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Diastereoselective Synthesis of Six-Membered Carbocyclic Spirooxindoles *via* 6π-Electrocyclization of 3-Dienylidene-2-oxindoles

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Abstract: The Wittig reaction of isatin derivatives with Morita–Baylis–Hillman bromides of cinnamaldehydes afforded 3-dienylidene-2-oxindoles. These trienes were converted into the corresponding spirooxindoles in a stereoselective manner in refluxing toluene in good yields. The diastereomeric spirooxindoles could be obtained stereoselectively by adding a catalytic amount of palladium(II) acetate *via* the palladium-catalyzed isomerization of *EEE*-trienes to *ZEE*-trienes followed by a more facile 6π-electrocyclization process. The obtained spirooxindoles could be further functionalized by palladium-catalyzed oxidative arylation, thionation with Lawesson's reagent, catalytic hydrogenation and Friedel–Crafts-type reaction.

Keywords: dienylidene-2-oxindoles; 6π-electrocyclization; palladium; spirooxindoles

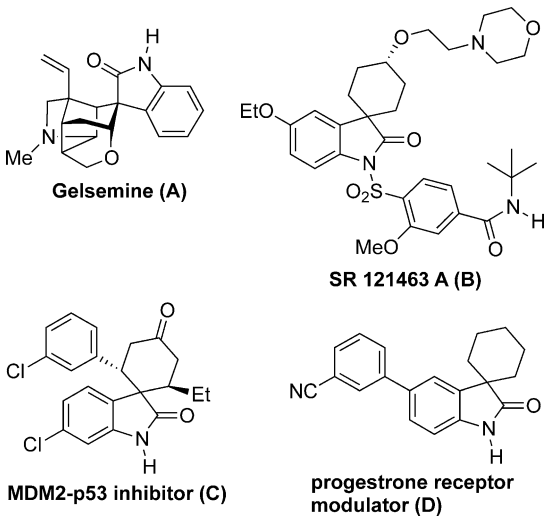

Figure 1. Natural products and biologically active six-membered spirocyclic oxindoles.

Introduction

Spirooxindole derivatives have attracted tremendous interest of researchers in the area of synthetic organic chemistry and medicinal chemistry because they occur in many natural products and pharmaceutically important molecules.[1–4] Spirooxindoles with six-membered carbocyclic backbones are relevant synthetic targets found in both natural products and bioactive compounds, such as the hexacyclic alkaloid Gelsemine (**A**),[2a,b] selective vasopressin V_2 receptor antagonist SR 121463A (**B**),[2c,d] MDM2-p53 inhibitor **C**,[2e,f] and progesterone receptor modulator **D**[2g,h] (Figure 1). Thus, considerable efforts have been devoted to developing efficient protocols to access these interesting motifs over the past years.[1–4] Although considerable progress has been made for the synthesis of diversely functionalized six-membered carbocyclic spirooxindoles, a new protocol to efficiently synthesize this core structure remains valuable.

Very recently, we reported the palladium-catalyzed construction of spirooxindoles by arylative cyclization of 3-(γ,δ-disubstituted)allylidene-2-oxindoles.[5] A sequential palladium-catalyzed oxidative arylation, allylic palladium migration, and an aryl C–H bond functionalization/arylation cascade reaction provided an interesting spirodihydronaphthalene-2-oxindole [Scheme 1, Eq. (1)]. During the studies we envisaged that 3-dienylidene-2-oxindoles could be used as an efficient precursor for the synthesis of spirooxindoles bearing a cyclohexadiene ring [Scheme 1, Eq. (2)]. Both double bonds (C_α=C_β and C_ε=C_ζ) are positioned in a *cis*-relationships around the central double bond

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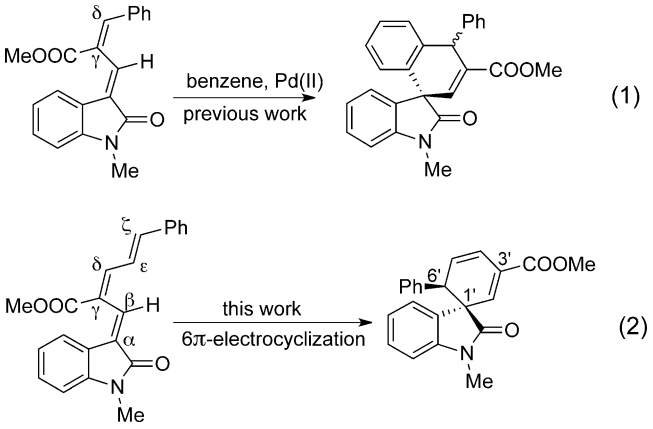
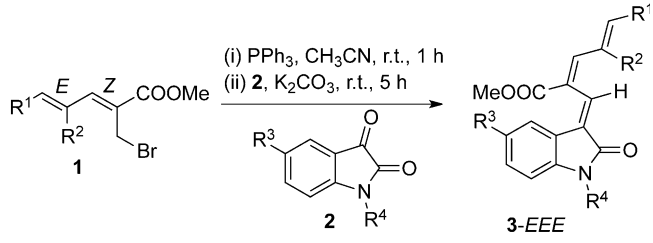


Scheme 1. Synthesis of spirooxindoles.

(C_γ=C_δ), thus a thermal 6π-electrocyclization proceeds readily to produce the spirooxindole.

Results and Discussion

The synthesis of starting material was carried out by the Wittig reaction between isatin and the phosphorus ylide generated from the corresponding Morita–Baylis–Hillman (MBH) bromide of cinnamaldehydes,[5–8] as shown in Scheme 2. The triene **3a**-*EEE* was isolated in good yield (79%) as a major product.[6] The formation of the corresponding stereoisomer **3a**-*ZEE* was also observed at the right position on TLC; however, we failed to isolate the compound due to the presence of some impurity near the spot.[9] Some representative trienes **3b–g** were prepared similarly in moderate to good yields (55–79%) by the combination of MBH bromides **1a–c** and isatins **2a–e**.



1a: R^1 = Ph, R^2 = H
1b: R^1 = *p*-FC_6H_4, R^2 = H
1c: R^1 = Ph, R^2 = Me

2a: R^3 = H, R^4 = Me
2b: R^3 = Cl, R^4 = Me
2c: R^3 = MeO, R^4 = Me
2d: R^3 = NO_2, R^4 = Me
2e: R^3 = H, R^4 = H

3a: 79% (**1a** + **2a**)
3b: 79% (**1b** + **2a**)
3c: 55% (**1c** + **2a**)[a]
3d: 68% (**1a** + **2b**)
3e: 78% (**1a** + **2c**)
3f: 71% (**1a** + **2d**)
3g: 75% (**1a** + **2e**)

[a] Compound **5c** (26%) was isolated as well (see the Supporting Information).

Scheme 2. Preparation of starting materials.

The 6π-electrocyclization of **3a**-*EEE* was examined in refluxing toluene,[10] as shown in Scheme 3. As expected, spirooxindole derivative **4a** was obtained in good yield (73%) for 20 h *via* a disrotatory ring-closure of the triene **3a**-*EEE*. However, a long reaction time was required presumably due to the steric hindrance between the two aryl moieties in the transition state. The starting material **3a**-*ZEE* was required in order to obtain the other stereoisomer **5a**; however, **3a**-*ZEE* could not be isolated as mentioned above. In our previous paper, we observed a palladium-catalyzed isomerization of the C_α=C_β double bond of 3-(γ,δ-disubstituted)allylidene-2-oxindoles.[5] Thus, we assumed that the C_α=C_β double bond of **3a**-*EEE* could also be isomerized in the presence of a catalytic amount (5 mol%) of $Pd(OAc)_2$ at elevated temperature to furnish **3a**-*ZEE*. Thus we examined the reaction of **3a**-*EEE* in refluxing toluene in the presence of a catalytic amount (5 mol%) of $Pd(OAc)_2$. To our delight, compound **5a** was isolated as a major product (73%) along with a low yield of **4a** (19%). Compound **5a** could be formed most likely by a thermal 6π-electrocyclization of **3a**-*ZEE* which is formed *in-situ* by a palladium-catalyzed isomerization process *via* the intermediate **I**.[5,11] During the whole reaction progress the formation of **3a**-*ZEE* was not observed on TLC, although **5a** was a major product. The results indicated that the 6π-electrocyclization of **3a**-*ZEE* would be markedly more rapid than that of **3a**-*EEE*. In order to check the possibility for the formation of **5a** from **4a** by a palladium-catalyzed epimerization the reaction of **4a** and $Pd(OAc)_2$ was examined in refluxing toluene, but no reaction was observed. The structure of **5a** was confirmed unequivocally by its X-ray crystal structure.[12]

Encouraged by the results, we examined the synthesis of both spirooxindoles with other starting materials under the following two conditions: *Conditions A* (toluene, reflux) and *Conditions B* [toluene, 5 mol% $Pd(OAc)_2$, reflux]. The results are summarized in Table 1. As shown in Table 1, variations of the triene part (entries 2 and 3) and oxindole part (entries 4–6) did not affect the reaction. The products **4b–g** were obtained in good yields (78–82%) under the *Conditions A*, and the opposite stereoisomers **5b–f** were produced as major products (76–85%) under the *Conditions B* along with a low yield of **4b–f** (4–13%). However, the reaction of NH derivative **3g** (entry 7) produced **5g** in low yield under *Conditions B* along with **4g** as a major product.[13] The result showed that double bond isomerization of **3g** by $Pd(OAc)_2$ was sluggish presumably due to partial coordination of palladium to the amide moiety.

As next entries we examined the reactions of **3h–j**, as shown in Scheme 4. The triene **3h** was prepared from MBH bromide **1d** and *N*-methylisatin (**2a**) in moderate yield (70%); however, the reaction of **3h**

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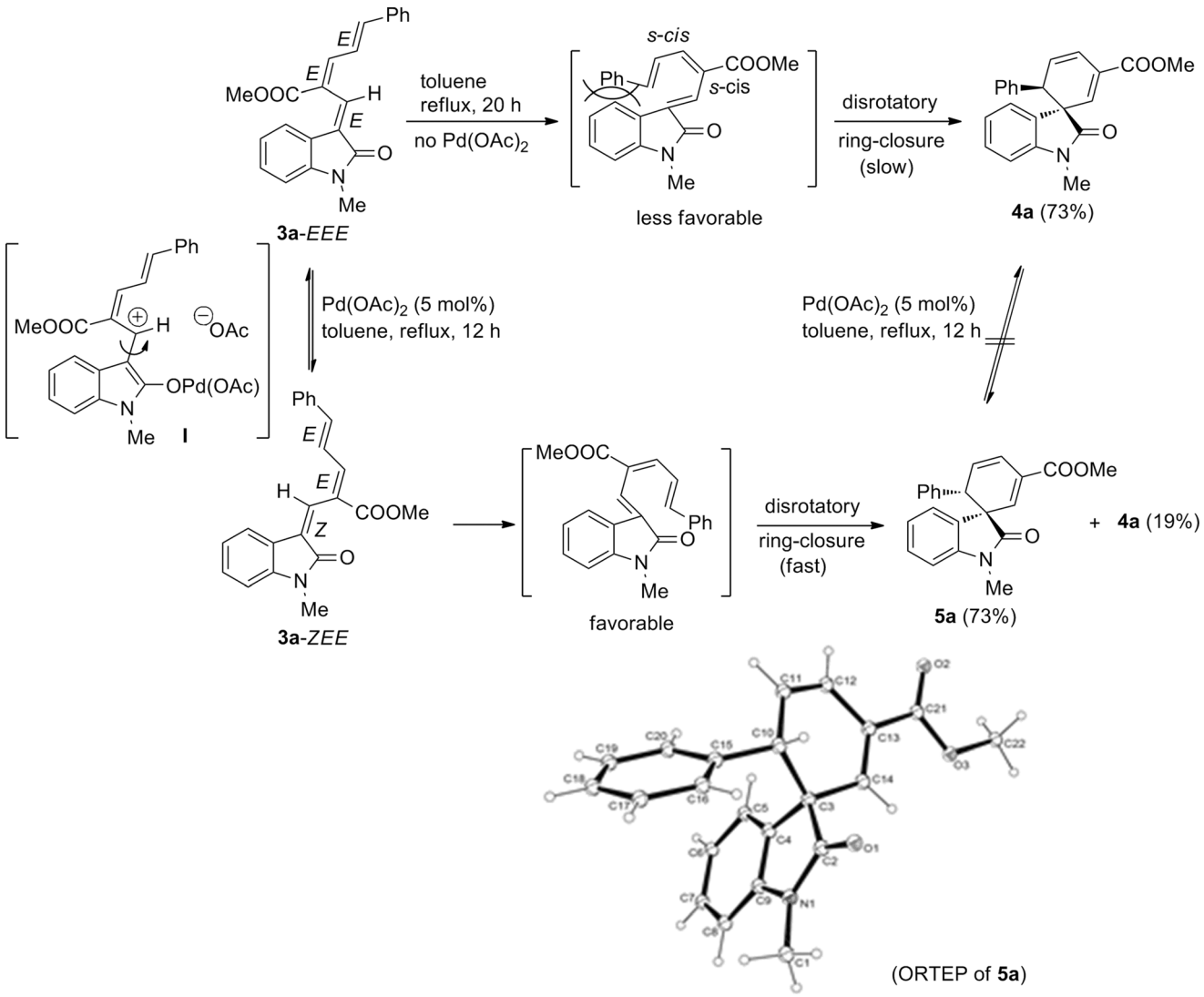

Scheme 3. Controlled synthesis of both isomers **4a** and **5a** from **3a**-*EEE*.

was completely ineffective in the reactions (*Conditions A and B*) presumably due to steric effects in the 6π-electrocyclization. The furan derivative **3i** was prepared by the reaction of *N*-methylisatin and the corresponding Boc derivative **1e** in moderate yield (69%, see the Supporting Information). The preparation of the corresponding MBH bromide of **1e** was unsuccessful presumably due to decomposition of the furan ring under acidic condition. The reaction of **3i** under the *Conditions A* afforded 6′-furyl derivative **4i** in good yield (70%), while **5i** was isolated in good yield (82%) under the *Conditions B* along with a trace amount of **4i** (4%). The methyl-substituted triene **3j** was also prepared by the reaction of Boc derivative **1f** and **2a** in good yield (71%). Similarly, the reaction of **3j** produced **4j** and **5j** in good yields under *Conditions A* and *Conditions B*, respectively.

In order to further modify the spirooxindoles, we examined the palladium-catalyzed oxidative arylation reaction[14,15] of spirooxindole **5a**, as shown in Scheme 5. *syn*-Carbopalladation of **5a** with phenylpalladium species afforded the intermediate **II**, and a subsequent *syn* β-H elimination produced **6a** in good yield (81%). The stereo- and regioselective formation of **II** might be ascribed to the stabilization of palladium center by chelation with the carbonyl group of oxindole moiety.[5,14f] In addition, the product **6a** could be obtained from **3a**-*EEE* directly in good yield (75%) *via* the sequential palladium-catalyzed isomerization of **3a**-*EEE* to **3a**-*ZEE* (*vide supra*), 6π-electrocyclization to form **5a**, and the final palladium-catalyzed oxidative phenylation to **6a**. The structure of **6a** was confirmed unequivocally by its X-ray crystal structure.[16] It is interesting to note that the formation of stereoisomer **7a** was not observed in a reasonable yield. We expected the formation of **7a**, albeit as a minor product, because the palladium-catalyzed 6π-electrocyclization of **3a**-*EEE* produced a mixture of

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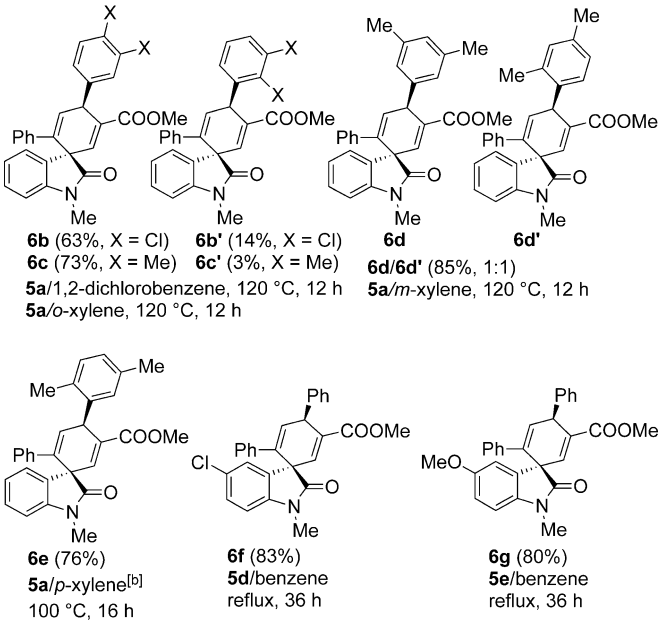
Table 1. Synthesis of spirooxindoles.

Entry	Triene	Conditions A[a]	Conditions B[b]
1	**3a**-*EEE*	**4a** (73%)	+ **4a** (19%), **5a** (73%)
2	**3b**-*EEE*	**4b** (82%)[c]	+ **4b** (9%), **5b** (80%)[c]
3	**3c**-*EEE*	**4c** (78%)	+ **4c** (4%), **5c** (76%)
4	**3d**-*EEE*	**4d** (80%)	+ **4d** (13%), **5d** (76%)
5	**3e**-*EEE*	**4e** (81%)	+ **4e** (5%), **5e** (85%)
6	**3f**-*EEE*	**4f** (82%)	+ **4f** (5%), **5f** (80%)
7	**3g**-*EEE*	**4g** (80%)	+ **4g** (50%), **5g** (26%)

[a] *Conditions A*: triene **3** (0.2 mmol), toluene, reflux, 20 h.
[b] *Conditions B*: triene **3** (0.2 mmol), $Pd(OAc)_2$ (5 mol%), toluene, reflux, 12 h.
[c] Ar is 4-fluorophenyl.

Table 2. Pd-catalyzed arylation of spirooxindoles.[a]



[a] *Conditions*: substrate **5**, arene (50 equiv.), $Pd(OAc)_2$ (5 mol%), PivOH (6.0 equiv.), AgOAc (4.0 equiv.).
[b] *p*-Xylene (100 equiv.) was used.

5a and **4a** (Scheme 3). The result stated that palladium-catalyzed phenylation of **4a** does not proceed efficiently. Actually, the palladium-catalyzed phenylation of **4a** was very sluggish, and compound **7a** was isolated in low yield (18%) even after a long time (36 h) along with phenanthridinone **8** (10%)[17,18] and recovered **4a** (22%). The formation of many intractable side products was also observed. The carbopalladation of **4a** to form an intermediate **III** is sterically hindered by the arene moiety of the oxindole ring. Thus, the formation of **7a** was difficult. In order to increase the yield of unexpected compound **8**, the reaction of **4a** was examined in the absence of benzene. Thus, the reaction of **4a** was carried out in pivalic acid as solvent. The yield of **8** was improved slightly (18%), and the pivalate derivative **9** was formed as a major product (39%). The yield of **8** could be increased to 37% by performing the reaction in mesitylene along with recovered **4a** (25%) even after 60 h. The highest yield of **8** was obtained in 1,2-dichlorobenzene at 120 °C; however, the yield was moderate (51%) due to the formation of some side products including **9**. The formation of **8** might involve a sequential allylic palladation *via* a π-allylpalladium intermediate to form **IV**, ring-opening β-carbon elimination to produce **V**,[19] and the formation of a seven-membered palladacycle intermediate **VI**.[20] A similar conversion of spirooxindole to phenanthridinone has been reported.[18]

Based on the successful synthesis of **6a** by the reaction of **5a** and benzene, the palladium-catalyzed arylations of **5a**, **5d** and **5e** with other arenes were examined as shown in Table 2. The reaction of **5a** and 1,2-dichlorobenzene afforded **6b** in good yield (63%) along with its regioisomer **6b′** (14%). The reaction of **5a** with *o*-xylene gave **6c** in good yield (73%) along with its regioisomer **6c′** in low yield (3%). The reaction of **5a** with *m*-xylene afforded an inseparable regioisomeric mixture (1:1) of **6d**/**6d′** in good yield (85%), while the reaction with *p*-xylene gave **6e** in moderate yield (76%). Both compounds **6d** and **6d′** could be synthesized from **5a** with 1-iodo-3,5-dimethylbenzene and 1-iodo-2,4-dimethylbenzene, respectively, under the influence of $Pd(OAc)_2$/AgOAc in acetic acid (see the Supporting Information). The yield of **6e** was low when the reaction with *p*-xylene was carried out at 120 °C due to the formation of in-

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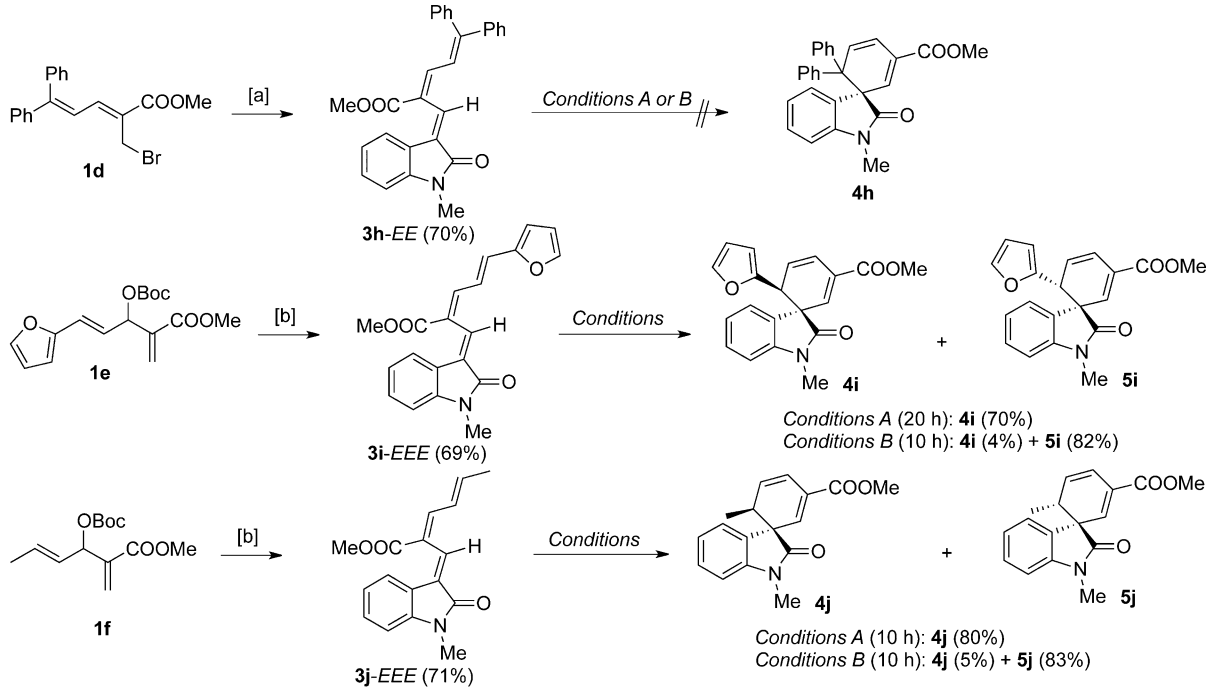
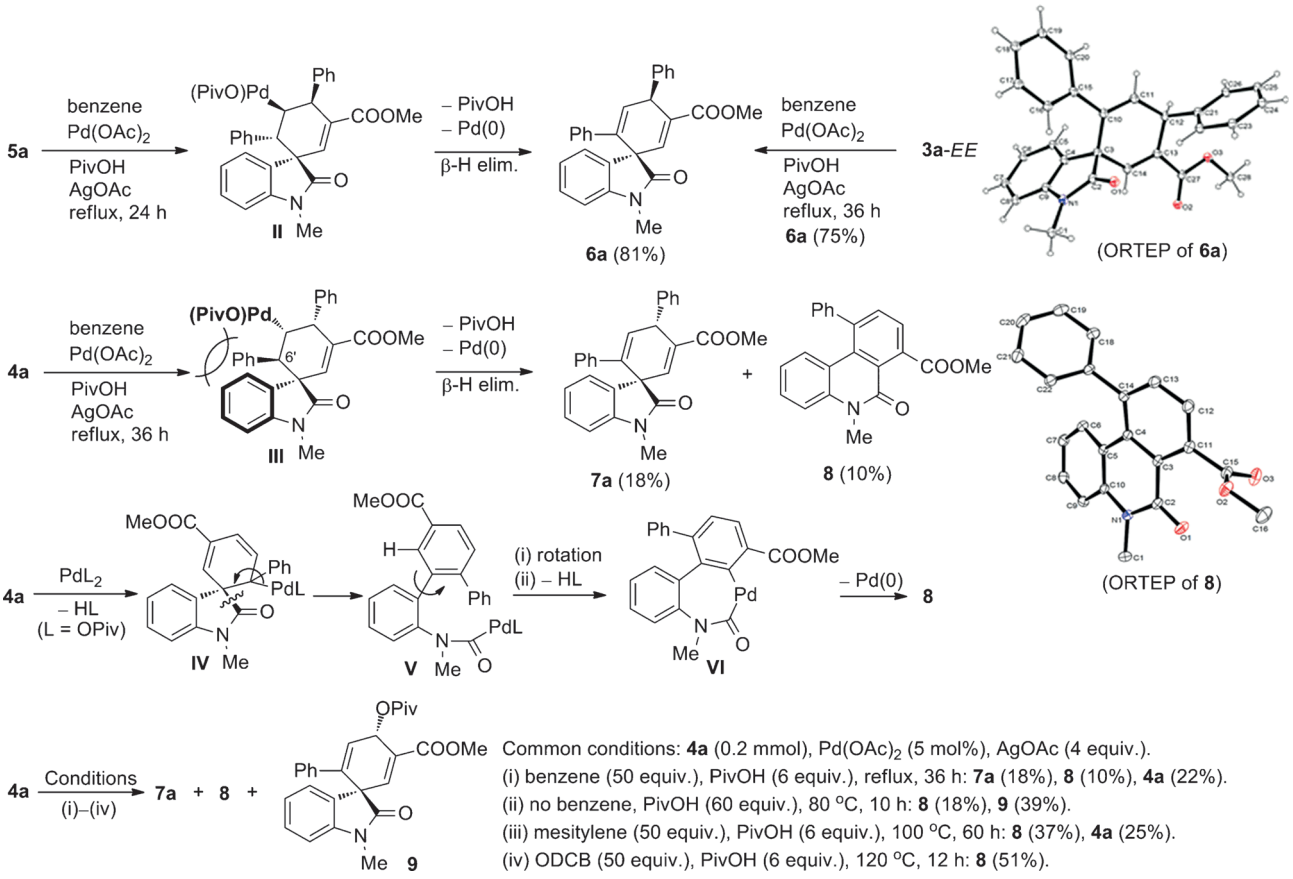


Conditions [a]: (i) PPh_3, CH_3CN, room temperature, 1 h, (ii) **2a**, K_2CO_3, room temperature, 5 h.
Conditions [b]: **2a**, PPh_3, toluene, room temperature, 3–12 h.

Scheme 4. Synthesis of related spirooxindoles.



Scheme 5. Pd-catalyzed oxidative phenylation of **5a** and **4a**.

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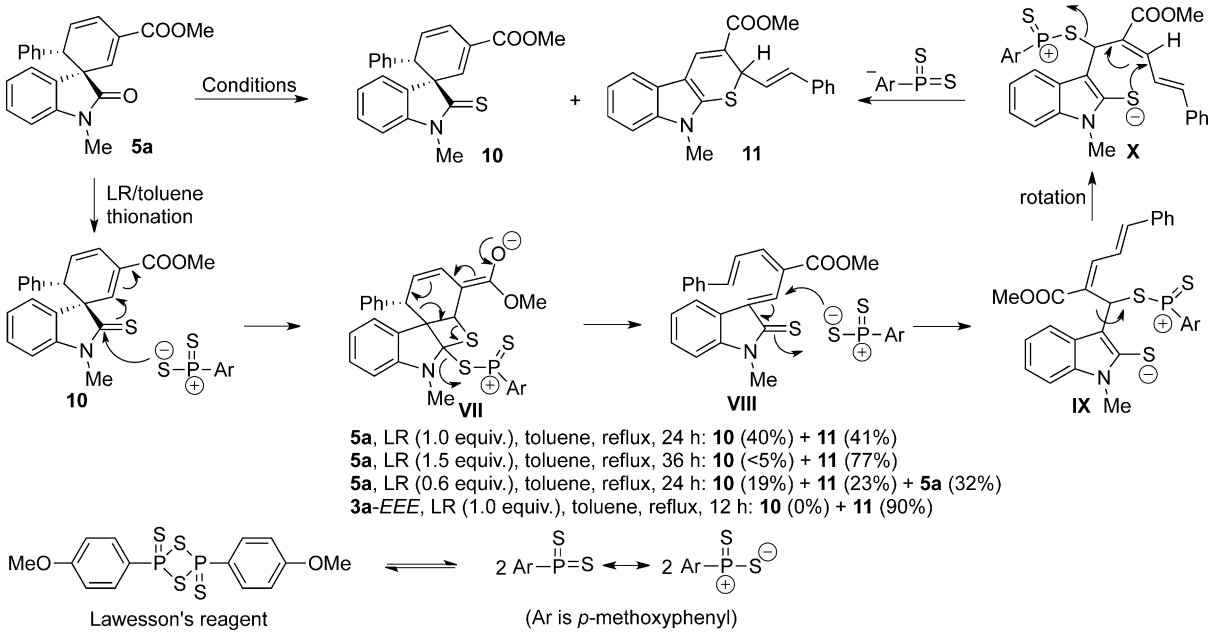
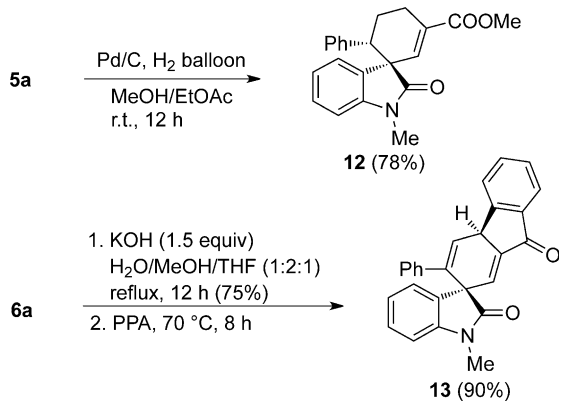


Scheme 6. The reactions of **5a** and **3a** with Lawesson's reagent.

tractable side products, thus the reaction was performed at 100 °C. In addition, the reactions of **5d** and **5e** with benzene afforded **6f** and **6g** in good yields (83 and 80%), respectively.

In order to synthesize spirothiooxindole derivative **10**, the reaction of **5a** and Lawesson's reagent (LR)[21] was examined, as shown in Scheme 6. The reaction of **5a** and 1.0 equiv. of LR afforded **10** in moderate yield (40%) along with 2-styryl-1-thia-9-azafluorene derivative **11** (41%).[6,22] The compound **11** could be produced from **10** *via* a sequential addition of $ArPS_2$ to form **VII**, ring-opening of **VII** to form **VIII**, conjugate addition of $ArPS_2$ to **VIII** to form **IX**, and the final intramolecular addition-elimination process to **11**. The yield of **11** increased to 77% on increasing the amount of LR. However, the yield of **10** could not be improved even in the presence of a limited amount of LR (0.6 equiv.). The reaction of **3a**-*EEE* and LR (1.0 equiv.) also afforded **11** in good yield (90%), and the result showed that the mechanism involving the ring-opened triene intermediate **VIII** would be reasonable.



Scheme 7. Transformations of spirooxindoles **5a** and **6a**.

As shown in Scheme 7, cyclohexene derivative **12** was prepared from **5a** by catalytic hydrogenation in moderate yield (78%). In addition, spirooxindole dihydrofluorenone derivative **13** was prepared from **6a** by a sequential hydrolysis of the ester group of **6a** and a following Friedel–Crafts reaction in polyphosphoric acid (PPA).

Conclusions

In summary, an efficient synthetic method for spirooxindoles has been developed involving a Wittig reaction between isatin and the ylide derived from MBH bromide and the following 6π-electrocyclization process. Controlled synthesis of both stereoisomers could be achieved by the presence of a palladium catalyst from the same starting material 3-dienylidene-2-oxindoles.

Experimental Section

General information and the details for the preparation of starting materials **3a–j** and products **6–13** can be found in the Supporting Information.

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Typical Procedure for the Synthesis of 4a (Conditions A)

A solution of **3a**-*EEE* (69 mg, 0.2 mmol) in toluene (1 mL) was heated to reflux for 20 h under an N_2 balloon atmosphere. After removal of toluene and column chromatographic purification process (hexanes/Et_2O, 3:1) the spirooxindole **4a** was obtained as a white solid; yield: 50 mg (73%).

Methyl 1′-methyl-2′-oxo-6-phenylspiro[cyclohexa[2,4]diene-1,3′-indoline]-3-carboxylate (4a): yield: 73%; white solid; mp 122–123 °C; IR (KBr): $\nu = 1715$, 1612, 1493, 1256 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 2.72$ (s, 3H), 3.79 (s, 3H), 4.26–4.29 (m, 1H), 6.06 (ddd, $J = 10.2$, 3.0 and 0.9 Hz, 1H), 6.53 (d, $J = 7.5$ Hz, 1H), 6.54 (d, $J = 0.9$ Hz, 1H), 6.71 (ddd, $J = 10.2$, 3.3 and 1.5 Hz, 1H), 6.85 (dd, $J = 8.1$ and 1.2 Hz, 2H), 7.03–7.16 (m, 4H), 7.25 (t, $J = 7.5$ Hz, 1H), 7.47 (d, $J = 7.5$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 25.71$, 49.78, 51.98, 55.15, 107.72, 122.05, 122.69, 123.90, 127.23, 127.58, 128.74, 129.07, 129.98, 131.19, 133.11, 133.97, 137.72, 143.48, 165.51, 173.27; ESI-MS: $m/z = 346$ $[M+H]^+$; anal. calcd. for $C_{22}H_{19}NO_3$: C 76.50, H 5.54, N 4.06; found: C 76.54, H 5.46, N 3.89.

Methyl 6-(4-fluorophenyl)-1′-methyl-2′-oxospiro[cyclohexa[2,4]diene-1,3′-indoline]-3-carboxylate (4b): yield: 82%; white solid; mp 122–123 °C; IR (KBr): $\nu = 1716$, 1612, 1511, 1256 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 2.76$ (s, 3H), 3.78 (s, 3H), 4.24–4.27 (m, 1H), 6.00 (ddd, $J = 9.9$, 2.7 and 1.2 Hz, 1H), 6.53 (dd, $J = 2.1$ and 1.2 Hz, 1H), 6.56 (d, $J = 7.5$ Hz, 1H), 6.70 (ddd, $J = 9.9$, 3.3 and 1.5 Hz, 1H), 6.71–6.85 (m, 4H), 7.13 (t, $J = 7.5$ Hz, 1H), 7.26 (t, $J = 7.5$ Hz, 1H), 7.45 (d, $J = 7.5$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 25.78$, 48.97, 52.00, 55.10, 107.86, 114.46 (d, $J = 20.6$ Hz), 122.24, 122.82, 123.86, 128.88, 129.65, 130.65 (d, $J = 8.0$ Hz), 131.17, 132.94, 133.52 (d, $J = 3.5$ Hz), 133.93, 143.44, 161.96 (d, $J = 243.8$ Hz), 165.42, 173.18; ESI-MS: $m/z = 364$ $[M+H]^+$; anal. calcd. for $C_{22}H_{18}FNO_3$: C 72.72, H 4.99, N 3.85; found: C 72.91, H 5.10, N 3.89.

Methyl 1′,5-dimethyl-2′-oxo-6-phenylspiro[cyclohexa[2,4]diene-1,3′-indoline]-3-carboxylate (4c): yield: 78%; pale yellow solid; mp 146–147 °C; IR (KBr): $\nu = 1717$, 1610, 1492, 1257 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 1.71$ (s, 3H), 3.00 (s, 3H), 3.62 (s, 1H), 3.79 (s, 3H), 6.54–6.58 (m, 2H), 6.71 (d, $J = 7.8$ Hz, 1H), 6.98–7.10 (m, 3H), 7.12–7.22 (m, 3H), 7.27 (t, $J = 7.8$ Hz, 1H), 7.42 (d, $J = 7.8$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 22.43$, 26.17, 51.90, 54.53, 55.13, 108.07, 117.90, 122.68, 123.28, 127.47, 127.82, 128.81, 129.41, 130.62, 132.18, 132.74, 136.11, 138.02, 142.61, 165.83, 175.41; ESI-MS: $m/z = 382$ $[M+Na]^+$; anal. calcd. for $C_{23}H_{21}NO_3$: C 76.86, H 5.89, N 3.90; found: C 76.98, H 5.96, N 3.64.

Methyl 5′-chloro-1′-methyl-2′-oxo-6-phenylspiro[cyclohexa[2,4]diene-1,3′-indoline]-3-carboxylate (4d): yield: 80%; pale yellow solid; mp 150–151 °C; IR (KBr): $\nu = 1723$, 1610, 1493, 1275 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 2.71$ (s, 3H), 3.80 (s, 3H), 4.19–4.26 (m, 1H), 6.05 (ddd, $J = 9.9$, 3.0 and 0.9 Hz, 1H), 6.45 (d, $J = 8.4$ Hz, 1H), 6.50 (d, $J = 1.2$ Hz, 1H), 6.71 (ddd, $J = 9.9$, 3.3 and 1.2 Hz, 1H), 6.86–6.89 (m, 2H), 7.05–7.16 (m, 3H), 7.23 (dd, $J = 8.4$ and 2.1 Hz, 1H), 7.47 (d, $J = 2.1$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz); $\delta = 25.84$, 49.85, 52.05, 55.38, 108.66, 122.15, 124.36, 127.45, 127.75, 127.94, 128.69, 129.05, 129.90, 131.55, 132.86, 134.81, 137.32, 142.08, 165.32, 172.86; ESI-MS: $m/z = 380$ $[M+H]^+$, 382 $[M+H+2]^+$; anal. calcd. for $C_{22}H_{18}ClNO_3$: C 69.57, H 4.78, N 3.69; found: C 69.89, H 4.85, N 3.73.

Methyl 5′-methoxy-1′-methyl-2′-oxo-6-phenylspiro[cyclohexa[2,4]diene-1,3′-indoline]-3-carboxylate (4e): yield: 81%; white solid; mp 152–153 °C; IR (KBr): $\nu = 1716$, 1602, 1499, 1277 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 2.70$ (s, 3H), 3.79 (s, 3H), 3.85 (s, 3H), 4.23–4.26 (m, 1H), 6.05 (ddd, $J = 9.9$, 2.7 and 0.9 Hz, 1H), 6.43 (d, $J = 8.4$ Hz, 1H), 6.53 (dd, $J = 2.4$ and 1.2 Hz, 1H), 6.70 (ddd, $J = 9.9$, 3.0 and 1.2 Hz, 1H), 6.77 (dd, $J = 8.4$ and 2.4 Hz, 1H), 6.86–6.91 (m, 2H), 7.03–7.15 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 25.78$, 49.80, 51.95, 55.63, 55.88, 108.08, 111.21, 113.01, 122.00, 127.21, 127.59, 129.09, 129.97, 131.14, 133.88, 134.39, 137.03, 137.73, 156.05, 165.48, 172.94; ESI-MS: $m/z = 376$ $[M+H]^+$; anal. calcd. for $C_{23}H_{21}NO_4$: C 73.58, H 5.64, N 3.73; found: C 73.39, H 5.96, N 3.50.

Methyl 1′-methyl-5′-nitro-2′-oxo-6-phenylspiro[cyclohexa[2,4]diene-1,3′-indoline]-3-carboxylate (4f): yield: 82%; pale yellow solid; mp 160–161 °C; IR (KBr): $\nu = 1725$, 1614, 1521, 1335, 1275 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 2.79$ (s, 3H), 3.82 (s, 3H), 4.30–4.33 (m, 1H), 6.08 (ddd, $J = 9.9$, 2.7 and 0.9 Hz, 1H), 6.50 (dd, $J = 2.4$ and 1.2 Hz, 1H), 6.60 (d, $J = 8.4$ Hz, 1H), 6.75 (ddd, $J = 9.9$, 3.3 and 1.2 Hz, 1H), 6.82–6.88 (m, 2H), 7.05–7.17 (m, 3H), 8.24 (dd, $J = 8.4$ and 2.4 Hz, 1H), 8.40 (d, $J = 2.4$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 26.17$, 50.05, 52.19, 55.15, 107.27, 119.78, 122.44, 126.05, 127.78, 127.94, 128.95, 129.78, 131.55, 132.29, 134.03, 136.80, 143.40, 149.10, 165.07, 173.40; ESI-MS: $m/z = 391$ $[M+H]^+$; anal. calcd. for $C_{22}H_{18}N_2O_5$: C 67.69, H 4.65, N 7.18; found: C 67.87, H 4.96, N 7.01.

Methyl 2′-oxo-6-phenylspiro[cyclohexa[2,4]diene-1,3′-indoline]-3-carboxylate (4g): yield: 80%; white solid; mp 165–166 °C; IR (KBr): $\nu = 3261$, 1723, 1619, 1472, 1258 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 3.79$ (s, 3H), 4.24–4.27 (m, 1H), 6.07 (ddd, $J = 9.9$, 3.0 and 0.9 Hz, 1H), 6.54 (d, $J = 0.9$ Hz, 1H), 6.66 (d, $J = 7.5$ Hz, 1H), 6.71 (ddd, $J = 9.9$, 3.0 and 1.2 Hz, 1H), 6.87–6.95 (m, 2H), 6.98–7.07 (m, 2H), 7.08–7.16 (m, 2H), 7.21 (t, $J = 7.5$ Hz, 1H), 7.45 (d, $J = 7.5$ Hz, 1H), 8.17 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 49.38$, 52.00, 55.39, 109.86, 121.88, 122.67, 124.11, 127.32, 127.82, 128.74, 129.20, 129.97, 130.75, 133.49, 133.80, 137.58, 140.59, 165.46, 176.26; ESI-MS: $m/z = 332$ $[M+H]^+$; anal. calcd. for $C_{21}H_{17}NO_3$: C 76.12, H 5.17, N 4.23; found: C 76.41, H 5.40, N 4.05.

Methyl 6-(furan-2-yl)-1′-methyl-2′-oxospiro[cyclohexa[2,4]diene-1,3′-indoline]-3-carboxylate (4i): yield: 70%; pale yellow solid; mp 142–143 °C; IR (KBr): $\nu = 1722$, 1612, 1493, 1258 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 3.00$ (s, 3H), 3.77 (s, 3H), 4.31–4.33 (m, 1H), 5.92 (d, $J = 3.0$ Hz, 1H), 6.02 (ddd, $J = 9.9$, 3.6 and 0.9 Hz, 1H), 6.17 (dd, $J = 3.0$ and 1.8 Hz, 1H), 6.55 (d, $J = 0.9$ Hz, 1H), 6.71 (ddd, $J = 9.9$, 3.0 and 1.2 Hz, 1H), 6.72 (d, $J = 7.5$ Hz, 1H), 7.09 (t, $J = 7.5$ Hz, 1H), 7.15 (d, $J = 1.8$ Hz, 1H), 7.30 (t, $J = 7.5$ Hz, 1H), 7.40 (d, $J = 7.5$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 26.16$, 42.72, 51.98, 53.49, 107.76, 107.94, 110.18, 122.09, 122.81, 123.63, 126.76, 128.91, 130.52, 132.45, 134.55, 141.77, 143.36, 151.52, 165.34, 173.78; ESI-MS: $m/z = 336$ $[M+H]^+$; anal. calcd. for $C_{20}H_{17}NO_4$: C 71.63, H 5.11, N 4.18; found: C 71.46, H 5.37, N 4.15.

Methyl 1′,6-dimethyl-2′-oxospiro[cyclohexa[2,4]diene-1,3′-indoline]-3-carboxylate (4j): yield: 80%; white solid; mp 146–147 °C; IR (KBr): $\nu = 1715$, 1611, 1493, 1344, 1256 cm^{-1};

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^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.90 (d, J = 7.2 Hz, 3H), 3.01–3.09 (m, 1H), 3.17 (s, 3H), 3.73 (s, 3H), 5.78 (dd, J = 9.9 and 3.0 Hz, 1H), 6.43 (s, 1H), 6.49 (ddd, J = 9.9, 3.0 and 1.5 Hz, 1H), 6.83 (d, J = 7.5 Hz, 1H), 7.07 (t, J = 7.5 Hz, 1H), 7.29 (d, J = 7.5 Hz, 1H), 7.30 (t, J = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.52, 26.09, 36.69, 51.83, 53.36, 107.93, 120.42, 122.87, 123.53, 128.60, 130.55, 132.12, 133.29, 134.77, 143.51, 165.52, 174.29; ESI-MS: m/z = 306 $[M+Na]^+$; anal. calcd. for $C_{17}H_{17}NO_3$: C 72.07, H 6.05, N 4.94; found: C 72.41, H 6.39, N 4.75.

Typical Procedure for the Synthesis of 5a (Conditions B)

A solution of **3a**-*EEE* (69 mg, 0.2 mmol) and $Pd(OAc)_2$ (2 mg, 5 mol%) in toluene (1 mL) was heated to reflux for 12 h under an N_2 balloon atmosphere. After removal of toluene and a column chromatographic purification process (hexanes/Et_2O, 4:1) the spirooxindole **5a** was obtained as a white solid (yield: 50 mg, 73%) along with **4a** (yield: 13 mg, 19%).

Methyl 1′-methyl-2′-oxo-6-phenylspiro[cyclohexa[2,4]-diene-1,3′-indoline]-3-carboxylate (5a): yield: 73%; white solid; mp 138–140 °C; IR (KBr) ν = 1715, 1609, 1470, 1275 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.94 (s, 3H), 3.78 (s, 3H), 4.59–4.62 (m, 1H), 6.12 (ddd, J = 9.9, 2.7 and 1.2 Hz, 1H), 6.45 (d, J = 7.5 Hz, 1H), 6.73 (d, J = 1.5 Hz, 1H), 6.75 (ddd, J = 9.9, 3.3 and 1.2 Hz, 1H), 6.89–6.95 (m, 3H), 6.97–7.07 (m, 3H), 7.13 (t, J = 7.5 Hz, 1H), 7.39 (d, J = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 26.07, 48.04, 51.97, 56.11, 107.94, 122.31, 122.77, 124.99, 126.49, 127.01, 127.43, 129.04, 129.25, 129.34, 131.03, 134.28, 137.36, 141.98, 165.50, 178.80; ESI-MS: m/z = 368 $[M+Na]^+$; anal. calcd. for $C_{22}H_{19}NO_3$: C 76.50, H 5.54, N 4.06; found: C 76.81, H 5.79, N 3.93.

Methyl 6-(4-fluorophenyl)-1′-methyl-2′-oxospiro[cyclohexa[2,4]diene-1,3′-indoline]-3-carboxylate (5b): yield: 80%; white solid; mp 130–131 °C; IR (KBr): ν = 1715, 1609, 1510, 1274 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.96 (s, 3H), 3.78 (s, 3H), 4.57–4.60 (m, 1H), 6.06 (ddd, J = 9.9, 2.7 and 1.2 Hz, 1H), 6.49 (d, J = 7.5 Hz, 1H), 6.67–6.74 (m, 3H), 6.75 (ddd, J = 9.9, 3.3 and 1.5 Hz, 1H), 6.84–6.90 (m, 2H), 6.93 (t, J = 7.5 Hz, 1H), 7.15 (t, J = 7.5 Hz, 1H), 7.38 (d, J = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 26.12, 47.33, 52.01, 56.11, 108.15, 114.35 (d, J = 20.6 Hz), 122.43, 123.03, 124.93, 126.24, 129.36, 129.45, 130.57 (d, J = 8.0 Hz), 130.72, 133.16 (d, J = 3.5 Hz), 134.29, 141.98, 161.80 (d, J = 244.4 Hz), 165.44, 178.69; ESI-MS: m/z = 364 $[M+H]^+$; anal. calcd. for $C_{22}H_{18}FNO_3$: C 72.72, H 4.99, N 3.85; found: C 73.05, H 5.27, N 3.66.

Methyl 1′,5-dimethyl-2′-oxo-6-phenylspiro[cyclohexa[2,4]-diene-1,3′-indoline]-3-carboxylate (5c): yield: 76%; white solid; mp 136–137 °C; IR (KBr): ν = 1707, 1607, 1485, 1253 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.72 (s, 3H), 2.94 (s, 3H), 3.77 (s, 3H), 4.12 (s, 1H), 6.50–6.61 (m, 3H), 6.64–6.74 (m, 1H), 6.85 (t, J = 7.5 Hz, 1H), 6.88–7.02 (m, 3H), 7.06–7.14 (m, 2H), 7.18 (t, J = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 22.35, 26.13, 51.91, 52.60, 56.02, 107.93, 118.40, 122.21, 125.60, 127.20, 127.66, 128.09, 128.96, 130.50, 131.29, 132.16, 135.65, 138.35, 142.73, 165.84, 177.89; ESI-MS: m/z = 360 $[M+H]^+$; anal. calcd. for $C_{23}H_{21}NO_3$: C 76.86, H 5.89, N 3.90; found: C 77.11, H 6.15, N 3.74.

Methyl 5′-chloro-1′-methyl-2′-oxo-6-phenylspiro[cyclohexa[2,4]diene-1,3′-indoline]-3-carboxylate (5d): yield: 76%; white solid; mp 157–158 °C; IR (KBr): ν = 1720, 1606, 1487, 1261 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.92 (s, 3H), 3.80 (s, 3H), 4.58–4.61 (m, 1H), 6.13 (ddd, J = 9.9, 2.7 and 0.6 Hz, 1H), 6.37 (d, J = 8.1 Hz, 1H), 6.70 (dd, J = 2.4 and 1.5 Hz, 1H), 6.77 (ddd, J = 9.9, 3.3 and 1.5 Hz, 1H), 6.89–6.94 (m, 2H), 7.00–7.08 (m, 3H), 7.11 (dd, J = 8.1 and 2.1 Hz, 1H), 7.35 (d, J = 2.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 26.19, 48.10, 52.09, 56.11, 108.86, 123.00, 125.24, 127.25, 127.58, 127.66, 128.14, 129.01, 129.19, 129.84, 130.98, 133.39, 136.96, 140.64, 165.30, 178.35; ESI-MS: m/z = 402 $[M+Na]^+$, 404 $[M+Na+2]^+$; anal. calcd. for $C_{22}H_{18}ClNO_3$: C 69.57, H 4.78, N 3.69; found: C 69.88, H 4.86, N 3.54.

Methyl 5′-methoxy-1′-methyl-2′-oxo-6-phenylspiro[cyclohexa[2,4]diene-1,3′-indoline]-3-carboxylate (5e): yield: 85%; white solid; mp 160–161 °C; IR (KBr): ν = 1712, 1601, 1495, 1275 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.91 (s, 3H), 3.74 (s, 3H), 3.78 (s, 3H), 4.58–4.61 (m, 1H), 6.12 (ddd, J = 9.6, 2.4 and 1.2 Hz, 1H), 6.36 (d, J = 8.4 Hz, 1H), 6.66 (dd, J = 8.4 and 2.4 Hz, 1H), 6.72 (d, J = 1.2 Hz, 1H), 6.75 (ddd, J = 9.6, 3.3 and 1.2 Hz, 1H), 6.92–6.97 (m, 2H), 6.98–7.08 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 26.18, 47.95, 51.99, 55.85, 56.39, 108.20, 112.45, 113.51, 122.76, 127.04, 127.51, 127.79, 129.07, 129.39, 131.01, 134.41, 135.71, 137.40, 155.59, 165.48, 178.36; ESI-MS: m/z = 376 $[M+H]^+$, 398 $[M+Na]^+$; anal. calcd. for $C_{23}H_{21}NO_4$: C 73.58, H 5.64, N 3.73; found: C 73.87, H 5.96, N 3.52.

Methyl 1′-methyl-5′-nitro-2′-oxo-6-phenylspiro[cyclohexa[2,4]diene-1,3′-indoline]-3-carboxylate (5f): yield: 80%; pale yellow solid; mp 162–163 °C; IR (KBr): ν = 1725, 1613, 1493, 1334, 1275 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.00 (s, 3H), 3.82 (s, 3H), 4.60–4.65 (m, 1H), 6.17 (ddd, J = 9.9, 2.7 and 0.9 Hz, 1H), 6.53 (d, J = 8.7 Hz, 1H), 6.69 (d, J = 0.9 Hz, 1H), 6.84 (ddd, J = 9.9, 3.3 and 1.2 Hz, 1H), 6.86–6.91 (m, 2H), 6.99–7.10 (m, 3H), 8.11 (dd, J = 8.7 and 2.1 Hz, 1H), 8.21 (d, J = 2.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 26.49, 48.26, 52.22, 55.73, 107.55, 120.61, 123.34, 126.34, 127.43, 127.56, 127.85, 128.86, 130.54, 130.75, 132.00, 136.43, 143.05, 147.57, 164.99, 179.03; ESI-MS: m/z = 391 $[M+H]^+$; anal. calcd. for $C_{22}H_{18}N_2O_5$: C 67.69, H 4.65, N 7.18; found: C 67.44, H 4.93, N 7.06.

Methyl 2′-oxo-6-phenylspiro[cyclohexa[2,4]diene-1,3′-indoline]-3-carboxylate (5g): yield: 26%; white solid; mp 159–160 °C; IR (KBr): ν = 3276, 1714, 1616, 1470, 1274 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.79 (s, 3H), 4.58–4.61 (m, 1H), 6.13 (dd, J = 10.8 and 2.7 Hz, 1H), 6.58 (d, J = 7.5 Hz, 1H), 6.75 (s, 1H), 6.76 (ddd, J = 10.8, 3.3 and 1.2 Hz, 1H), 6.91 (t, J = 7.5 Hz, 1H), 6.96–7.12 (m, 6H), 7.40 (d, J = 7.5 Hz, 1H), 8.15 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 47.73, 52.04, 56.53, 109.81, 122.41, 122.68, 125.43, 127.14, 127.24, 127.72, 129.20, 129.32, 131.23, 134.01, 137.47, 138.99, 165.53, 180.94, one carbon was overlapped; ESI-MS: m/z = 332 $[M+H]^+$; anal. calcd. for $C_{21}H_{17}NO_3$: C 76.12, H 5.17, N 4.23; found: C 76.48, H 5.36, N 4.02.

Methyl 6-(furan-2-yl)-1′-methyl-2′-oxospiro[cyclohexa[2,4]diene-1,3′-indoline]-3-carboxylate (5i): yield: 82%; white solid; mp 151–152 °C; IR (KBr): ν = 1718, 1609, 1470, 1274 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.16 (s, 3H), 3.76 (s, 3H), 4.71–4.76 (m, 1H), 5.84 (d, J = 3.3 Hz, 1H), 6.04 (dd, J = 3.3 and 1.5 Hz, 1H), 6.11 (dd, J = 9.9 and

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2.7 Hz, 1H), 6.65 (d, J=7.5 Hz, 1H), 6.66 (s, 1H), 6.72 (ddd, J=9.9, 3.3 and 0.9 Hz, 1H), 6.88 (t, J=7.5 Hz, 1H), 7.03 (d, J=1.5 Hz, 1H), 7.18 (t, J=7.5 Hz, 1H), 7.29 (d, J=7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=26.51, 41.13, 51.96, 54.57, 107.09, 108.01, 109.86, 122.48, 122.51, 124.64, 126.95, 127.30, 128.85, 129.29, 134.60, 141.47, 142.07, 151.87, 165.33, 178.62; ESI-MS: m/z=336 $[M+H]^+$; anal. calcd. for $C_{20}H_{17}NO_4$: C 71.63, H 5.11, N 4.18; found: C 71.52, H 5.37, N 4.01.

Methyl 1′,6-dimethyl-2′-oxospiro[cyclohexa[2,4]diene-1,3′-indoline]-3-carboxylate (5j): yield. 83%; colorless oil; IR (film): ν=1717, 1608, 1471, 1274 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=0.76 (d, J=7.5 Hz, 3H), 3.26 (s, 3H), 3.34–3.46 (m, 1H), 3.74 (s, 3H), 5.76 (ddd, J=9.9, 2.4 and 0.9 Hz, 1H), 6.55 (ddd, J=9.9, 3.3 and 1.2 Hz, 1H), 6.63 (d, J=0.9 Hz, 1H), 6.84 (d, J=7.8 Hz, 1H), 6.96 (t, J=7.8 Hz, 1H), 7.29 (t, J=7.8 Hz, 1H), 7.34 (d, J=7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=14.11, 26.47, 35.06, 51.82, 54.47, 108.28, 121.30, 122.75, 124.51, 126.79, 128.96, 129.24, 133.13, 134.95, 142.44, 165.57, 179.38; ESI-MS: m/z=284 $[M+H]^+$; anal. calcd. for $C_{17}H_{17}NO_3$: C 72.07, H 6.05, N 4.94; found: C 72.34, H 6.18, N 4.75.

Spectroscopic Data for 6a–g and 7a–13

Methyl 1′-methyl-2′-oxo-2,4-diphenylspiro[cyclohexa[2,5]-diene-1,3′-indoline]-5-carboxylate (6a): yield: 81%; white solid; mp 222–223 °C; IR (KBr): ν=1719, 1609, 1491, 1275 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=3.18 (s, 3H), 3.59 (s, 3H), 4.71 (dd, J=3.9 and 1.2 Hz, 1H), 6.11 (d, J=3.9 Hz, 1H), 6.60 (d, J=1.2 Hz, 1H), 6.76 (d, J=7.8 Hz, 1H), 6.82–6.86 (m, 2H), 6.94–7.09 (m, 4H), 7.17 (d, J=7.8 Hz, 1H), 7.21–7.30 (m, 2H), 7.38 (t, J=7.5 HZ, 2H), 7.74 (d, J=8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=26.67, 43.03, 51.70, 56.27, 108.36, 123.12, 125.07, 126.82, 127.24, 127.69, 127.96, 128.53, 129.07, 129.26, 131.71, 132.08, 132.13, 132.20, 134.45, 139.12, 141.37, 143.18, 166.18, 175.42; ESI-MS: m/z=422 $[M+H]^+$; anal. calcd. for $C_{28}H_{23}NO_3$: C 79.79, H 5.50, N 3.32; found: C 80.05, H 5.81, N 3.18.

Methyl 4-(3,4-dichlorophenyl)-1′-methyl-2′-oxo-2-phenyl-spiro[cyclohexa[2,5]diene-1,3′-indoline]-5-carboxylate (6b): yield: 63%; white solid; mp 231–232 °C; IR (KBr): ν=1717, 1610, 1469, 1343, 1275 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=3.20 (s, 3H), 3.62 (s, 3H), 4.66 (dd, J=4.2 and 0.9 Hz, 1H), 6.04 (d, J=4.2 Hz, 1H), 6.63 (d, J=0.9 Hz, 1H), 6.76 (d, J=7.8 Hz, 1H), 6.80–6.84 (m, 2H), 6.99–7.10 (m, 4H), 7.14 (d, J=7.8 Hz, 1H), 7.26 (t, J=7.8 Hz, 1H), 7.43 (d, J=8.4 Hz, 1H), 7.63 (dd, J=8.4 and 2.1 Hz, 1H), 7.91 (d, J=2.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=26.81, 42.22, 51.87, 56.32, 108.49, 123.20, 125.06, 127.45, 127.79, 127.84, 128.72, 129.22, 130.46, 130.84, 130.91, 131.30, 131.35, 131.42, 132.39, 133.40, 135.41, 138.74, 141.76, 143.14, 165.78, 175.10; ESI-MS: m/z=490 $[M+H]^+$, 492 $[M+H+2]^+$, 494 $[M+H+4]^+$; anal. calcd. for $C_{28}H_{21}Cl_2NO_3$: C 68.58, H 4.32, N 2.86; found: C 68.76, H 4.56, N 2.80.

Methyl 4-(2,3-dichlorophenyl)-1′-methyl-2′-oxo-2-phenyl-spiro[cyclohexa[2,5]diene-1,3′-indoline]-5-carboxylate (6b′): yield: 14%; white solid; mp 225–226 °C; IR (KBr): ν=1720, 1610, 1470, 1343, 1276 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=3.17 (s, 3H), 3.61 (s, 3H), 5.40 (d, J=3.9 Hz, 1H), 6.07 (d, J=3.9 Hz, 1H), 6.72–6.82 (m, 4H), 6.96–7.10 (m, 4H), 7.16 (d, J=7.5 Hz, 1H), 7.22–7.30 (m, 2H), 7.34 (dd, J=7.8 and 1.5 Hz, 1H), 7.83 (dd, J=7.8 and 1.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=26.70, 39.72, 51.95, 56.27, 108.46, 123.27, 125.08, 127.40, 127.73, 127.85, 127.88, 128.53, 128.81, 129.21, 129.96, 131.19, 131.28, 131.85, 132.81, 133.03, 136.45, 138.74, 141.76, 143.14, 165.76, 175.21; ESI-MS: m/z=490 $[M+H]^+$, 492 $[M+H+2]^+$, 494 $[M+H+4]^+$; anal. calcd. for $C_{28}H_{21}Cl_2NO_3$: C 68.58, H 4.32, N 2.86; found: C 68.87, H 4.60, N 2.68.

Methyl 4-(3,4-dimethylphenyl)-1′-methyl-2′-oxo-2-phenyl-spiro[cyclohexa[2,5]diene-1,3′-indoline]-5-carboxylate (6c): yield: 73%; white solid; mp 210–211 °C; IR (KBr): ν=1720, 1609, 1490, 1342, 1275 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.27 (s, 3H), 2.34 (s, 3H), 3.21 (s, 3H), 3.63 (s, 3H), 4.66 (dd, J=4.2 and 1.2 Hz, 1H), 6.11 (d, J=4.2 Hz, 1H), 6.61 (d, J=1.2 Hz, 1H), 6.78 (d, J=7.8 Hz, 1H), 6.84–6.88 (m, 2H), 7.00–7.11 (m, 4H), 7.15–7.22 (m, 2H), 7.29 (t, J=7.8 Hz, 1H), 7.48 (d, J=7.6 Hz, 1H), 7.52 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz); δ=19.43, 19.91, 26.67, 42.57, 51.67, 56.25, 108.31, 123.07, 125.06, 126.51, 127.14, 127.64, 127.98, 129.01, 129.81, 130.43, 131.75, 131.83, 132.21, 132.42, 134.24, 134.99, 136.61, 138.83, 139.22, 143.18, 166.26, 175.44; ESI-MS: m/z=472 $[M+Na]^+$; anal. calcd. for $C_{30}H_{27}NO_3$: C 80.15, H 6.05, N 3.12; found: C 79.98, H 6.37, N 2.94.

Methyl 4-(2,3-dimethylphenyl)-1′-methyl-2′-oxo-2-phenyl-spiro[cyclohexa[2,5]diene-1,3′-indoline]-5-carboxylate (6c′): yield: 3%; white solid; mp 208–210 °C; IR (KBr): ν=1720, 1609, 1470, 1342, 1274 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=2.34 (s, 3H), 2.50 (s, 3H), 3.16 (s, 3H), 3.58 (s, 3H), 5.08 (dd, J=3.6 and 1.5 Hz, 1H), 6.02 (d, J=3.6 Hz, 1H), 6.66 (d, J=1.5 Hz, 1H), 6.76 (d, J=7.5 Hz, 1H), 6.77–6.82 (m, 2H), 6.96–7.11 (m, 5H), 7.18 (t, J=7.5 Hz, 1H), 7.21 (d, J=7.5 Hz, 1H), 7.28 (t, J=7.5 Hz, 1H), 7.70 (d, J=7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=14.95, 21.15, 26.58, 38.20, 51.73, 56.17, 108.33, 123.08, 125.01, 126.06, 126.88, 127.15, 127.61, 128.06, 128.35, 129.06, 131.62, 131.69, 131.79, 132.62, 134.01, 134.71, 136.43, 139.19, 139.74, 143.28, 166.33, 175.52; ESI-MS: m/z=450 $[M+H]^+$; anal. calcd. for $C_{30}H_{27}NO_3$: C 80.15, H 6.05, N 3.12; found: C 80.42, H 6.37, N 3.00.

Methyl 4-(3,5-dimethylphenyl)-1′-methyl-2′-oxo-2-phenyl-spiro[cyclohexa[2,5]diene-1,3′-indoline]-5-carboxylate (6d): yield: 76%; white solid; mp 231–232 °C; IR (KBr): ν=1720, 1609, 1470, 1342, 1274 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz): δ=2.36 (s, 6H), 3.19 (s, 3H), 3.61 (s, 3H), 4.63 (dd, J=4.2 and 1.2 Hz, 1H), 6.09 (d, J=4.2 Hz, 1H), 6.59 (d, J=1.2 Hz, 1H), 6.76 (d, J=7.8 Hz, 1H), 6.82–6.84 (m, 2H), 6.88 (s, 1H), 6.99–7.03 (m, 2H), 7.04–7.07 (m, 2H), 7.17 (d, J=7.8 Hz, 1H), 7.27 (t, J=7.8 Hz, 1H), 7.33 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=21.38, 26.68, 42.88, 51.65, 56.24, 108.29, 123.06, 125.05, 126.94, 127.15, 127.65, 127.95, 128.57, 129.01, 131.76, 131.82, 132.11, 132.35, 134.35, 137.87, 139.22, 141.30, 143.18, 166.23, 175.45; ESI-MS: m/z=450 $[M+H]^+$; anal. calcd. for $C_{30}H_{27}NO_3$: C 80.15, H 6.05, N 3.12; found: C 80.50, H 6.41, N 3.02.

Methyl 4-(2,4-dimethylphenyl)-1′-methyl-2′-oxo-2-phenyl-spiro[cyclohexa[2,5]diene-1,3′-indoline]-5-carboxylate (6d′): yield: 72%; white solid; mp 208–209 °C; IR (KBr): ν=1720, 1609, 1490, 1342, 1274 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz): δ=2.28 (s, 3H), 2.56 (s, 3H), 3.15 (s, 3H), 3.58 (s, 3H), 4.94 (d, J=3.6 Hz, 1H), 5.99 (d, J=3.6 Hz, 1H), 6.64 (s, 1H), 6.75 (d, J=7.8 Hz, 1H), 6.78 (d, J=7.8 Hz, 2H), 6.97–7.09 (m, 6H), 7.19 (d, J=7.8 Hz, 1H), 7.26 (t, J=7.8 Hz, 1H),

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7.71 (d, $J=7.8$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): $\delta=$ 19.56, 21.03, 26.60, 37.71, 51.72, 56.15, 108.33, 123.08, 125.01, 127.14, 127.54, 127.60, 128.04, 128.99, 129.04, 130.92, 131.59, 131.68, 131.77, 132.42, 134.70, 135.25, 135.96, 136.86, 139.17, 143.23, 166.29, 175.52; ESI-MS: $m/z=472$ $[M+Na]^+$; anal. calcd. for $C_{30}H_{27}NO_3$: C 80.15, H 6.05, N 3.12; found: C 80.02, H 6.37, N 2.96.

Methyl 4-(2,5-dimethylphenyl)-1′-methyl-2′-oxo-2-phenylspiro[cyclohexa[2,5]diene-1,3′-indoline]-5-carboxylate (6e): yield: 76%; white solid; mp 211–213 °C; IR (KBr): $\nu=1718$, 1705, 1608, 1469, 1343, 1275 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=2.37$ (s, 3H), 2.55 (s, 3H), 3.18 (s, 3H), 3.59 (s, 3H), 4.96 (dd, $J=3.9$ and 1.5 Hz, 1H), 6.00 (d, $J=3.9$ Hz, 1H), 6.66 (d, $J=1.5$ Hz, 1H), 6.76 (d, $J=7.8$ Hz, 1H), 6.81 (dd, $J=7.8$ and 1.8 Hz, 2H), 6.94 (d, $J=7.0$ Hz, 1H), 6.97–7.10 (m, 5H), 7.19 (d, $J=7.8$ Hz, 1H), 7.27 (t, $J=7.8$ Hz, 1H), 7.67 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=19.15$, 21.15, 26.66, 38.02, 51.71, 56.19, 108.32, 123.08, 125.02, 127.16, 127.34, 127.64, 128.02, 129.04, 129.78, 129.94, 131.62, 131.66, 131.81, 132.32, 132.38, 134.81, 136.09, 139.22, 139.55, 143.24, 166.29, 175.58; ESI-MS: $m/z=450$ $[M+H]^+$; anal. calcd. for $C_{30}H_{27}NO_3$: C 80.15, H 6.05, N 3.12; found: C 80.29, H 6.07, N 3.07.

Methyl 5′-chloro-1′-methyl-2′-oxo-2,4-diphenylspiro[cyclohexa[2,5]diene-1,3′-indoline]-5-carboxylate (6f): yield: 83%; white solid; mp 220–221 °C; IR (KBr): $\nu=1721$, 1608, 1488, 1337, 1274 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=3.18$ (s, 3H), 3.62 (s, 3H), 4.71 (dd, $J=3.9$ and 1.2 Hz, 1H), 6.12 (d, $J=3.9$ Hz, 1H), 6.57 (d, $J=1.2$ Hz, 1H), 6.69 (d, $J=7.8$ Hz, 1H), 6.86 (dd, $J=7.8$ and 1.8 Hz, 2H), 7.02–7.13 (m, 3H), 7.16 (d, $J=1.8$ Hz, 1H), 7.21–7.27 (m, 2H), 7.38 (t, $J=$ 7.8 Hz, 2H), 7.72 (d, $J=7.8$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=26.80$, 43.00, 51.79, 56.29, 109.32, 125.43, 126.91, 127.43, 127.86, 127.90, 128.48, 128.56, 129.06, 129.22, 131.63, 132.47, 132.65, 133.32, 133.54, 138.77, 141.05, 141.73, 165.95, 174.99; ESI-MS: $m/z=478$ $[M+Na]^+$, 480 $[M+Na+2]^+$; anal. calcd. for $C_{28}H_{22}ClNO_3$: C 73.76, H 4.86, N 3.07; found: C 73.89, H 5.06, N 2.88.

Methyl 5′-methoxy-1′-methyl-2′-oxo-2,4-diphenylspiro[cyclohexa[2,5]diene-1,3′-indoline]-5-carboxylate (6g): yield: 80%; white solid; mp 225–226 °C; IR (KBr): $\nu=1716$, 1602, 1495, 1275 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=3.16$ (s, 3H), 3.60 (s, 3H), 3.77 (s, 3H), 4.71 (dd, $J=3.9$ and 0.9 Hz, 1H), 6.12 (d, $J=3.9$ Hz, 1H), 6.59 (d, $J=0.9$ Hz, 1H), 6.67 (d, $J=8.1$ Hz, 1H), 6.77–6.82 (m, 2H), 6.87 (dd, $J=8.1$ and 1.8 Hz, 2H), 7.00–7.10 (m, 3H), 7.24 (t, $J=7.5$ Hz, 1H), 7.38 (t, $J=7.5$ Hz, 2H), 7.74 (d, $J=8.1$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=26.74$, 43.03, 51.68, 55.80, 56.60, 108.80, 111.89, 113.74, 126.80, 127.24, 127.74, 127.89, 128.51, 129.26, 132.05, 132.13, 132.96, 134.52, 136.65, 139.09, 141.31, 156.36, 166.15, 175.03, one carbon was overlapped; ESI-MS: $m/z=452$ $[M+H]^+$; anal. calcd. for $C_{29}H_{25}NO_4$: C 77.14, H 5.58, N 3.10; found: C 77.48, H 5.79, N 2.95.

Methyl 1′-methyl-2′-oxo-2,4-diphenylspiro[cyclohexa[2,5]diene-1,3′-indoline]-5-carboxylate (7a): yield: 18%; white solid; mp 199–201 °C; IR (KBr): $\nu=1722$, 1609, 1490, 1343, 1275 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=3.14$ (s, 3H), 3.59 (s, 3H), 4.82 (dd, $J=3.9$ and 1.5 Hz, 1H), 6.16 (d, $J=$ 3.9 Hz, 1H), 6.70 (d, $J=1.5$ Hz, 1H), 6.76–6.83 (m, 3H), 6.99–7.14 (m, 4H), 7.24–7.35 (m, 3H), 7.36–7.43 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=26.64$, 42.64, 51.74, 56.27, 108.53, 123.30, 124.95, 126.83, 127.35, 127.75, 127.90, 127.91, 128.81, 129.22, 130.90, 131.87, 132.06, 132.74, 135.37, 138.97, 142.16, 143.61, 166.13, 175.73; ESI-MS: $m/z=422$ $[M+H]^+$; anal. calcd. for $C_{28}H_{23}NO_3$: C 79.79, H 5.50, N 3.32; found: C 79.98, H 5.72, N 3.14.

Methyl 5-methyl-6-oxo-10-phenyl-5,6-dihydrophenanthridine-7-carboxylate (8): yield: 10%; white solid; mp 196–197 °C; IR (KBr): $\nu=1733$, 1653, 1591, 1477, 1356, 1262 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=3.78$ (s, 3H), 4.06 (s, 3H), 6.76–6.82 (m, 1H), 7.33–7.40 (m, 5H), 7.41–7.48 (m, 3H), 7.51 (d, $J=7.5$ Hz, 1H), 7.62 (d, $J=7.5$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=30.49$, 52.91, 114.67, 118.99, 121.26, 124.26, 125.82, 127.86, 128.81, 129.13, 129.27, 129.39, 132.71, 135.35, 135.68, 138.22, 140.77, 142.66, 160.34, 171.24; ESI-MS: $m/z=344$ $[M+H]^+$; anal. calcd. for $C_{22}H_{17}NO_3$: C 76.95, H 4.99, N 4.08; found: C 77.17, H 5.23, N 3.89.

Methyl 1′-methyl-2′-oxo-2-phenyl-4-(pivaloyloxy)spiro[cyclohexa[2,5]diene-1,3′-indoline]-5-carboxylate (9): yield: 39%; white solid; mp 150–151 °C; IR (KBr): $\nu=1726$, 1608, 1490, 1343, 1277, 1146 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=1.25$ (s, 9H), 3.10 (s, 3H), 3.75 (s, 3H), 6.30 (d, $J=$ 4.8 Hz, 1H), 6.43 (d, $J=4.8$ Hz, 1H), 6.78–6.82 (m, 3H), 6.87 (s, 1H), 7.04–7.17 (m, 4H), 7.19 (d, $J=7.5$ Hz, 1H), 7.33 (t, $J=7.5$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=$ 26.62, 27.12, 38.69, 51.98, 56.45, 63.75, 108.68, 123.51, 124.87, 126.33, 127.51, 127.97, 128.31, 129.59, 138.11, 139.61, 140.15, 143.89, 165.08, 174.38, 177.48, two carbons were overlapped; ESI-MS: $m/z=468$ $[M+Na]^+$; anal. calcd. for $C_{27}H_{27}NO_5$: C 72.79, H 6.11, N 3.14; found: C 72.96, H 6.38, N 3.00.

Methyl 1′-methyl-6-phenyl-2′-thioxospiro[cyclohexa[2,4]diene-1,3′-indoline]-3-carboxylate (10): yield: 40%; white solid; mp 152–153 °C; IR (KBr): $\nu=1721$, 1610, 1465, 1435, 1372, 1275, 1193 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=3.32$ (s, 3H), 3.79 (s, 3H), 4.95–4.98 (m, 1H), 6.05 (ddd, $J=9.9$, 2.7 and 0.9 Hz, 1H), 6.59 (d, $J=7.5$ Hz, 1H), 6.67 (dd, $J=$ 2.4 and 1.5 Hz, 1H), 6.75 (ddd, $J=9.9$, 3.6 and 1.5 Hz, 1H), 6.86–7.04 (m, 5H), 7.05 (t, $J=7.5$ Hz, 1H), 7.19 (t, $J=$ 7.5 Hz, 1H), 7.55 (d, $J=7.5$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=31.17$, 52.02, 52.68, 66.77, 109.26, 122.67, 123.83, 124.91, 127.08, 127.21, 128.37, 129.04, 129.39, 131.29, 131.37, 135.39, 137.09, 143.67, 165.61, 208.00; ESI-MS: $m/z=$ 362 $[M+H]^+$; anal. calcd. for $C_{22}H_{19}NO_2S$: C 73.10, H 5.30, N 3.88; found: C 73.17, H 5.39, N 3.71.

(*E*)-Methyl 9-methyl-2-styryl-2,9-dihydrothiopyrano[2,3-*b*]indole-3-carboxylate (11): yield: 41%; white solid; mp 169–170 °C; IR (KBr): $\nu=1693$, 1597, 1482, 1262, 1230 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=3.70$ (s, 3H), 3.84 (s, 3H), 5.04 (d, $J=7.8$ Hz, 1H), 6.31 (dd, $J=15.6$ and 7.8 Hz, 1H), 6.54 (d, $J=15.6$ Hz, 1H), 7.16–7.30 (m, 8H), 7.63–7.66 (m, 1H), 8.09 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=30.90$, 42.36, 51.86, 109.10, 110.26, 110.84, 117.05, 121.32, 121.99, 126.24, 126.46, 126.67, 127.73, 128.39, 130.66, 131.60, 136.39, 136.61, 138.48, 166.93; ESI-MS: $m/z=362$ $[M+H]^+$; anal. calcd. for $C_{22}H_{19}NO_2S$: C 73.10, H 5.30, N 3.88; found: C 73.34, H 5.51, N 3.79.

Methyl 1′-methyl-2′-oxo-6-phenylspiro[cyclohex[2]ene-1,3′-indoline]-3-carboxylate (12): yield: 78%; white solid; mp 132–133 °C; IR (KBr): $\nu=1714$, 1612, 1470, 1378, 1259 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=2.55$ (d, $J=$ 17.7 Hz, 1H), 2.62–2.74 (m, 1H), 2.75 (s, 3H), 2.82–2.98 (m, 1H), 3.02–3.11 (m, 1H), 3.37 (dd, $J=12.0$ and 5.4 Hz, 1H), 3.77 (s, 3H), 6.58 (d, $J=7.8$ Hz, 1H), 6.64 (d, $J=7.8$ Hz,

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2H), 6.96–7.10 (m, 4H), 7.23–7.33 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 25.65, 29.76, 32.51, 44.81, 51.28, 51.80, 107.77, 122.24, 124.10, 127.07, 127.47, 127.94, 128.24, 128.61, 130.95, 138.48, 138.66, 143.64, 166.99, 178.31; ESI-MS: m/z = 348 $[M+H]^+$; anal. calcd. for $C_{22}H_{21}NO_3$: C 76.06, H 6.09, N 4.03; found: C 76.22, H 6.21, N 4.00.

1′-Methyl-3-phenylspiro[fluorene-2,3′-indoline]-2′,9(4a*H*)-dione (13): yield: 90%; white solid; mp 192–193 °C; IR (KBr): ν = 1715, 1604, 1468, 1346, 1276 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.04 (s, 3H), 4.76–4.81 (m, 1H), 6.68 (d, J = 2.1 Hz, 1H), 6.79–6.83 (m, 3H), 6.85 (d, J = 7.5 Hz, 1H), 7.09–7.22 (m, 4H), 7.30 (d, J = 7.5 Hz, 1H), 7.37 (t, J = 7.5 Hz, 1H), 7.44–7.52 (m, 1H), 7.66–7.72 (m, 2H), 7.89 (d, J = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 26.32, 41.02, 56.54, 108.64, 123.50, 124.07, 124.23, 124.62, 127.19, 127.74, 127.75, 128.05, 128.16, 129.32, 129.83, 130.60, 135.03, 137.73, 139.20, 140.05, 141.49, 143.81, 150.04, 176.29, 190.76; ESI-MS: m/z = 390 $[M+H]^+$; anal. calcd. for $C_{27}H_{19}NO_2$: C 83.27, H 4.92, N 3.60; found: C 83.51, H 5.19, N 3.43.

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References

[1] For selected reviews on spirooxindoles, see: a) M. M. M. Santos, *Tetrahedron* **2014**, *70*, 9735–9757; b) A. Voituriez, A. Marinetti, M. Gicquel, *Synlett* **2015**, *26*, 142–166; c) D. Cheng, Y. Ishihara, B. Tan, C. F. Barbas III, *ACS Catal.* **2014**, *4*, 743–762; d) R. Narayan, M. Potowski, Z.-J. Jia, A. P. Antonchick, H. Waldmann, *Acc. Chem. Res.* **2014**, *47*, 1296–1310; e) A. K. Franz, N. V. Hanhan, N. R. Ball-Jones, *ACS Catal.* **2013**, *3*, 540–553; f) L. Hong, R. Wang, *Adv. Synth. Catal.* **2013**, *355*, 1023–1052; g) G. S. Singh, Z. Y. Desta, *Chem. Rev.* **2012**, *112*, 6104–6155; h) N. R. Ball-Jones, J. J. Badillo, A. K. Franz, *Org. Biomol. Chem.* **2012**, *10*, 5165–5181; i) B. M. Trost, M. K. Brennan, *Synthesis* **2009**, 3003–3025; j) C. V. Galliford, K. A. Scheidt, *Angew. Chem.* **2007**, *119*, 8902–8912; *Angew. Chem. Int. Ed.* **2007**, *46*, 8748–8758.

[2] For natural and biologically important six-membered carbocyclic spirooxindoles, see: a) H. Lin, S. J. Danishefsky, *Angew. Chem.* **2003**, *115*, 38–53; *Angew. Chem. Int. Ed.* **2003**, *42*, 36–51; b) A. Madin, C. J. O'Donnell, T. Oh, D. W. Old, L. E. Overman, M. J. Sharp, *J. Am. Chem. Soc.* **2005**, *127*, 18054–18065; c) C. Serradeil-Le Gal, C. Lacour, G. Valette, G. Garcia, L. Foulon, G. Galindo, L. Bankir, B. Pouzet, G. Guillon, C. Barberis, D. Chicot, S. Jard, P. Vilain, C. Garcia, E. Marty, D. Raufaste, G. Brossard, D. Nisato, J. P. Maffrand, G. Le Fur, *J. Clin. Invest.* **1996**, *98*, 2729–2738; d) H. Venkatesan, M. C. Davis, Y. Altas, J. P. Snyder, D. C. Liotta, *J. Org. Chem.* **2001**, *66*, 3653–3661; e) J.-J. Liu, Z. Zhang, *PCT Int. Appl.* WO2008/055812, **2008**; f) G. Bencivenni, L.-Y. Wu, A. Mazzanti, B. Giannichi, F. Pesciaioli, M.-P. Song, G. Bartoli, P. Melchiorre, *Angew. Chem.* **2009**, *121*, 7336–7339; *Angew. Chem. Int. Ed.* **2009**, *48*, 7200–7203; g) A. Fensome, R. Bender, J. Cohen, M. A. Collins, V. A. Mackner, L. L. Miller, J. W. Ullrich, R. Winneker, J. Wrobel, P. Zhang, Z. Zhang, Y. Zhu, *Bioorg. Med. Chem. Lett.* **2002**, *12*, 3487–3490; h) A. Fensome, W. R. Adams, A. L. Adams, T. J. Berrodin, J. Cohen, C. Huselton, A. Illenberger, J. C. Kern, V. A. Hudak, M. A. Marella, E. G. Melenski, C. C. McComas, C. A. Mugford, O. D. Slayden, M. Yudt, Z. Zhang, P. Zhang, Y. Zhu, R. C. Winneker, J. E. Wrobel, *J. Med. Chem.* **2008**, *51*, 1861–1873.

[3] For some selected synthesis of spirocarbocyclic oxindoles, see: a) F. Manoni, S. J. Connon, *Angew. Chem.* **2014**, *126*, 2666–2670; *Angew. Chem. Int. Ed.* **2014**, *53*, 2628–2632; b) Z. Bian, C. C. Marvin, M. Pettersson, S. F. Martin, *J. Am. Chem. Soc.* **2014**, *136*, 14184–14192; c) L.-W. Qi, Y. Yang, Y.-Y. Gui, Y. Zhang, F. Chen, F. Tian, L. Peng, L.-X. Wang, *Org. Lett.* **2014**, *16*, 6436–6439; d) Y.-J. Xie, J. Sun, C.-G. Yan, *ACS Comb. Sci.* **2014**, *16*, 271–280; e) E. V. Mercado-Marin, P. Garcia-Reynaga, S. Romminger, E. F. Pimenta, D. K. Romney, M. W. Lodewyk, D. E. Williams, R. J. Andersen, S. J. Miller, D. J. Tantillo, R. G. S. Berlinck, R. Sarpong, *Nature* **2014**, *509*, 318–324; f) S. Xu, C. Li, X. Jia, J. Li, *J. Org. Chem.* **2014**, *79*, 11161–11169; g) L.-Z. Ding, T.-S. Zhong, H. Wu, Y.-M. Wang, *Eur. J. Org. Chem.* **2014**, 5139–5143; h) M. Gicquel, C. Gomez, P. Retailleau, A. Voituriez, A. Marinetti, *Org. Lett.* **2013**, *15*, 4002–4005; i) Q.-Q. Zhou, X. Yuan, Y.-C. Xiao, L. Dong, Y.-C. Chen, *Tetrahedron* **2013**, *69*, 10369–10374; j) K. Jiang, Z.-J. Jia, S. Chen, L. Wu, Y.-C. Chen, *Chem. Eur. J.* **2010**, *16*, 2852–2856; k) Y. Wang, L. Liu, T. Zhang, N.-J. Zhong, D. Wang, Y.-J. Chen, *J. Org. Chem.* **2012**, *77*, 4143–4147; l) W. Sun, G. Zhu, C. Wu, L. Hong, R. Wang, *Chem. Eur. J.* **2012**, *18*, 13959–13963; m) K. A. P. Lingam, P. Shanmugam, K. Selvakumar, *Synlett* **2012**, *23*, 278–284; n) K. A. P. Lingam, A. B. Mandal, P. Shanmugam, *Tetrahedron Lett.* **2011**, *52*, 3610–3613; o) E. Richmond, N. Duguet, A. M. Z. Slawin, T. Lebl, A. D. Smith, *Org. Lett.* **2012**, *14*, 2762–2765; p) F. Zhong, X. Han, Y. Wang, Y. Lu, *Angew. Chem.* **2011**, *123*, 7983–7987; *Angew. Chem. Int. Ed.* **2011**, *50*, 7837–7841; q) G. Bencivenni, L.-Y. Wu, A. Mazzanti, B. Giannichi, F. Pesciaioli, M.-P. Song, G. Bartoli, P. Melchiorre, *Angew. Chem.* **2009**, *121*, 7336–7339; *Angew. Chem. Int. Ed.* **2009**, *48*, 7200–7203; r) X.-M. Shi, W.-P. Dong, L.-P. Zhu, X.-X. Jiang, R. Wang, *Adv. Synth. Catal.* **2013**, *355*, 3119–3123.

[4] For palladium-catalyzed synthesis of spirooxindoles, see: a) B. M. Trost, N. Cramer, S. M. Silverman, *J. Am. Chem. Soc.* **2007**, *129*, 12396–12397; b) B. M. Trost, D. A. Bringley, T. Zhang, N. Cramer, *J. Am. Chem. Soc.* **2013**, *135*, 16720–16735; c) R. T. Ruck, M. A. Huffman, M. M. Kim, M. Shevlin, W. V. Kandur, I. W. Davies, *Angew. Chem.* **2008**, *120*, 4789–4792; *Angew. Chem. Int. Ed.* **2008**, *47*, 4711–4714; d) T. Piou, L. Neuville, J. Zhu, *Angew. Chem.* **2012**, *124*, 11729–11733; *Angew. Chem. Int. Ed.* **2012**, *51*, 11561–11565; e) T.

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Piou, A. Bunescu, Q. Wang, L. Neuville, J. Zhu, *Angew. Chem.* **2013**, *125*, 12611–12615; *Angew. Chem. Int. Ed.* **2013**, *52*, 12385–12389; f) S. Jaegli, W. Erb, P. Retailleau, J.-P. Vors, L. Neuville, J. Zhu, *Chem. Eur. J.* **2010**, *16*, 5863–5867; g) S. Jaegli, J. Dufour, H.-I. Wei, T. Piou, X.-H. Duan, J.-P. Vors, L. Neuville, J. Zhu, *Org. Lett.* **2010**, *12*, 4498–4501; h) C. L. Ladd, D. S. Roman, A. B. Charette, *Org. Lett.* **2013**, *15*, 1350–1353; i) D. Katayev, Y.-X. Jia, A. K. Sharma, D. Banerjee, C. Besnard, R. B. Sunoj, E. P. Kundig, *Chem. Eur. J.* **2013**, *19*, 11916–11927; j) L. E. Overman, D. A. Watson, *J. Org. Chem.* **2006**, *71*, 2587–2599; k) A. Ashimori, B. Bachand, L. E. Overman, D. J. Poon, *J. Am. Chem. Soc.* **1998**, *120*, 6477–6487; l) A. Ashimori, L. E. Overman, *J. Org. Chem.* **1992**, *57*, 4571–4572; m) K. A. P. Lingam, P. Shanmugam, *Tetrahedron Lett.* **2013**, *54*, 4202–4206; n) R. Shintani, S.-y. Hayashi, M. Murakami, M. Takeda, T. Hayashi, *Org. Lett.* **2009**, *11*, 3754–3756; o) C. Tsukano, M. Okuno, Y. Takemoto, *Chem. Lett.* **2013**, *42*, 753–755; p) H. Kamisaki, Y. Yasui, Y. Takemoto, *Tetrahedron Lett.* **2009**, *50*, 2589–2592; q) S. M. Hande, M. Nakajima, H. Kamisaki, C. Tsukano, Y. Takemoto, *Org. Lett.* **2011**, *13*, 1828–1831; r) D. M. D′Souza, F. Rominger, T. J. J. Muller, *Angew. Chem.* **2005**, *117*, 156–161; *Angew. Chem. Int. Ed.* **2005**, *44*, 153–158; s) D. M. D′Souza, A. Kiel, D.-P. Herten, F. Rominger, T. J. J. Muller, *Chem. Eur. J.* **2008**, *14*, 529–547.

[5] K. H. Kim, H. R. Moon, J. Lee, J. N. Kim, *Adv. Synth. Catal.* **2015**, *357*, 701–708. During the palladium-catalyzed isomerization of **3a**-*EEE* the allylic carbocation **I** might be involved because of the stability of **I** by the nearby enamine and enolate moieties.

[6] H. R. Moon, K. H. Kim, J. Lee, J. N. Kim, *Bull. Korean Chem. Soc.* **2015**, *36*, 219–225.

[7] For general reviews on the MBH reaction, see: a) D. Basavaiah, A. J. Rao, T. Satyanarayana, *Chem. Rev.* **2003**, *103*, 811–891; b) D. Basavaiah, B. S. Reddy, S. S. Badsara, *Chem. Rev.* **2010**, *110*, 5447–5674; c) V. Singh, S. Batra, *Tetrahedron* **2008**, *64*, 4511–4574; d) S. Gowrisankar, H. S. Lee, S. H. Kim, K. Y. Lee, J. N. Kim, *Tetrahedron* **2009**, *65*, 8769–8780; e) M. Shi, F.-J. Wang, M.-X. Zhao, Y. Wei, *The Chemistry of the Morita–Baylis–Hillman Reaction*, RSC Publishing: Cambridge, **2011**.

[8] For synthetic applications of the ylides derived from MBH bromides, see: a) R. M. Crist, P. V. Reddy, B. Borhan, *Tetrahedron Lett.* **2001**, *42*, 619–621; b) M. M. Sa, L. Meier, *Heteroat. Chem.* **2013**, *24*, 384–391; c) R. Zhou, C. Wang, H. Song, Z. He, *Org. Lett.* **2010**, *12*, 976–979; d) C. Muthiah, K. S. Kumar, J. J. Vittal, K. C. K. Swamy, *Synlett* **2002**, 1787–1790; e) K. H. Kim, C. H. Lim, J. W. Lim, J. N. Kim, *Adv. Synth. Catal.* **2014**, *356*, 697–704; f) C. H. Lim, K. H. Kim, J. W. Lim, J. N. Kim, *Tetrahedron Lett.* **2013**, *54*, 5808–5813; g) C. H. Lim, S. H. Kim, K. H. Kim, J. N. Kim, *Tetrahedron Lett.* **2013**, *54*, 2476–2479; h) C. H. Lim, S. H. Kim, K. H. Park, J. Lee, J. N. Kim, *Tetrahedron Lett.* **2013**, *54*, 387–391.

[9] Although the separation of minor compound **3a**-*ZEE* failed, we expected that the 6π-electrocyclization of a crude reaction mixture of the Wittig reaction would produce the diastereomeric spirooxindole **5a**, albeit in low yield. As expected, the spirooxindole **5a** could be isolated in low yield (7%) along with **4a** (72%) as a major product when we used a crude mixture of **3a**-*EEE* and **3a**-*ZEE*. The result clearly shows that **3a**-*ZEE* was formed together as a minor product during the Wittig reaction of **1a** and **2a**. The two stereoisomers were produced in almost equal amounts for the allylidene derivatives in our previous paper;[5] however, one isomer (**3a**-*EEE*) was formed as a major product in this case and the reason is unclear at this stage.

[10] For our recent papers on 6π-electrocyclizations, see: a) J. W. Lim, K. H. Kim, S. H. Kim, J. N. Kim, *Tetrahedron Lett.* **2012**, *53*, 5449–5454; b) J. W. Lim, K. H. Kim, S. H. Kim, J. N. Kim, *Tetrahedron Lett.* **2013**, *54*, 2595–2599; c) J. W. Lim, K. H. Kim, S. H. Kim, J. N. Kim, *Tetrahedron* **2014**, *70*, 6831–6840.

[11] For the palladium-catalyzed double bond isomerization and a following 6π-electrocyclization, see: a) J. E. Moses, J. E. Baldwin, R. Marquez, R. M. Adlington, A. R. Cowley, *Org. Lett.* **2002**, *4*, 3731–3734; b) S. Bruckner, J. E. Baldwin, R. M. Adlington, T. D. W. Claridge, B. Odell, *Tetrahedron* **2004**, *60*, 2785–2788.

[12] CCDC 1020657 (**5a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

[13] The stereochemistry of **4b–4g** and **5b–5g** was assigned based on the chemical shift of the proton at the C-6′ position. The protons of **5a–5g** appeared downfield ($\delta = 4.57$–4.65 ppm for **5a**, **5b** and **5d–5g**; $\delta = 4.12$ ppm for **5c**) relative to those of **4a–4g** ($\delta = 4.19$–4.33 ppm for **4a**, **4b** and **4d–4g**; $\delta = 3.62$ ppm for **4c**) presumably due to anisotropy of the carbonyl (C=O) group of oxindole moiety.

[14] For palladium-catalyzed oxidative arylation, see: a) L. Zhou, W. Lu, *Chem. Eur. J.* **2014**, *20*, 634–642; b) J. L. Bras, J. Muzart, *Chem. Rev.* **2011**, *111*, 1170–1214; c) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215–1292; d) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu, *Angew. Chem.* **2009**, *121*, 5196–5217; *Angew. Chem. Int. Ed.* **2009**, *48*, 5094–5115; e) H. S. Lee, K. H. Kim, S. H. Kim, J. N. Kim, *Adv. Synth. Catal.* **2012**, *354*, 2419–2426, and further references cited therein; f) H. J. Lee, K. H. Kim, S. H. Kim, J. N. Kim, *Tetrahedron Lett.* **2013**, *54*, 170–175.

[15] For palladium-catalyzed arylation using the Pd/AgOAc/PivOH system, see: a) S. H. Kim, K. H. Kim, H. J. Lee, J. N. Kim, *Tetrahedron Lett.* **2013**, *54*, 329–334, and further references cited therein for the conditions employing PivOH as a proton shuttle during the aryl C–H activation; b) K. H. Kim, J. W. Lim, H. J. Lee, J. N. Kim, *Tetrahedron Lett.* **2013**, *54*, 419–423; c) K. H. Kim, S. Lee, S. H. Kim, C. H. Lim, J. N. Kim, *Tetrahedron Lett.* **2012**, *53*, 5088–5093; d) K. H. Kim, H. S. Lee, S. H. Kim, J. N. Kim, *Tetrahedron Lett.* **2012**, *53*, 2761–2764; e) K. H. Kim, H. S. Lee, S. H. Kim, J. N. Kim, *Tetrahedron Lett.* **2012**, *53*, 1323–1327; f) D.-J. Tang, B.-X. Tang, J.-H. Li, *J. Org. Chem.* **2009**, *74*, 6749–6755.

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[16] CCDC 1020658 (**6a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.
[17] CCDC 1039494 (**8**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.
[18] For conversion of spirooxindoles to phenanthridone derivatives, see: a) E. M. Beccalli, F. Clerici, M. L. Gelmi, *Tetrahedron* **1999**, *55*, 8579–8586; b) E. M. Beccalli, F. Clerici, M. L. Gelmi, *Tetrahedron* **2003**, *59*, 4615–4622; c) G. Rousseau, F. Robert, Y. Landais, *Chem. Eur. J.* **2009**, *15*, 11160–11173; d) H. Iwasaki, T. Eguchi, N. Tsutsui, H. Ohno, T. Tanaka, *J. Org. Chem.* **2008**, *73*, 7145–7152.
[19] For β-carbon elimination, see: a) T. Satoh, M. Miura, *Top. Organomet. Chem.* **2005**, *14*, 1–20; b) K. Ruhland, *Eur. J. Org. Chem.* **2012**, 2683–2706; c) K. H. Kim, S. H. Kim, H. J. Lee, J. N. Kim, *Adv. Synth. Catal.* **2013**, *355*, 1977–1983; d) Y. Nagao, A. Ueki, K. Asano, S. Tanaka, S. Sano, M. Shiro, *Org. Lett.* **2002**, *4*, 455–457; e) Y. Terao, H. Wakui, T. Satoh, M. Miura, M. Nomura, *J. Am. Chem. Soc.* **2001**, *123*, 10407–10408; f) Y. Terao, H. Wakui, M. Nomoto, T. Satoh, M. Miura, M. Nomura, *J. Org. Chem.* **2003**, *68*, 5236–5243; g) M. Catellani, G. P. Chiusoli, *J. Organomet. Chem.* **1983**, *247*, C59–C62.
[20] For selected examples of seven-membered palladacycles, see: a) J.-X. Yan, H. Li, X.-W. Liu, J.-L. Shi, X. Wang, Z.-J. Shi, *Angew. Chem.* **2014**, *126*, 5045–5049; *Angew. Chem. Int. Ed.* **2014**, *53*, 4945–4949; b) T. Saget, N. Cramer, *Angew. Chem.* **2012**, *124*, 13014–13017; *Angew. Chem. Int. Ed.* **2012**, *51*, 12842–12845; c) S. Rousseaux, B. Liegault, K. Fagnou, *Chem. Sci.* **2012**, *3*, 244–248.
[21] For thionation with Lawesson's reagent, see: a) T. Ozturk, E. Ertas, O. Mert, *Chem. Rev.* **2007**, *107*, 5210–5278; b) M. P. Cava, M. I. Levinson, *Tetrahedron* **1985**, *41*, 5061–5087; c) M. Jesberger, T. P. Davis, L. Barner, *Synthesis* **2003**, 1929–1958; d) R. S. Varma, D. Kumar, *Org. Lett.* **1999**, *1*, 697–700.
[22] For the similar 1-thia-9-azafluorene derivatives, see: a) X. Chen, Z.-H. Qi, S.-Y. Zhang, L.-P. Kong, Y. Wang, X.-W. Wang, *Org. Lett.* **2015**, *17*, 42–45; b) M. Jha, C. Davis, J. Fazzari, M. Vitali, *Tetrahedron Lett.* **2014**, *55*, 7043–7046.

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