Iodobenzene-Mediated Intramolecular Oxidative Coupling of Substituted 4-Hydroxyphenyl-*N*-phenylbenzamides for the Synthesis of Spirooxindoles

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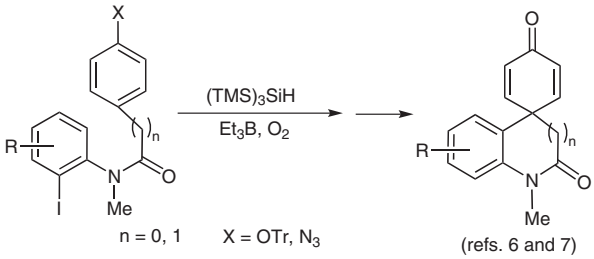
Abstract: Phenyliodine(III) bis(trifluoroacetate) (PIFA) can effect the intramolecular oxidative coupling of substituted 4-hydroxyphenyl-*N*-phenylbenzamides. The transformations could be realized in a catalytic manner by using iodobenzene as catalyst and *m*-chloroperoxybenzoic acid or urea·H_2O_2 as terminal oxidant. This reaction constitutes an efficient method for the synthesis of spirooxindoles.

Key words: hypervalent iodine , oxidative coupling, phenolic coupling, spirooxindoles, iodobenzene

Organic hypervalent iodine reagents have found wide applications in organic synthesis over the last two decades. The versatility and ready availability of hypervalent iodine compounds, combined with their environmentally benign character, render them superior oxidants for a variety of organic transformations.[1] Recently, there has been much interest in applying hypervalent iodine reagents, such as $PhI(OAc)_2$ (DIB or PIDA) and $PhI(OCOCF_3)_2$ (BTI or PIFA) in particular, to the oxidative coupling of electron-rich aromatic compounds.[2] The PIDA and PIFA-mediated intramolecular phenolic coupling reactions constitute powerful biomimetic strategies for the synthesis of fused and spiral cyclic compounds.[3,4]

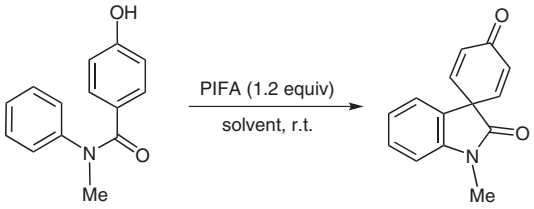
Spirooxindoles are key intermediates in the syntheses of some important biologically active compounds.[5] Recently, two novel synthetic approaches employing aryl free radical cyclizations have been developed to gain access to spirooxindoles as well as spirodihydroquinolones (Scheme 1).[6,7] In another study, Doris et al. showed that the spirodihydroquinolones could be prepared through PIFA-promoted intramolecular coupling of 2-(4-hydroxyphenyl)-*N*-methyl-*N*-acetamide.[8] However, the general scope of the reaction was not explored, and the protocol was not extended to the synthesis of spirooxindoles. In light of the synthetic importance of spirooxindoles, we reinvestigated these reactions, and found that the method was very effective for the synthesis of spirooxindoles from substituted 4-hydroxyphenyl *N*-phenylbenzamides. The transformations could be realized catalytically by employing the catalytic system developed by Kita et al.[9] and Ochiai et al.[10]

During the initial stages of the study, 4-hydroxyphenyl-*N*-methyl-*N*-benzamide (**1a**) was chosen as the substrate,



Scheme 1

and was subjected to reaction with PIFA and PIDA at room temperature. With PIFA as the oxidant, the reaction took place smoothly in various solvents, and the corresponding spirooxindole (**2a**) was obtained in good to excellent yield (Scheme 2). In contrast, PIDA was found to be ineffective in the reaction.



Solvent	Yield (%)
MeCN	90
MeOH	84
CF_3CH_2OH	93
CH_2Cl_2	82
THF	84

Scheme 2

It is generally accepted that PIFA or PIDA-mediated oxidative dearomatization of 4- or 2-substituted phenols proceeds either though cationic phenoxenium intermediates, or through a concerted addition–elimination reaction after initial conversion of the phenoxy group at the iodine center.[1a] There is evidence to indicate that the former mechanism might be more favorable.[11] Consistent with this notion, these types of reaction usually gave better results in highly polar solvents, such as trifluoroethanol (TFE). In the case of **1a**, however, the formation of the cationic phenoxenium intermediate (**I**) might not be a favored process due to the electron-withdrawing effect of the carbonyl group (Scheme 3). Therefore, we assumed that the reac-

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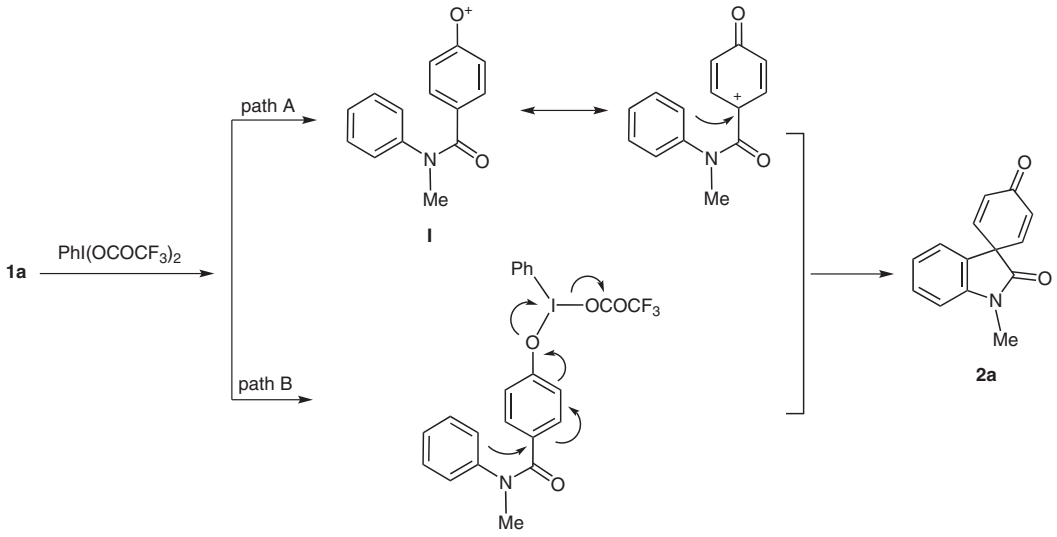


Scheme 3

tion of **1a** might follow the concerted addition–elimination pathway (Scheme 3, path B). This hypothesis was supported by the observed solvent effect as shown in Scheme 2. Although acetonitrile and trifluoroethanol were still the better solvents, good results were also obtained in less polar dichloromethane and tetrahydrofuran.

This protocol could be used to prepare a variety of substituted spirooxindoles, as shown in Table 1. The yields were generally satisfactory. When *N*-(3-chlorophenyl)-4-hydoxyphenyl-*N*-methylbenzamide (**1h**) was used as the substrate, two isomeric products **2h-1** and **2h-2** (Figure 1) were generated. The yield of **2h-1** was higher than that of **2h-1**, probably as a result of steric effects, which render the formation of **2h-2** less favorable. Their structures were confirmed by X-ray crystallographic analysis (Figure 2).[12]

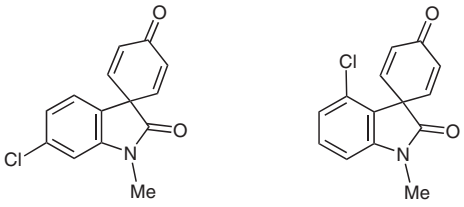


Figure 1

It is noteworthy that in this PIFA-promoted oxidative coupling, there is no need for prehalogenation of substrate **1**. Therefore, this method provides a more convenient approach to the synthesis of **2**. Spirooxindole **2j** is a synthetic intermediate that plays a pivotal role in the synthesis of the vasopressin inhibitor SR121463A.[13] By using this protocol, **2j** was obtained in 80% yield from **1j**. By comparison, the synthesis of spirodihydroquinolones (**4**) from the corresponding 2-(4-hydroxyphenyl)-*N*-methyl-*N*-acetamides (**3**) was less efficient (Scheme 4). However, the yields were still comparable to those obtained by using the free radical methods.[6,7]

Recently, there has been much interest in developing catalytic systems that require only catalytic amounts of hy-

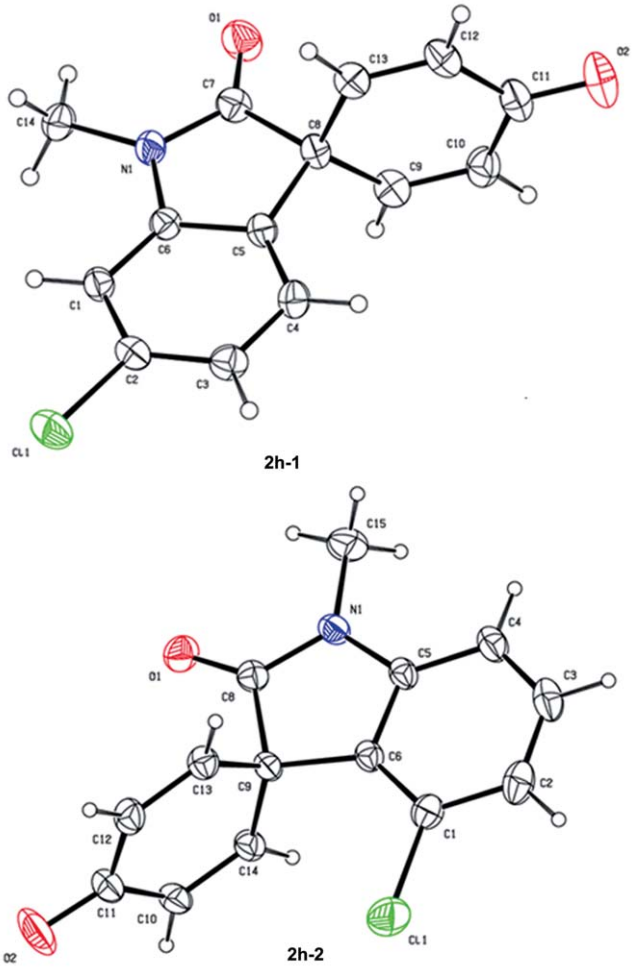
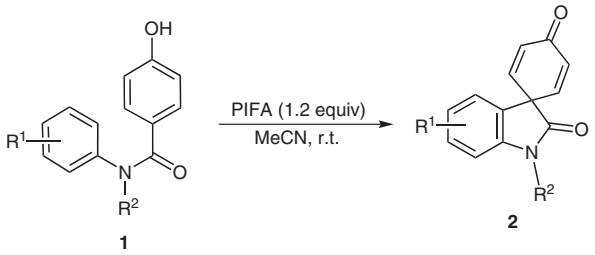


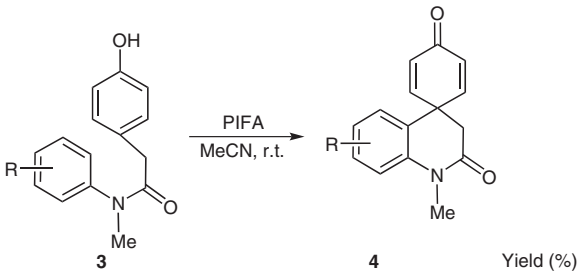
Figure 2

Table 1 PIFA-Mediated Intramolecular Oxidative Coupling of *N*-Phenylbenzamides (**1**)



Entry	Substrate **1**	R^1	R^2	Product(s)	Yield (%)[a]
1	**1a**	H	Me	**2a**	90
2	**1b**	4-EtO	Me	**2b**	82
3	**1c**	4-Me	Me	**2c**	83
4	**1d**	2-MeO	Me	**2d**	88
5	**1e**	2-Me	Me	**2e**	78
6	**1f**	4-Cl	Me	**2f**	90
7	**1g**	2-Cl	Me	**2g**	61
8	**1h**	3-Cl	Me	**2h-1** and **2h-2**	55 and 37
9	**1i**	H	Bn	**2i**	95
10	**1j**	4-EtO	Bn	**2j**	80
11	**1k**	4-Me	Bn	**2k**	84
12	**1l**	2-MeO	Bn	**2l**	75
13	**1m**	2-Cl	Bn	**2m**	79

[a] Isolated yield.

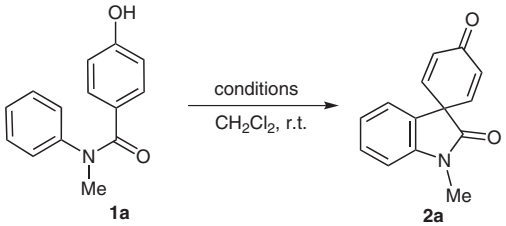


Scheme 4

pervalent iodine reagents to perform the oxidizing function.[14] The hypervalent iodine reagents could be recycled by using another terminal oxidant. This strategy is very attractive from both environmental and economical points of view. Studies by Kita and Ochiai show that *m*-chloroperoxybenzoic acid (MCPBA) and urea·H_2O_2 are suitable terminal oxidants to effect the oxidation of iodoarenes to hypervalent iodine(III) reagents in situ in the catalytic cycle. Various types of oxidation reactions, including oxidative C–O,[9] C–N,[15] and C–C[16] coupling, have been achieved by using hypervalent iodine(III)-based catalytic systems. Precedent work by Kita et al. demonstrated that the oxidizing systems using iodoarene as catalyst were applicable to the intramolecular C–C coupling of phenolic substrates incorporating various tethers, with the formation of five- to seven-membered spirodienones.[16] Therefore, we investigated whether catalytic systems could be applied to the synthesis of spirooxindoles.

To this end, two systems employing MCPBA and urea·H_2O_2, respectively, as the terminal oxidants, were examined for their effectiveness in promoting the transformation of **1a** into **2a**;[16] the results are outlined in Table 2. Because compounds **1** did not readily dissolve in trifluoroethanol, dichloromethane was chosen as the solvent. The results showed that when 0.1 equivalent of iodobenzene was used as the catalyst, and MCPBA was used as the terminal oxidant, the reaction took place smoothly in the presence of one equivalent of trifluoroacetic acid (TFA), and **2a** was obtained in satisfactory yield (Table 2, entries 1–3). It is noteworthy that only one equivalent of MCPBA was enough to guarantee clean conversion, although it took longer for the reaction to reach completion (Table 2, entry 3). By comparison, no reaction took place in the absence of iodobenzene (Table 2, entry 5). The urea·H_2O_2/iodobenzene/trifluoroacetic acid anhydride (TFAA) system also worked very well for the transformation. With two equivalents of urea·H_2O_2 as oxidant and four equivalents of TFAA as additive, **2a** was formed in excellent yield (Table 2, entry 7).

Table 2 Examination of the Iodobenzene-Based Catalytic Systems

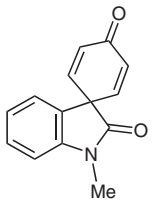
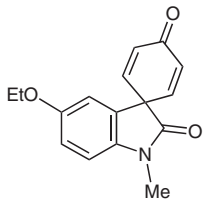
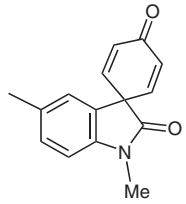
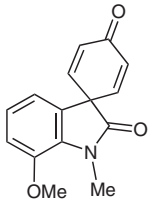
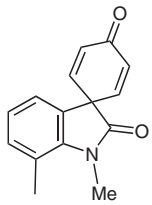
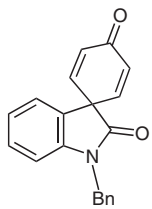
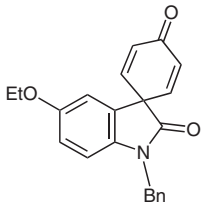
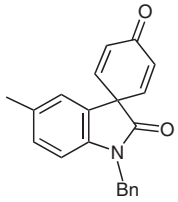
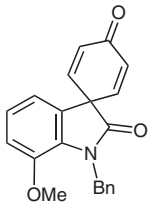
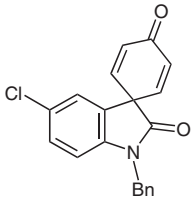
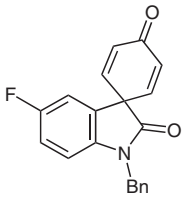
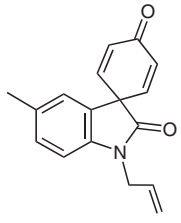


Entry	Oxidant (equiv)	PhI (equiv)	Additive (equiv)	Time (h)	Yield (%)[a]
1	MCPBA (4.0)	0.1	TFA (1.0)	4	86
2	MCPBA (2.0)	0.1	TFA (1.0)	7	83
3	MCPBA (1.1)	0.1	TFA (1.0)	23	83
4	MCPBA (2.0)	0.05	TFA (1.0)	12	52
5	MCPBA (2.0)	none	TFA (1.0)	24	N.R.[b]
6	urea·H_2O_2 (2.0)	0.1	TFAA (1.0)	8	trace[c]
7	urea·H_2O_2 (2.0)	0.1	TFAA (4.0)	15 min	96
8	urea·H_2O_2 (1.0)	0.1	TFAA (4.0)	15 min	41
9	MCPBA (2.0)	0.1[d]	TFA (1.0)	10	84
10	urea·H_2O_2 (2.0)	0.1[d]	TFAA (4.0)	20 min	89

[a] Isolated yield.
[b] No reaction took place.
[c] Most of the starting material was recovered.
[d] 4-Iodotoluene was used as catalyst.

However, the reaction barely took place when only one equivalent of TFAA was used (Table 2, entry 6), probably due to the complexation of TFAA with urea. In addition to iodobenzene, 4-iodotoluene was also found to be capable of catalyzing the reaction with high efficiency (Table 2, entries 9 and 10).

Table 3 Synthesis of Spirooxindoles **2** Using 10 mol% Iodobenzene as Catalyst

Entry	Product	Conditions[a]	Time (h)	Yield (%)[b]
1	 **2a**	A B	7 20 min	83 96
2	 **2b**	A	3	90
3	 **2c**	A	11	73
4	 **2d**	A	24	73
5	 **2e**	A	17	86
6	 **2i**	A	4	83
7	 **2j**	A	3	86
8	 **2k**	A	5	79
9	 **2l**	A B	18 30 min	52 57
10	 **2n**	A B	10 30 min	85[c] 74
11	 **2o**	A B	10 30 min	80[c] 74
12	 **2p**	A	7	71

[a] Conditions A: MCPBA (2.0 equiv) was used as terminal oxidant; TFA (1.0 equiv) was used unless otherwise specified. Conditions B: urea·H_2O_2 (2.0 equiv) and TFAA (4.0 equiv) were used.
[b] Isolated yield.
[c] TFA (4.0 equiv) was used.

The iodobenzene-mediated systems were then applied to the synthesis of variously substituted spirooxindoles (Table 3); the yields were generally satisfactory. In the case of substrates **2n** and **2o**, when MCPBA was used as the oxidant, four equivalents of trifluoroacetic acid was needed to complete the conversion (Table 3, entries 10 and 11; conditions A). Because only 0.1 equivalent of iodobenzene was used instead of a stoichiometric amount of PIFA, the toxicity and cost associated with the synthesis were greatly reduced, thus rendering the method more synthetically attractive.

In summary, the PIFA-mediated intramolecular oxidative coupling of substituted 4-hydroxyphenyl-*N*-phenylbenzamides constitutes an efficient method for the synthesis of spirooxindoles. The synthesis could be accomplished by using 0.1 equivalent of iodobenzene as catalyst and 2.0 equivalents of MCPBA or urea·H_2O_2 as the terminal oxidant. As 3,3-spirocyclohexadienone-attached oxindoles **2** could be easily accessed from simple precursors **1** using this protocol, it is hoped that they might serve as intermediates in the synthesis of a wide range of 3,3-disubstituted oxindoles and other useful compounds.

^{1}H and ^{13}C NMR spectra were recorded with a Bruker AM-400 MHz spectrometer with TMS as the internal standard in $CDCl_3$. The MS (EI) spectra were measured with an HP 5988A spectrometer by direct inlet at 70 eV. The high-resolution mass spectra (HRMS) were measured with a Bruker Daltonics APEX II 47e spectrometer by ESI. Melting points were measured with an XT-4 melting point apparatus and are uncorrected.

Synthesis of 2; General Procedure (Conditions A)

To a slurry of MCPBA (345 mg, 2.0 mmol) in CH_2Cl_2 (10 mL) was added TFA (75 μL, 1.0 mmol). After the MCPBA was completely dissolved, PhI (11 μL, 0.10 mmol) and **1** (1.0 mmol) were added quickly to the solution, and the mixture was stirred at r.t. until the reaction was complete as indicated by TLC. The mixture was diluted with CH_2Cl_2 (15 mL) and washed sequentially with sat. $Na_2S_2O_3$ (2 × 12 mL), sat. Na_2CO_3 (12 mL), and brine (12 mL), and then dried with anhydrous Na_2SO_4. After filtration, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography to give product **2**.

Synthesis of 2; General Procedure (Conditions B)

To CH_2Cl_2 (10 mL) was added urea·H_2O_2 (188 mg, 2.0 mmol), and TFAA (563 μL, 4.0 mmol). The mixture was stirred at r.t. until urea·H_2O_2 was completely dissolved, then PhI (11 μL, 0.10 mmol) and **1** (1.0 mmol) were added quickly to the solution, and the mixture was stirred at r.t. until the reaction was complete as indicated by TLC. The solvent was then evaporated under reduced pressure and the residue was purified by silica gel chromatography to give product **2**.

5′-Ethyloxy-1′-methyl-4*H*-spiro[cyclohexa-2,5-diene-1,3′-indol]-2′,4(1′*H*)-dione (2b)

White solid; mp 148–150 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.39 (t, *J* = 7.2 Hz, 3 H), 3.29 (s, 3 H), 3.97 (q, *J* = 7.2 Hz, 2 H), 6.54 (d, *J* = 9.6 Hz, 2 H), 6.61 (dd, *J* = 10.0, 2.0 Hz, 2 H), 6.62–6.64 (m, 1 H), 6.86–6.94 (m, 2 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.7, 27.3, 56.2, 64.2, 109.6, 112.1, 115.2, 127.0, 131.3, 136.9, 143.7, 156.0, 170.9, 185.3.

MS (EI): *m*/*z* (%) = 269 (100) $[M]^+$, 241 (78), 213 (57), 184 (58), 170 (16), 155 (19), 115 (26), 63 (27).

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{16}NO_3$: 270.1125; found: 270.1128.

3′-Methyloxy-1′-methyl-4*H*-spiro[cyclohexa-2,5-diene-1,3′-indol]-2′,4(1′*H*)-dione (2d)

White solid; mp 150–153 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.57 (s, 3 H), 3.91 (s, 3 H), 6.53 (dd, *J* = 8.0, 2.0 Hz, 2 H), 6.59 (dd, *J* = 8.0, 2.0 Hz, 2 H), 6.63 (d, *J* = 7.6 Hz, 1 H), 6.95 (d, *J* = 7.6 Hz, 1 H), 7.04 (t, *J* = 7.6 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 30.7, 56.0, 56.1, 113.5, 117.1, 124.2, 127.1, 131.2, 131.7, 143.8, 145.9, 171.4, 185.4.

MS (EI): *m*/*z* (%) = 255 (100) $[M]^+$, 240 (40), 227 (29), 212 (63), 197 (18), 184 (53).

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{14}NO_3$: 256.0968; found: 256.0973.

3′-Methyl-1′-methyl-4*H*-spiro[cyclohexa-2,5-diene-1,3′-indol]-2′,4(1′*H*)-dione (2e)

White solid; mp 174–178 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.64 (s, 3 H), 3.58 (s, 3 H), 6.52 (dd, *J* = 8.0, 2.0 Hz, 2 H), 6.58 (dd, *J* = 8.0, 2.0 Hz, 2 H), 6.84 (d, *J* = 7.2 Hz, 1 H), 6.97 (t, *J* = 7.6 Hz, 1 H), 7.12 (d, *J* = 7.6 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 19.0, 30.6, 55.4, 120.9, 122.7, 123.5, 126.3, 131.2, 133.6, 141.6, 143.8, 172.1, 185.3.

MS (EI): *m*/*z* (%) = 239 (100) $[M]^+$, 224 (15), 211 (28), 196 (47).

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{14}NO_2$: 240.1019; found: 240.1012.

5′-Chloro-1′-methyl-4*H*-spiro[cyclohexa-2,5-diene-1,3′-indol]-2′,4(1′*H*)-dione (2f)

White solid; mp 231–232 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.30 (s, 3 H), 6.56 (s, 4 H), 6.90 (d, *J* = 8.4 Hz, 1 H), 7.03 (d, *J* = 2.0 Hz, 1 H), 7.38 (dd, *J* = 8.4, 2.0 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 27.4, 55.6, 110.0, 125.2, 127.7, 129.1, 129.9, 131.8, 142.3, 142.5, 170.9, 184.8.

MS (EI): *m*/*z* (%) = 259 (71) $[M]^+$, 231 (100), 215 (31), 202 (34), 168 (36).

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{11}ClNO_2$: 260.0473; found: 260.0467.

3′-Chloro-1′-methyl-4*H*-spiro[cyclohexa-2,5-diene-1,3′-indol]-2′,4(1′*H*)-dione (2g)

White solid; mp 143–145 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.67 (s, 3 H), 6.54 (d, *J* = 10.4 Hz, 2 H), 6.57 (d, *J* = 10.4 Hz, 2 H), 6.91 (dd, *J* = 7.6, 0.8 Hz, 1 H), 7.02 (t, *J* = 8.0 Hz, 1 H), 7.33 (dd, *J* = 8.0, 0.8 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 30.7, 55.3, 116.3, 123.3, 124.2, 131.5, 132.2, 139.7, 142.8, 171.5, 184.9.

MS (EI): *m*/*z* (%) = 259 (100) $[M]^+$, 231 (58), 216 (40), 188 (22).

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{11}ClNO_2$: 260.0473; found: 260.0472.

4′-Chloro-1′-methyl-4*H*-spiro[cyclohexa-2,5-diene-1,3′-indol]-2′,4(1′*H*)-dione (2h-1)

White solid; mp 178–180 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.30 (s, 3 H), 6.55 (s, 4 H), 6.95–6.97 (m, 2 H), 7.08–7.10 (m, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 27.4, 55.3, 109.9, 123.5, 124.3, 125.6, 131.7, 136.0, 142.7, 144.9, 171.3, 184.9.

MS (EI): *m*/*z* (%) = 259 (90) $[M]^+$, 231 (100), 216 (45), 202 (22), 196 (24), 188 (24), 168 (32), 139 (42), 126 (26).

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{11}ClNO_2$: 260.0473; found: 260.0469.

6′-Chloro-1′-methyl-4*H*-spiro[cyclohexa-2,5-diene-1,3′-indol]-2′,4(1′*H*)-dione (2h-2)
White solid; mp 205–207 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.31 (s, 3 H), 6.55 (d, *J* = 8.4 Hz, 2 H), 6.64 (d, *J* = 8.4 Hz, 2 H), 6.88 (d, *J* = 7.6 Hz, 1 H), 7.07 (d, *J* = 8.0 Hz, 1 H), 7.37 (t, *J* = 8.0 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 27.7, 56.0, 107.4, 123.5, 124.5, 131.1, 132.1, 133.0, 141.5, 145.2, 170.2, 185.2.

MS (EI): *m*/*z* (%) = 259 (62) $[M]^+$, 231 (78), 224 (38), 196 (19), 168 (29), 141 (50), 121 (100).

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{11}ClNO_2$: 260.0473; found: 260.0477.

1′-Benzyl-4*H*-spiro[cyclohexa-2,5-diene-1,3′-indol]-2′,4(1′*H*)-dione (2i)
Light-yellow solid; mp 119–121 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.98 (s, 2 H), 6.59 (d, *J* = 10.0 Hz, 2 H), 6.67 (d, *J* = 10.4 Hz, 2 H), 6.88 (d, *J* = 8.0 Hz, 1 H), 7.03–7.10 (m, 2 H), 7.26–7.34 (m, 6 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 44.8, 56.0, 110.2, 123.7, 124.8, 125.8, 127.3, 128.0, 129.9, 131.4, 135.0, 142.9, 143.8, 171.4, 185.5.

MS (EI): *m*/*z* (%) = 301 (100) $[M]^+$, 210 (40), 154 (16), 139 (10), 128 (22).

HRMS (ESI): *m*/*z* calcd for $C_{20}H_{16}NO_2$: 302.1176; found: 302.1184.

5′-Ethyloxy-1′-Benzyl-4*H*-spiro[cyclohexa-2,5-diene-1,3′-indol]-2′,4(1′*H*)-dione (2j)
White solid; mp 126–128 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.35 (t, *J* = 7.2 Hz, 3 H), 3.92 (q, *J* = 7.2 Hz, 2 H), 4.94 (s, 2 H), 6.55–6.58 (dd, *J* = 12.4, 2.0 Hz, 2 H,), 6.62–6.66 (m, 3 H), 6.73–6.80 (m, 2 H), 7.28–7.37 (m, 5 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.7, 44.8, 56.3, 64.2, 110.7, 112.1, 115.3, 127.2, 127.3, 128.0, 129.0, 131.5, 135.2, 136.0, 143.5, 156.0, 171.1, 185.2.

MS (EI): *m*/*z* (%) = 345 (4) $[M]^+$, 91 (100).

HRMS (ESI): *m*/*z* calcd for $C_{22}H_{20}NO_3$: 346.1438; found: 346.1440.

5′-Methyl-1′-benzyl-4*H*-spiro[cyclohexa-2,5-diene-1,3′-indol]-2′,4(1′*H*)-dione (2k)
White solid; mp 128–130 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.28 (s, 3 H), 4.96 (s, 2 H), 6.58 (d, *J* = 10.4 Hz, 2 H), 6.66 (d, *J* = 10.0 Hz, 2 H), 6.76 (d, *J* = 8.0 Hz, 1 H), 6.86 (s, 1 H), 7.08 (dd, *J* = 8.0, 0.8 Hz, 1 H), 7.27–7.36 (m, 5 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 21.0, 44.8, 56.2, 110.1, 125.6, 125.9, 127.4, 128.1, 129.0, 130.3, 131.4, 133.7, 135.2, 140.5, 144.1, 171.5, 185.7.

MS (EI): *m*/*z* (%) = 315 (5) $[M]^+$, 91 (100).

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{18}NO_2$: 316.1332; found: 316.1337.

3′-Methyloxy-1′-benzyl-4*H*-spiro[cyclohexa-2,5-diene-1,3′-indol]-2′,4(1′*H*)-dione (2l)
White solid; mp 172–174 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.78 (s, 3 H), 5.23 (s, 2 H), 6.54 (d, *J* = 10.0 Hz, 2 H), 6.61 (d, *J* = 10.0 Hz, 2 H), 6.64 (d, *J* = 8.0 Hz, 1 H), 7.03 (t, *J* = 8.4 Hz, 1 H), 7.35 (d, *J* = 8.0 Hz, 1 H), 7.23–7.32 (m, 5 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 46.6, 55.9, 56.0, 113.7, 117.2, 124.3, 127.3, 127.4, 128.5, 131.1, 131.3, 137.7, 143.6, 145.6, 171.6, 185.2.

MS (EI): *m*/*z* (%) = 331 (7) $[M]^+$, 91 (100).

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{18}NO_3$: 332.1281; found: 332.1276.

3′-Chloro-1′-benzyl-4*H*-spiro[cyclohexa-2,5-diene-1,3′-indol]-2′,4(1′*H*)-dione (2m)
White solid; mp 188–190 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.41 (s, 2 H), 6.58–6.65 (m, 4 H), 6.94 (dd, *J* = 7.2, 1.2 Hz, 1 H), 7.02 (m, 1 H), 7.25–7.36 (m, 6 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 45.9, 55.4, 116.4, 123.5, 124.5, 126.6, 127.6, 128.5, 128.8, 131.6, 132.6, 136.7, 139.1, 143.0, 172.0, 185.1.

MS (EI): *m*/*z* (%) = 335 (2) $[M]^+$, 91 (100).

HRMS (ESI): *m*/*z* calcd for $C_{20}H_{15}ClNO_2$: 336.0786; found: 336.0782.

5′-Chloro-1′-benzyl-4*H*-spiro[cyclohexa-2,5-diene-1,3′-indol]-2′,4(1′*H*)-dione (2n)
Light-yellow solid; mp 137–139 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.96 (s, 2 H), 6.57–6.76 (m, 4 H), 6.77 (d, *J* = 8.4 Hz, 1 H), 7.03 (d, *J* = 2.0 Hz, 1 H), 7.24–7.38 (m, 6 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 44.9, 55.7, 111.1, 125.3, 127.3, 127.8, 128.2, 129.1, 129.2, 129.8, 131.9, 134.6, 141.4, 142.5, 171.1, 184.8.

MS (EI): *m*/*z* (%) = 335 (5) $[M]^+$, 91 (100).

HRMS (ESI): *m*/*z* calcd for $C_{20}H_{15}ClNO_2$: 336.0786; found: 336.0783.

5′-Fluoro-1′-benzyl-4*H*-spiro[cyclohexa-2,5-diene-1,3′-indol]-2′,4(1′*H*)-dione (2o)
Light-yellow solid; mp 150–152 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.96 (s, 2 H), 6.59 (d, *J* = 10.4 Hz, 2 H), 6.63 (d, *J* = 10.4 Hz, 2 H), 6.77–6.82 (m, 2 H), 6.98 (m, 1 H), 7.29–7.38 (m, 5 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 44.9, 55.9, 110.8, 110.9, 112.7, 113.0, 116.2, 116.4, 127.3, 127.7, 128.2, 129.1, 129, 131.8, 134.8, 138.8, 138.8, 142.7, 158.3, 160.8, 171.2, 184.8.

MS (EI): *m*/*z* (%) = 319 (5) $[M]^+$, 91 (100).

HRMS (ESI): *m*/*z* calcd for $C_{20}H_{15}FNO_2$: 320.1081; found: 320.1085.

5′-Methyl-1′-allyl-4*H*-spiro[cyclohexa-2,5-diene-1,3′-indol]-2′,4(1′*H*)-dione (2p)
White solid; mp 104–105 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.31 (s, 3 H), 4.39 (d, *J* = 7.2 Hz, 2 H), 5.25–5.29 (m, 2 H), 5.82–5.90 (m, 1 H), 6.55 (d, *J* = 10.0 Hz, 2 H), 6.62 (d, *J* = 10.0 Hz, 2 H), 6.84–6.86 (m, 2 H), 7.16 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 20.9, 43.3, 56.0, 109.8, 118.2, 125.5, 125.9, 130.1, 130.7, 131.3, 133.5, 140.5, 143.8, 171.0, 185.4.

MS (EI): *m*/*z* (%) = 265 (27) $[M]^+$, 250 (28), 224 (71), 168 (37), 41 (100).

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{16}NO_2$: 266.1175; found: 266.1181.

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