d, *J* = 0.8 Hz, 2H), 2.83 (dq, *J* = 6.8, 4.0 Hz, 1H), 2.77–2.65 (m, 2H), 2.39–2.25 (m, 2H), 2.14–2.05 (m, 1H), 1.99 (dtt, *J* = 11.0, 8.1, 5.7 Hz, 1H), 1.14–1.06 (m, 3H), 1.03 (ddd, *J* = 13.4, 6.3, 3.0 Hz, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 195.9, 179.1, 167.6, 147.7, 145.2, 144.0, 143.6, 136.0, 128.2, 123.0, 122.7, 114.1, 111.4, 109.5, 105.1, 101.7, 98.4, 48.9, 36.9, 28.0, 22.7, 20.4, 6.3, 6.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{24}H_{20}NO_5$ 402.1336; found 402.1335.

7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-dione (3ra). White solid; 30.7 mg, 85% yield; mp 294–296 °C; column chromatography eluent, petroleum

ether/EtOAc = 3:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.16 (t, *J* = 7.4 Hz, 1H), 6.90 (m, 3H), 6.58 (s, 1H), 6.20 (s, 1H), 5.87 (s, 1H), 5.87 (s, 1H), 2.81–2.66 (m, 2H), 2.48–2.30 (m, 2H), 2.13 (tt, *J* = 10.6, 5.2 Hz, 1H), 2.08–1.97 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 196.0, 180.0, 168.0, 147.8, 145.4, 143.4, 140.5, 137.1, 128.3, 123.4, 122.8, 113.6, 111.0, 110.0, 105.4, 101.7, 98.4, 49.1, 36.9, 28.1, 20.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{16}NO_5$ 362.1023; found 362.1027.

1'-benzyl-10,11-dihydrospiro[benzo[c]xanthene-7,3'-indoline]-2',8(9H)-dione (3sa). White solid; 33.4 mg, 73% yield; mp 272–274 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.3 Hz, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.57 (m, 3H), 7.50 (t, *J* = 7.3 Hz, 1H), 7.43–7.35 (m, 3H), 7.30 (t, *J* = 7.3 Hz, 1H), 7.17–7.07 (m, 1H), 6.94–6.84 (m, 2H), 6.79 (d, *J* = 7.8 Hz, 1H), 6.64 (d, *J* = 8.6 Hz, 1H), 5.18 (d, *J* = 15.7 Hz, 1H), 5.01 (d, *J* = 15.6 Hz, 1H), 2.94 (t, *J* = 6.2 Hz, 2H), 2.55–2.36 (m, 2H), 2.20 (tt, *J* = 11.7, 5.7 Hz, 1H), 2.15–2.05 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 195.9, 178.6, 167.7, 143.7, 142.9, 136.7, 136.4, 133.5, 128.8 (2C), 128.3, 127.7 (2C), 127.6, 127.6, 127.0, 126.8, 125.3, 123.8, 123.5, 123.3, 123.0, 121.3, 116.5, 112.1, 109.3, 48.9, 44.8, 37.0, 28.2, 20.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{31}H_{24}NO_3$ 458.1751; found 458.1748.

1-benzyl-7',7'-dimethyl-7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-dione (3ab). White solid; 46.5 mg, 97% yield; mp 221–223 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 7.4 Hz, 1H), 7.14–7.07 (m, 1H), 6.92–6.86 (m, 2H), 6.74 (d, *J* = 7.8 Hz, 1H), 6.58 (s, 1H), 6.01 (s, 1H), 5.86 (d, *J* = 1.2 Hz, 1H), 5.84 (d, *J* = 1.2 Hz, 1H), 5.08 (d, *J* = 15.7 Hz, 1H), 5.00 (d, *J* = 15.7 Hz, 1H), 2.66 (d, *J* = 17.3 Hz, 1H), 2.55 (d, *J* = 17.4 Hz, 1H),

2.31 (d, *J* = 16.2 Hz, 1H), 2.19 (d, *J* = 16.2 Hz, 1H), 1.16 (s, 3H), 1.10 (s, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 195.6, 178.5, 166.2, 147.8, 145.3, 143.6, 142.6, 136.4, 136.2, 128.8 (2C), 128.2, 127.6 (2C), 127.5, 122.9 (2C), 114.0, 109.7, 109.3, 105.1, 101.7, 98.5, 50.7, 48.7, 44.6, 41.8, 32.2, 29.0, 27.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{30}H_{26}NO_5$ 480.1805; found 480.1814.

1-benzyl-7'-methyl-7',8'-dihydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-dione (3ac). White solid; 41.9 mg, 90% yield; mp 224–226 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.5 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 7.4 Hz, 1H), 7.15–7.06 (m, 1H), 6.94–6.84 (m, 2H), 6.74 (d, *J* = 7.8 Hz, 1H), 6.59 (s, 1H), 6.00 (d, *J* = 2.7 Hz, 1H), 5.85 (d, *J* = 7.9 Hz, 2H), 5.15–4.93 (m, 2H), 2.75 (m, 1H), 2.55–2.22 (m, 3H), 2.11 (m, 1H), 1.11 (t, *J* = 6.1 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 195.8, 178.5, 166.9, 147.8, 145.3, 143.6, 142.7, 136.5, 136.2, 128.8 (2C), 128.2, 127.6 (2C), 127.6, 123.0, 123.0, 113.9, 110.4, 109.3, 105.2, 101.7, 98.5, 48.8, 45.1, 44.7, 36.0, 28.0, 20.7; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{29}H_{24}NO_5$ 466.1649; found 466.1659.

1'-benzyl-6,7-dihydro-8H-spiro[cyclopenta[b][1,3]dioxolo[4,5-g]chromene-9,3'-indoline]-2',8-dione (3ad). White solid; 40.6 mg, 93% yield; mp 224–226 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.3 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 7.4 Hz, 1H), 7.16 (ddd, *J* = 8.9, 7.6, 1.7 Hz, 1H), 6.99–6.91 (m, 2H), 6.75 (d, *J* = 7.9 Hz, 1H), 6.70 (s, 1H), 6.00 (s, 1H), 5.91 (s, 2H), 5.12 (d, *J* = 15.8 Hz, 1H), 4.95 (d, *J* = 15.8 Hz, 1H), 2.95–2.81 (m, 2H), 2.49 (qdd, *J* = 18.1, 6.7, 3.2 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 200.5, 179.4, 176.9, 148.2, 145.7, 145.5, 142.8, 135.5, 134.0, 128.8 (3C), 127.6, 127.3

(2C), 124.1, 123.3, 114.2, 113.6, 109.6, 105.9, 102.0, 99.1, 48.7, 44.5, 33.3, 25.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{27}H_{20}NO_5$ 438.1336; found 438.1347.

7'-acetyl-1-benzyl-6'-methylspiro[indoline-3,8'-[1,3]dioxolo[4,5-g]chromen]-2-one (3ae). White solid; 32.9 mg, 75% yield; mp 212–214 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.5 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.27 (t, *J* = 7.3 Hz, 1H), 7.13 (td, *J* = 7.7, 1.4 Hz, 1H), 6.98–6.88 (m, 2H), 6.77 (d, *J* = 7.8 Hz, 1H), 6.56 (s, 1H), 5.91 (s, 1H), 5.84 (s, 1H), 5.83 (s, 1H), 5.08 (d, *J* = 15.6 Hz, 1H), 4.91 (d, *J* = 15.6 Hz, 1H), 2.46 (s, 3H), 2.17 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 197.3, 178.9, 159.9, 147.7, 144.9, 143.9, 142.8, 136.3, 136.1, 128.8 (2C), 128.3, 127.7 (2C), 127.6, 123.1 (2C), 113.7, 113.5, 109.2, 104.8, 101.6, 98.2, 51.3, 44.6, 31.6, 20.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{27}H_{22}NO_5$ 440.1492; found 440.1489.

7'-benzoyl-1-benzyl-6'-phenylspiro[indoline-3,8'-[1,3]dioxolo[4,5-g]chromen]-2-one (3af). White solid; 46.7 mg, 83% yield; mp 227–229 °C; column chromatography eluent, petroleum ether/EtOAc = 15:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57–7.51 (m, 2H), 7.48 (d, *J* = 7.4 Hz, 2H), 7.44–7.39 (m, 2H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 7.4 Hz, 1H), 7.18–7.06 (m, 6H), 7.02 (t, *J* = 7.7 Hz, 2H), 6.87 (t, *J* = 7.2 Hz, 1H), 6.76 (s, 1H), 6.72 (d, *J* = 7.8 Hz, 1H), 5.99 (s, 1H), 5.89 (s, 2H), 5.14 (d, *J* = 15.7 Hz, 1H), 4.94 (d, *J* = 15.7 Hz, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 195.6, 178.1, 158.7, 148.0, 145.3, 145.0, 143.2, 138.7, 136.1, 134.6, 133.7, 131.8, 130.3, 129.7 (2C), 129.2 (2C), 128.8 (2C), 128.7, 127.9 (2C), 127.6 (2C), 127.6, 127.5 (2C), 123.7, 123.1, 113.9, 110.2, 109.4, 105.2, 101.7, 98.8, 52.7, 44.6; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{37}H_{26}NO_5$ 564.1805; found 564.1811.

benzyl

1-benzyl-6'-methyl-2-oxospiro[indoline-3,8'-[1,3]dioxolo[4,5-g]chromene]-7'-carboxylate (3ag). White solid; 37.2 mg, 70% yield; mp 150–152 °C; column chromatography eluent, petroleum ether/EtOAc = 40:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.27 (m, 7H), 7.26 (dt, *J* = 3.7, 2.0 Hz, 1H), 7.12 (td, *J* = 7.7, 1.2 Hz, 1H), 7.01–6.98 (m, 1H), 6.94 (t, *J* = 7.4 Hz, 1H), 6.91–6.87 (m, 2H), 6.55 (t, *J* = 3.8 Hz, 2H), 5.84 (d, *J* = 1.3 Hz, 1H), 5.83 (s, 1H), 5.82 (d, *J* = 1.3 Hz, 1H), 4.90 (d, *J* = 15.4 Hz, 1H), 4.77 (d, *J* = 11.9 Hz, 1H), 4.69 (d, *J* = 12.0 Hz, 1H), 3.78 (d, *J* = 15.4 Hz, 1H), 2.52 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 178.9, 165.9, 162.7, 147.8, 144.9, 143.7, 142.5, 137.0, 136.4, 135.2, 128.9 (2C), 128.7 (2C), 128.4 (2C), 128.1, 128.1, 127.8 (2C), 127.7, 123.5, 123.1, 112.9, 109.3, 104.8, 101.6, 101.3, 98.4, 66.6, 50.8, 43.9, 20.2; HRMS (ESI-TOF) m/z: [M + H]$^{+}$ calcd for $C_{33}H_{26}NO_6$ 532.1755; found 532.1769.

ethyl

1-benzyl-2-oxo-6'-phenylspiro[indoline-3,8'-[1,3]dioxolo[4,5-g]chromene]-7'-carboxylate (3ah). White solid; 32.4 mg, 61% yield; mp 183–185 °C; column chromatography eluent, petroleum ether/EtOAc = 15:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 6.5 Hz, 2H), 7.47 (d, *J* = 7.5 Hz, 2H), 7.45–7.39 (m, 3H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.29 (t, *J* = 7.3 Hz, 1H), 7.18 (t, *J* = 7.7 Hz, 1H), 7.14 (d, *J* = 7.3 Hz, 1H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.80 (d, *J* = 7.8 Hz, 1H), 6.64 (s, 1H), 5.95 (s, 1H), 5.87 (d, *J* = 4.2 Hz, 2H), 5.12 (d, *J* = 15.5 Hz, 1H), 4.88 (d, *J* = 15.5 Hz, 1H), 3.71 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.60 (dq, *J* = 10.8, 7.1 Hz, 1H), 0.56 (t, *J* = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 178.3, 166.1, 159.9, 147.9, 145.0, 144.8, 143.0, 136.1, 135.6, 134.8, 129.8, 128.8 (2C), 128.6 (3C), 128.0 (2C), 127.8 (2C), 127.7, 123.9, 123.2, 113.2, 109.1, 105.0, 103.8, 101.7,

98.7, 60.3, 51.6, 44.6, 13.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{33}H_{26}NO_6$ 532.1755; found 532.1759.

(E)-1-benzyl-3-(6-oxobenzo[d][1,3]dioxol-5(6H)-ylidene)indolin-2-one (A). This compound was detected and obtained by the reaction of oxindole-embedded *ortho*-hydroxybenzyl alcohol **1a** (0.1 mmol, 37.5 mg) with 1,3-cyclohexanedione **2a** (0.12 mmol, 13.5 mg) in the presence of 10 mol % TfOH (0.01 mmol, 1.5 mg) at 80 °C for 5 min. Reddish brown oil; <10% yield; *E/Z* >20:1; column chromatography eluent, petroleum ether/EtOAc = 18:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.77 (d, *J* = 8.0 Hz, 1H), 8.60 (s, 1H), 7.32 (m, 5H), 7.22 (t, *J* = 7.8 Hz, 1H), 6.93 (t, *J* = 7.6 Hz, 1H), 6.65 (d, *J* = 7.7 Hz, 1H), 5.97 (s, 2H), 5.95 (s, 1H), 4.94 (s, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 187.9, 169.2, 159.5, 150.3, 144.2, 136.6, 135.8, 132.7, 130.7, 128.8 (2C), 127.7, 127.6, 127.2 (2C), 122.4, 122.0, 108.7, 102.8, 101.5, 101.2, 43.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{16}NO_4$ 358.1047; found 358.1043.

1-benzyl-5a'-hydroxy-5a',7',8',9a'-tetrahydrospiro[indoline-3,10'-[1,3]dioxolo[4,5-b]xanthene]-2,9'(6'H)-dione (C). This compound was detected and obtained by the reaction of oxindole-embedded *ortho*-hydroxybenzyl alcohol **1a** (0.1 mmol, 37.5 mg) with 1,3-cyclohexanedione **2a** (0.12 mmol, 13.5 mg) in the presence of 10 mol % TfOH (0.01 mmol, 1.5 mg) at 80 °C for 1 h. White solid; 9.9 mg, 21% yield; mp 228–230 °C; column chromatography eluent, petroleum ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.81 (s, 1H), 7.50 (d, *J* = 7.3 Hz, 2H), 7.38 (t, *J* = 7.2 Hz, 2H), 7.30 (t, *J* = 7.2 Hz, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 6.99 (t, *J* = 7.3 Hz, 1H), 6.91 (d, *J* = 7.3 Hz, 1H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.50 (s, 1H), 5.83 (s, 2H), 5.75 (s, 1H), 5.09 (d, *J* = 15.6 Hz, 1H), 4.99 (d, *J* = 15.7 Hz, 1H), 3.72 (s, 1H), 2.53–2.40 (m, 2H), 2.33 (td, *J* = 13.1, 6.8 Hz, 1H), 2.24–2.08 (m, 2H), 2.03 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz,

$CDCl_3$) δ 204.1, 181.2, 148.5, 146.3, 143.9, 142.9, 135.4, 133.7, 128.9 (2C), 128.8, 127.9, 127.6 (2C), 123.7, 122.3, 112.3, 110.0, 105.2, 101.3, 100.2, 98.6, 59.6, 49.3, 44.9, 40.9, 36.8, 20.7; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{28}H_{24}NO_6$ 470.1598; found 470.1592.

Supporting Information

NMR spectra of products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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