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Diastereoselective Synthesis of Functionalized Spirocyclopropyl Oxindoles via $P(NMe_2)_3$-Mediated Reductive Cyclopropanation

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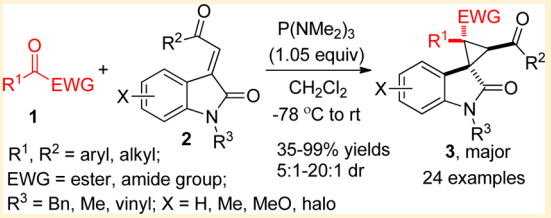
Supporting Information

ABSTRACT: A $P(NMe_2)_3$-mediated reductive cyclopropanation reaction of α-keto esters or amides with isatin-derived alkenes has been developed, providing efficient and diastereoselective synthesis of highly functionalized spirocyclopropyl oxindoles bearing two all-carbon quaternary centers. This reaction also represents a complementary and nonmetal-involving protocol for the challenging cyclopropanation of electron-deficient alkenes.



Spirocyclic oxindoles are important molecular architectures frequently present in a diverse range of natural products and pharmaceutical molecules.[1] This class of frameworks has accordingly attracted much interest from chemists due to their biological importance and the challenge embodied in their synthesis.[2] As a representative member of the spirocyclic oxindole cores, the spirocyclopropyl oxindole skeleton has its own appealing values and features with regard to its bioactivities and versatility.[3−5] For example, spirocyclopropyl oxindoles **A** and **B** exhibited nanomolar level activities as HIV-1 non-nucleoside reverse transcriptase inhibitors toward both wild-type and drug-resistant mutant viruses,[3] whereas a group of compounds of formula **C** showed distinct antitumor activity and also effectiveness in the treatment of obesity and diabetes (Figure 1).[4] Additionally, owing to the existence of the highly

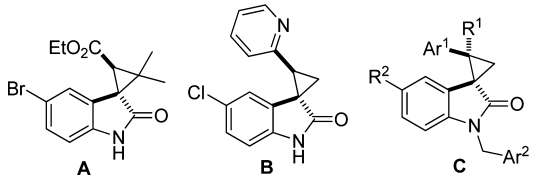
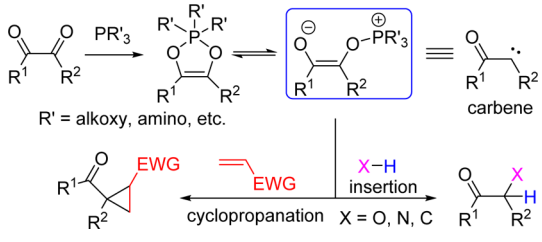


Figure 1. Representative bioactive spirocyclopropyl oxindoles.

strained cyclopropane moiety, spirocyclopropyl oxindoles are also proven to be versatile building blocks in syntheses of complex molecules such as natural spirotryprostatin B and welwitindolinone alkaloids.[5] Thus, substantial research efforts have been directed toward the construction of the spirocyclopropyl oxindole core and a number of efficient methods have been developed in both racemic and asymmetric fashions.[2,6,7] Among the reported methods, the transition-metal-catalyzed cyclopropanation of olefins with common substrates diazo oxindoles has emerged as a straightforward protocol to access spirocyclopropyl oxindoles.[6] But this protocol is only applicable to the relatively electron-rich olefins since the cyclopropanation of electron-deficient olefins with transition metal carbenoids remains challenging.[8] Fortunately, several organocatalytic cyclopropanation reactions of specifically functionalized substrates have unveiled sporadic and complementary successes in the synthesis of spirocyclopropyl oxindoles bearing electron-withdrawing groups.[7] Even though such encouraging progress has been made, developing new and efficient synthetic methods for spirocyclopropyl oxindole cores, particularly bearing electron-deficient groups, from readily available starting materials is still highly desirable.

1,2-Dicarbonyl compounds such as α-keto esters are versatile building blocks in organic synthesis due to their specific functionality-enriched structures.[9] It is well documented that 1,2-dicarbonyl compounds readily undergo the Kukhtin−Ramirez addition with trivalent phosphorus reagents to produce the five-coordinate 1,3,2-dioxaphospholene adducts, which are presumably in equilibrium with the four-coordinate dipolar phosphonium enolate species (Scheme 1).[9a,10] Through the dipolar structure, the Kukhtin−Ramirez adducts have exhibited a rich reaction chemistry,[11] particularly serving as

Scheme 1. Typical Reactivity of the Kukhtin−Ramirez Adducts



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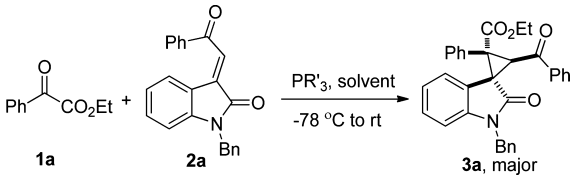
carbene surrogates.[12,13] In early 1971, Foucaud and co-workers first demonstrated a cyclopropanation reaction between the adduct trimethoxy-1,3,2-dioxaphospholene and benzylidene malononitriles to give polysubstituted cyclopropanes under mild conditions.[12a] Subsequently, Fauduet et al. successfully validated this cyclopropanation reaction for other simple electron-deficient alkenes by using the Kukhtin−Ramirez adducts derived from hexamethylphosphorous triamide.[12b] This phosphorus reagents-mediated cyclopropanation therefore illustrated a facile synthetic route to cyclopropane motifs from electron-poor alkenes although the reported reaction generally lacked stereoselectivity. However, after the initial disclosures, the cyclopropanation reaction and its potential in organic synthesis had not been further explored over the past decades.[12c] Recently, the renewed interest from the Radosevich research group has unveiled that the Kukhtin−Ramirez adducts could serve as carbene equivalents to engage in a couple of formal X−H bond (X = O, N, C) insertions, affording α-functionalized carbonyl derivatives in a metal-free fashion.[13] Furthermore, the same group has also developed a reductive homocondensation of the vinyl-substituted α-dicarbonyl substrates. The transformation is believed to be initiated by the Kukhtin−Ramirez addition of hexamethylphosphorous triamide to the dicarbonyl substrate.[11g] Intrigued by the attractive reactivity of the Kukhtin−Ramirez adducts and also motivated by the challenging goal to synthesize spirocyclopropyl oxindole cores bearing electron-deficient functional groups, we envisioned that a trivalent phosphorus reagent-mediated reductive cyclopropanation between 1,2-dicarbonyl compounds and isatin-derived electron-deficient alkenes would furnish a practical and efficient protocol to construct such spirocyclopropyl oxindoles. Herein, we report the results from such an investigation in detail.

We initiated our research with the substrates ethyl 2-oxo-2-phenylacetate **1a** and (*E*)-1-benzyl-3-(2-oxo-2-phenylethylidene) indolin-2-one **2a** (Table 1). To our delight, under predetermined conditions as listed in Table 1, a

Table 1. Survey on the Model Reaction Conditions[a]



1a **2a** **3a**, major

entry	solvent	PR'_3	yield (%)[b]	dr[c]
1	THF	$P(NMe_2)_3$	82	10:1
2	ether	$P(NMe_2)_3$	75	10:1
3	toluene	$P(NMe_2)_3$	79	14:1
4	CH_2Cl_2	$P(NMe_2)_3$	95	11:1
5	CH_2Cl_2	$P(OMe)_3$	64	7:1
6	CH_2Cl_2	PPh_3	trace	–
7	CH_2Cl_2	PBu_3	trace	–
8	CH_2Cl_2	$P(NMe_2)_3$	80	11:1[d]

[a]Conditions: under a N_2 atmosphere, a solution of phosphorus agent (0.21 mmol) in solvent (0.5 mL) was dropwise added to a stirred mixture of **1a** (36 mg, 0.2 mmol) and **2a** (71 mg, 0.21 mmol) in solvent (1.5 mL) at −78 °C. The resulting mixture was then slowly warmed to rt by removing the cooling bath and stirred at rt for 22 h. [b]Isolated yield. [c]Determined by H^1 NMR assay of the isolated product. [d]**1a** (38 mg, 0.21 mmol) and **2a** (68 mg, 0.2 mmol) were used.

$P(NMe_2)_3$-mediated model reaction between **1a** (0.2 mmol) and **2a** (0.21 mmol) afforded the expected cyclopropanation product, spirocyclopropyl oxindole **3a**, in 82% yield and 10:1 dr after column chromatographic isolation (Table 1, entry 1). The structure and relative stereochemistry of **3a** have been determined by its X-ray single crystal diffraction (see Supporting Information). This encouraging result confirmed the feasibility of the phosphorus reagent-mediated reductive cyclopropanation of α-keto esters with isatin-derived electron-deficient alkenes and also validated a new approach to highly functionalized spirocyclopropyl oxindoles as well. To further improve the reaction efficiency, a brief survey on the model reaction conditions was carried out (Table 1). Solvent screening indicated that CH_2Cl_2 was the preferred reaction medium, although such common solvents as THF, ether, and toluene were also effective and gave good results (entries 1−4). Among a couple of trivalent phosphorus agents examined, $P(NMe_2)_3$ remained the best. Trimethyl phosphite gave a moderate yield (entry 5), whereas phosphines such as triphenylphosphine and tributylphosphine were almost ineffective to this transformation (entries 6 and 7). Modifying the molar ratio of **1a**/**2a** to 1.05:1 resulted in a slight decrease in the yield (entry 8). Thus, the preferable conditions for the model cyclopropanation reaction were established as listed in Table 1.

With the optimized conditions in hand, the substrate scope of this cyclopropanation reaction was investigated (Table 2). With α-keto ester **1a** employed as a representative reactant, a variety of isatin-derived electron-deficient alkenes **2** were first explored. The variation of the substituent R^2 attached to the acyl group in **2** was checked. Both aryl- and heteroaryl-substituted alkenes **2** smoothly afforded their corresponding cyclopropanation products **3** in moderate to excellent yields and good to excellent diastereoselectivity (entries 1−7). Aliphatic methyl-substituted alkene **2h** also uneventfully gave its cyclopropanation product **3h** in 85% yield and excellent diastereoselectivity (entry 8). Different substituents X on the aromatic ring of the oxindole framework in **2** were further examined. Both electron-donating and -withdrawing substituents X were well tolerated. In the examined cases, the substrates **2i**−**l** readily gave out their corresponding cyclopropanation products in good yields and diastereoselectivity (entries 9−12). Other substituents R^3 at the nitrogen atom other than a benzyl group in **2** were also surveyed (entries 13 and 14). Both vinyl- and methyl-substituted oxindole derivatives **2m** and **2n** were all capable of delivering their normal cyclopropanation products, although the former gave a slightly lower yield and stereoselectivity (entries 13 and 14).

Differently substituted α-keto esters **1** were further tested in the cyclopropanation reactions with representative isatin-derived electron-deficient alkenes **2a** and **2i**. Under the standard conditions, aryl- and heteroaryl-substituted α-keto esters **1b**−**g** all smoothly afforded their corresponding cyclopropanation products **3** in moderate to excellent yields with good diastereoselectivity (Table 2, entries 15−20). However, ethyl pyruvate **1h** (R^1 = Me) only brought about a complex mixture (entry 21). Notably, the efficiency of this reductive cyclopropanation was further confirmed by a 1.0 mmol scale reaction of **1a** and **2a**, which gave product **3a** in 89% yield and 11:1 dr (entry 22).

The vinyl-substituted α-keto esters **1** were also surveyed (Scheme 2). In Radosevich's study, the vinyl-substituted α-keto ester **1i** was reported to undergo homocondensation with itself

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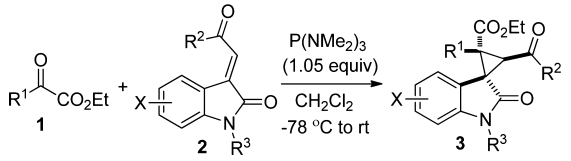
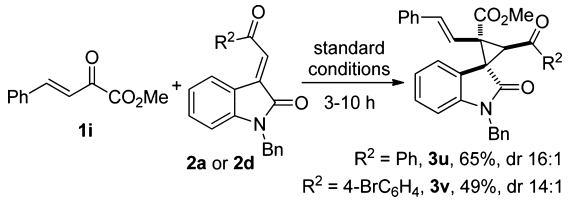
Table 2. Synthesis of Highly Functionalized Spirocyclopropyl Oxindoles[a]



entry	R^1 in **1**	R^2, X, R^3 in **2**	time (h)	yield (%)[b]	dr[c]
1	Ph (**1a**)	Ph, H, Bn (**2a**)	22	**3a**, 95	11:1
2	Ph	4-MeOC$_6$H$_4$, H, Bn (**2b**)	24	**3b**, 85	11:1
3	Ph	4-CF$_3$C$_6$H$_4$, H, Bn (**2c**)	12	**3c**, 75	20:1
4	Ph	4-BrC$_6$H$_4$, H, Bn (**2d**)	12	**3d**, 67	10:1
5	Ph	2-naphthyl, H, Bn (**2e**)	22	**3e**, 77	20:1
6	Ph	2-thienyl, H, Bn (**2f**)	20	**3f**, 93	14:1
7	Ph	3-pyridyl, H, Bn (**2g**)	21	**3g**, 99	20:1
8	Ph	Me, H, Bn (**2h**)	48	**3h**, 85	20:1
9	Ph	Ph, 5-MeO, Bn (**2i**)	21	**3i**, 96	8:1
10	Ph	Ph, 5-Me, Bn (**2j**)	24	**3j**, 99	10:1
11	Ph	Ph, 6-Br, Bn (**2k**)	5	**3k**, 99	5:1
12	Ph	Ph, 7-Cl, Bn (**2l**)	24	**3l**, 62	11:1
13	Ph	Ph, H, vinyl (**2m**)	20	**3m**, 62	5:1
14	Ph	Ph, H, Me (**2n**)	20	**3n**, 95	14:1
15	4-MeC$_6$H$_4$ (**1b**)	**2a**	22	**3o**, 92	20:1
16	4-FC$_6$H$_4$ (**1c**)	**2a**	18	**3p**, 91	11:1
17	4-ClC$_6$H$_4$ (**1d**)	**2a**	24	**3q**, 92	14:1
18	4-BrC$_6$H$_4$ (**1e**)	**2a**	11	**3r**, 95	14:1
19	2-naphthyl (**1f**)	**2a**	24	**3s**, 40	10:1
20	2-thienyl (**1g**)	**2i**	10	**3t**, 85	5:1
21	Me (**1h**)	**2a**	24	complex	–
22	Ph (**1a**)	**2a**	22	89	11:1[d]

[a]For a typical procedure, see Experimental Section. [b]Isolated yield. [c]Determined by H^1 NMR assay of the isolated product and referring to the major isomer versus the sum of others. [d]Run on a 1.0 mmol scale.

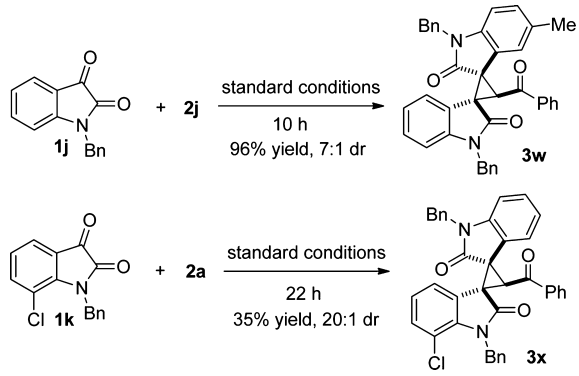
Scheme 2. Cyclopropanations of Vinyl-Substituted α-Keto Ester 1i



under the mediation of P(NMe$_2$)$_3$ in toluene.[11g] In this study, the ester **1i** was found to be a viable substrate for the cyclopropanation reaction. Under the standard conditions, the cyclopropanations of **1i** with alkenes **2a** and **2d** readily gave the normal spirooxindole products **3u** and **3v** in modest yields and high diastereoselectivity, although some unidentified byproducts were observed as well (Scheme 2). This result indicates that the plausible Kukhtin–Ramirez adduct from α-keto ester **1i** and P(NMe$_2$)$_3$ prefers to condense with the isatin-derived alkenes **2** rather than with the vinyl-substituted α-keto esters **1i**. It is also noteworthy that vinylcyclopropanes are often useful intermediates in various organic transformations.[14]

Gratifyingly, the substrate scope of this cyclopropanation could be even expanded to isatins which represent cyclic 1,2-dicarbonyl compounds. As shown in Scheme 3, when *N*-Bn

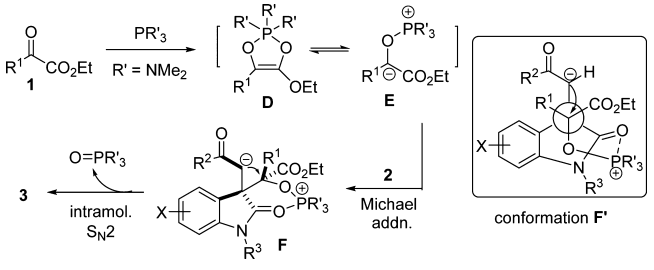
Scheme 3. Synthesis of Bis-spirooxindoles



isatin **1j** and its 7-chloro analog **1k** were respectively reacted with alkenes **2j** and **2a** under the standard conditions, the corresponding bis-spirooxindoles[7d] **3w** and **3x** were readily obtained. The structure and relative configuration of **3x** were confirmed by X-ray crystallographic analysis. All spirocyclic compounds **3** in this study were fully characterized by ^{1}H, ^{13}C NMR and HRMS-ESI measurements, and the stereochemistry assignments for other compounds **3b–v** and **3w** were made by analogy with representatives **3a** and **3x** (also see Supporting Information). Thus, the P(NMe$_2$)$_3$-mediated reductive cyclopropanation of α-keto esters **1** with isatin-derived electron-deficient alkenes **2** has a flexible substrate scope and accordingly constitutes a simple and efficient synthetic method for highly functionalized spirocyclopropyl oxindoles **3** bearing two all-carbon quaternary centers.[15]

Although an accurate interpretation of the mechanism and stereochemistry of the cyclopropanation reaction remains elusive, according to the experimental observation in this study and the closely related reports,[9a,10c,11g,12,13] a proposed formation mechanism for spirocyclopropyl oxindoles **3** is depicted in Scheme 4. Presumably, the cyclopropanation is

Scheme 4. Formation of 3



initiated with the Kukhtin–Ramirez addition of hexamethylphosphorous triamide to α-keto ester **1** to generate the dipolar intermediate **E**.[10c,11g,13] Subsequently, a Michael addition of intermediate **E** to isatin-derived electron-deficient alkene **2** leads to intermediate **F**, which prefers to adopt a sterically favored conformation **F′** to complete the cyclization step through an intramolecular S$_N$2 displacement to give cyclopropanation product **3** and release the byproduct phosphoric

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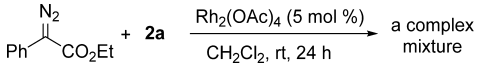
triamide. We believed that the stereochemistry outcome in **3** should be governed by the steric requirement of an S_N2 displacement and the Coulombic interaction between the phosphonium cation and the oxygen atom of the amide carbonyl in intermediate **F**.[16] Recently, it was reported by Bogdanov et al. that α-ketocarbene intermediates were most likely formed from the deoxygenation of 1,2-dicarbonyl compounds including *N*-alkyl isatins by hexaethylphosphorous triamide.[12c] Consequently, a mechanism involving such an α-ketocarbene intermediate in the cyclopropanation may not be completely ruled out. In view of the weak cyclopropanation reactivity of electrophilic carbenoids with electron-deficient alkenes,[8] the carbene intermediate-involved mechanism for this cyclopropanation may be therefore considered a remote possibility.

In our control experiment (Scheme 5), the reaction of ethyl α-diazo acetate and alkene **2a** failed to give out the cyclopropanation product under a favored condition for formation of carbenoids.[17] This result clearly indicated that the cyclopropanation of an electron-deficient alkene such as **2a** by a metal carbenoid strategy was infeasible. Thus, this $P(NMe_2)_3$-mediated reductive cyclopropanation reaction represents a complementary and efficient protocol for the cyclopropanation of electron-deficient alkenes under metal-free conditions.

Scheme 5. Control Experiment



CONCLUSION

In summary, we have developed a convenient and efficient method to construct highly functionalized spirocyclopropyl oxindole cores from readily available α-keto esters or amides and isatin-derived electron-deficient alkenes. This method originates from the characteristic reaction chemistry of the Kukhtin−Ramirez adducts of 1,2-dicarbonyl compounds and trivalent phosphorus reagents such as $P(NMe_2)_3$. It represents a complementary and nonmetal-involving cyclopropanation protocol that is particularly suitable for electron-deficient alkene substrates and accordingly provides an easy access to biologically important spirocyclopropyl oxindoles bearing electron-withdrawing functional groups. The formation of the spirocyclic skeleton is most likely through a tandem sequence of Michael addition/intramolecular S_N2 displacement, which is triggered by the *in situ* generated Kukhtin−Ramirez adduct. Given its merits including high efficiency, good diastereoselectivity, good generality, and easy handling, we anticipate this method should find its potential application in the preparation of spirocyclopropyl oxindole derivatives in the future.

EXPERIMENTAL SECTION

Unless otherwise noted, all reactions were carried out in a nitrogen atmosphere. Solvents were purified prior to use according to conventional procedures. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ with tetramethylsilane (TMS) as the internal standard. HRMS spectra were acquired in the ESI mode (positive ion) with the mass analyzer of TOF used. Column chromatography was performed on silica gel (200−300 mesh) using a mixture of petroleum ether/ethyl acetate as eluant. α-Keto esters **1** were prepared through the Friedel−Crafts acylation reactions.[18] Isatin-derived electron-deficient alkenes were prepared according to literature methods from corresponding isatins.[19]

General Procedure for the $P(NMe_2)_3$-Mediated Reductive Cyclopropanation (Table 2 and Schemes 2, 3). Under a N_2 atmosphere and at −78 °C, a solution of $P(NMe_2)_3$ (38 μL, 0.21 mmol) in CH_2Cl_2 (0.5 mL) was dropwise added by means of a syringe to a stirred solution of α-keto ester **1** (0.2 mmol) and isatin-derived electron-deficient alkene **2** (0.21 mmol) in CH_2Cl_2 (1.5 mL). The resulting mixture was then slowly warmed up to room temperature and stirred at rt until **1** was completely consumed, as monitored by TLC. The solvent was removed on a rotary evaporator under reduced pressure, and the residue was subjected to column chromatographic isolation on silica gel (gradient elution, petroleum ether (bp 60−90 °C)/ethyl acetate 15:1−5:1) to give product **3**.

*Ethyl 3-Benzoyl-1′-benzyl-2′-oxo-2-phenylspiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3a**).* Following the general procedure, α-keto ester **1a** (36 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2a** (71 mg, 0.21 mmol) were employed to give product **3a** (95 mg, 95% yield, 11:1 dr) as a white solid; mp 141−142 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 7.4 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 2H), 7.37−7.27 (m, 6H), 7.21 (t, *J* = 7.8 Hz, 2H), 7.15 (t, *J* = 7.7 Hz, 1H), 7.09 (d, *J* = 7.5 Hz, 2H), 6.86−6.75 (m, 2H), 6.63 (d, *J* = 7.8 Hz, 1H), 5.14 (d, *J* = 15.8 Hz, 1H), 4.94 (d, *J* = 15.8 Hz, 1H), 4.50 (s, 1H), 4.27−4.14 (m, 2H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.5, 173.1, 169.0, 143.5, 138.3, 135.7, 133.6, 131.7, 129.5, 128.9, 128.8, 128.7, 128.6, 128.5, 128.1, 127.9, 127.6, 127.1, 121.7, 121.4, 108.8, 62.2, 52.0, 44.2, 43.4, 41.9, 13.9; HRMS−ESI $[M + H]^+$ Calcd for $C_{33}H_{28}NO_4$ 502.2013, found 502.2012.

*Ethyl 1′-Benzyl-3-(4-methoxybenzoyl)-2′-oxo-2-phenylspiro-[cyclopropane-1,3′-indoline]-2-carboxylate (**3b**).* Following the general procedure, α-keto ester **1a** (36 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2b** (77 mg, 0.21 mmol) were employed to give product **3b** (90 mg, 85% yield, 11:1 dr) as a light yellow solid; mp 190−191 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.6 Hz, 2H), 7.39−7.30 (m, 6H), 7.22 (t, *J* = 7.7 Hz, 2H), 7.16 (t, *J* = 7.7 Hz, 1H), 7.11 (d, *J* = 7.8 Hz, 2H), 7.04 (d, *J* = 7.6 Hz, 2H), 6.81 (t, *J* = 7.6 Hz, 2H), 6.61 (d, *J* = 8.1 Hz, 1H), 5.16 (d, *J* = 15.8 Hz, 1H), 4.96 (d, *J* = 15.8 Hz, 1H), 4.48 (s, 1H), 4.29−4.16 (m, 2H), 3.94 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.8, 173.3, 169.2, 163.9, 143.4, 135.8, 131.7, 131.5, 130.9, 129.8, 128.8, 128.7, 128.6, 128.1, 127.9, 127.6, 127.2, 121.9, 121.3, 114.0, 108.8, 62.1, 55.5, 51.8, 44.2, 43.1, 41.7, 13.9; HRMS−ESI $[M + H]^+$ Calcd for $C_{34}H_{30}NO_5$ 532.2118, found 532.2122.

*Ethyl 1′-Benzyl-2′-oxo-2-phenyl-3-(4-(trifluoromethyl)benzoyl)-spiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3c**).* Following the general procedure, α-keto ester **1a** (36 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2c** (86 mg, 0.21 mmol) were employed to give product **3c** (85 mg, 75% yield, 20:1 dr) as a white solid; mp 185−187 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 8.2 Hz, 2H), 7.81 (d, *J* = 8.2 Hz, 2H), 7.34 (d, *J* = 4.3 Hz, 4H), 7.33−7.26 (m, 2H), 7.22 (t, *J* = 7.8 Hz, 2H), 7.17 (t, *J* = 7.7 Hz, 1H), 7.05 (d, *J* = 7.4 Hz, 2H), 6.85−6.78 (m, 2H), 6.61 (d, *J* = 7.5 Hz, 1H), 5.14 (d, *J* = 15.7 Hz, 1H), 4.93 (d, *J* = 15.7 Hz, 1H), 4.47 (s, 1H), 4.28−4.12 (m, 2H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.7, 172.9, 168.8, 143.6, 140.8, 135.7, 134.9 (q, *J* = 32.8 Hz), 131.7, 129.3, 128.9, 128.8, 128.7, 128.6, 128.3, 128.2, 127.7, 127.2, 126.0 (q, *J* = 3.6 Hz), 123.6 (q, *J* = 272.8 Hz), 121.5, 121.4, 108.9, 62.3, 52.3, 44.3, 43.6, 41.9, 13.9; HRMS−ESI $[M + H]^+$ Calcd for $C_{34}H_{27}F_3NO_4$ 570.1887, found 570.1893.

*Ethyl 1′-Benzyl-3-(4-bromobenzoyl)-2′-oxo-2-phenylspiro[cyclo-propane-1,3′-indoline]-2-carboxylate (**3d**).* Following the general procedure, α-keto ester **1a** (36 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2d** (88 mg, 0.21 mmol) were employed to give product **3d** (78 mg, 67% yield, 10:1 dr) as a white solid; mp 153−154 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.5 Hz, 2H), 7.68 (d, *J* = 8.5 Hz, 2H), 7.34 (d, *J* = 4.3 Hz, 4H), 7.32−7.25 (m, 2H), 7.21 (t, *J* = 7.7 Hz, 2H), 7.15 (t, 7.7 Hz, 1H), 7.05 (d, *J* = 7.3 Hz, 2H), 6.85−6.76 (m, 2H), 6.58 (d, *J* = 7.6 Hz, 1H), 5.14 (d, *J* = 15.7 Hz, 1H), 4.92 (d, *J* = 15.7 Hz, 1H), 4.42 (s, 1H), 4.27−4.11 (m, 2H), 1.23

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(t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.6, 172.9, 168.9, 143.5, 136.9, 135.6, 132.2, 131.6, 130.0, 129.4, 129.0, 128.8, 128.7, 128.6, 128.1, 128.0, 127.7, 127.1, 121.5, 121.4, 108.9, 62.2, 52.1, 44.2, 43.3, 41.7, 13.9; HRMS−ESI $[M + H]^+$ Calcd for $C_{33}H_{27}BrNO_4$ 580.1118, found 580.1123.

*Ethyl 3-(2-Naphthoyl)-1′-benzyl-2′-oxo-2-phenylspiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3e**).* Following the general procedure, α-keto ester **1a** (36 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2e** (82 mg, 0.21 mmol) were employed to obtain product **3e** (85 mg, 77% yield, 20:1) as a white solid; mp 156−157 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67−8.59 (m, 2H), 8.05 (d, J = 8.2 Hz, 1H), 7.91−7.85 (m, 1H), 7.62 (t, J = 7.5 Hz, 1H), 7.55−7.47 (m, 2H), 7.39−7.27 (m, 5H), 7.27−7.14 (m, 6H), 6.91 (d, J = 6.8 Hz, 1H), 6.88−6.80 (m, 2H), 5.15 (d, J = 15.7 Hz, 1H), 4.93 (d, J = 15.7 Hz, 1H), 4.54 (s, 1H), 4.28−4.13 (m, 2H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.0, 173.1, 169.1, 143.6, 136.2, 135.7, 133.9, 133.6, 131.8, 130.1, 129.8, 129.5, 129.2, 128.8, 128.5, 128.4, 128.2, 128.1, 128.0, 127.6, 127.2, 126.5, 125.7, 124.7, 121.8, 121.5, 108.8, 62.1, 52.2, 44.8, 44.4, 44.2, 13.9; HRMS−ESI $[M + H]^+$ Calcd for $C_{37}H_{30}NO_4$ 552.2169, found 552.2162.

*Ethyl 1′-Benzyl-2′-oxo-2-phenyl-3-(thiophene-2-carbonyl)spiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3f**).* Following the general procedure, α-keto ester **1a** (36 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2f** (73 mg, 0.21 mmol) were employed to obtain product **3f** (94 mg, 93% yield, 14:1 dr) as a light yellow solid; mp 160−162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (dd, J = 3.8, 0.9 Hz, 1H), 7.70 (dd, J = 4.9, 0.9 Hz, 1H), 7.37−7.27 (m, 6H), 7.25−7.20 (m, 3H), 7.16−7.08 (m, 3H), 6.82−6.76 (m, 2H), 6.70−6.65 (m, 1H), 5.14 (d, J = 15.8 Hz, 1H), 4.92 (d, J = 15.8 Hz, 1H), 4.42 (s, 1H), 4.25−4.10 (m, 2H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.7, 173.0, 168.8, 145.7, 143.5, 135.7, 134.7, 133.3, 131.7, 129.4, 128.8, 128.6, 128.0, 127.6, 127.1, 121.6, 121.4, 108.8, 62.1, 51.4, 44.2, 43.5, 41.9, 13.9; HRMS−ESI $[M + H]^+$ Calcd for $C_{31}H_{26}NO_4S$ 508.1577, found 508.1574.

*Ethyl 1′-Benzyl-3-nicotinoyl-2′-oxo-2-phenylspiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3g**).* Following the general procedure, α-keto ester **1a** (36 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2g** (72 mg, 0.21 mmol) were employed to yield product **3g** (99 mg, 99% yield, 20:1 dr) as a red solid; mp 139−140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.45 (br s, 1H), 8.87 (br s, 1H), 8.58 (d, J = 7.9 Hz, 1H), 7.53−7.48 (m, 1H), 7.38−7.20 (m, 8H), 7.16 (t, J = 7.6 Hz, 1H), 7.06 (d, J = 7.5 Hz, 2H), 6.86−6.79 (m, 2H), 6.63 (d, J = 7.6 Hz, 1H), 5.14 (d, J = 15.7 Hz, 1H), 4.92 (d, J = 15.7 Hz, 1H), 4.45 (s, 1H), 4.26−4.15 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.5, 172.9, 168.8, 153.6, 149.6, 143.6, 136.1, 135.7, 133.6, 131.7, 129.2, 128.9, 128.8, 128.6, 128.3, 128.2, 127.8, 127.2, 123.9, 121.5, 121.4, 109.0, 62.3, 52.3, 44.2, 43.6, 41.7, 13.9; HRMS−ESI $[M + H]^+$ Calcd for $C_{32}H_{27}N_2O_4$ 503.1965, found 503.1965.

*Ethyl 3-Acetyl-1′-benzyl-2′-oxo-2-phenylspiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3h**).* Following the general procedure, α-keto ester **1a** (36 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2h** (59 mg, 0.21 mmol) were employed to obtain product **3h** (75 mg, 85% yield, 20:1 dr) as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.21 (m, 8H), 7.15 (t, J = 7.7 Hz, 1H), 7.08 (d, J = 7.2 Hz, 2H), 6.79 (t, J = 8.7 Hz, 2H), 6.65 (d, J = 7.6 Hz, 1H), 5.16 (d, J = 15.7 Hz, 1H), 4.88 (d, J = 15.7 Hz, 1H), 4.20−4.04 (m, 2H), 3.82 (s, 1H), 2.44 (s, 3H), 1.15 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.9, 173.0, 168.6, 143.4, 135.6, 131.8, 129.0, 128.8, 128.4, 128.3, 128.0, 127.8, 127.7, 127.1, 121.6, 108.8, 62.0, 51.6, 44.2, 44.1, 43.6, 33.7, 13.8; HRMS−ESI $[M + Na]^+$ Calcd for $C_{28}H_{25}NNaO_4$ 462.1676, found 462.1679.

*Ethyl 3-Benzoyl-1′-benzyl-5′-methoxy-2′-oxo-2-phenylspiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3i**).* Following the general procedure, α-keto ester **1a** (36 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2i** (77 mg, 0.21 mmol) were employed to obtain product **3i** (102 mg, 96% yield, 8:1 dr) as a white solid; mp 76−77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 8.4 Hz, 2H), 7.64 (t, J = 7.3 Hz, 1H), 7. 54 (t, J = 7.7 Hz, 2H), 7.28−7.18 (m, 8H), 7.10 (d, J = 7.1 Hz, 2H), 6.72−6.65 (m, 2H), 6.26 (br s, 1H), 5.11 (d, J = 15.8 Hz, 1H), 4.90 (d, J = 15.8 Hz, 1H), 4.52 (s, 1H), 4.30−4.13 (m, 2H), 3.46 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.6, 172.8, 168.9, 154.5, 138.4, 136.9, 135.8, 133.6, 131.8, 129.5, 128.8, 128.7, 128.5, 128.4, 128.0, 127.6, 127.1, 122.9, 114.9, 114.1, 109.1, 62.1, 55.5, 52.1, 44.2, 43.7, 41.8, 13.9; HRMS−ESI $[M + H]^+$ Calcd for $C_{34}H_{30}NO_5$ 532.2118, found 532.2119.

*Ethyl 3-Benzoyl-1′-benzyl-5′-methyl-2′-oxo-2-phenylspiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3j**).* Following the general procedure, α-keto ester **1a** (36 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2j** (75 mg, 0.21 mmol) were employed to obtain product **3j** (102 mg, 99% yield, 10:1 dr) as a light yellow solid; mp 152−154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 7.4 Hz, 2H), 7.63 (t, J = 7.4 Hz, 1H), 7.53 (t, J = 7.4 Hz, 2H), 7.33−7.18 (m, 8H), 7.09 (d, J = 7.4 Hz, 2H), 6.94 (d, J = 7.9 Hz, 1H), 6.68 (d, J = 7.9 Hz, 1H), 6.42 (s, 1H), 5.12 (d, J = 15.8 Hz, 1H), 4.91 (d, J = 15.8 Hz, 1H), 4.50 (s, 1H), 4.26−4.12 (m, 2H), 2.09 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.6, 173.0, 169.1, 141.1, 138.4, 135.8, 133.5, 131.7, 130.7, 129.6, 129.4, 128.8, 128.7, 128.6, 128.5, 128.3, 127.9, 127.5, 127.1, 121.8, 108.5, 62.1, 51.9, 44.2, 43.4, 41.9, 21.1, 13.9; HRMS−ESI $[M + H]^+$ Calcd for $C_{34}H_{30}NO_4$ 516.2169, found 516.2180.

*Ethyl 3-Benzoyl-1′-benzyl-6′-bromo-2′-oxo-2-phenylspiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3k**).* Following the general procedure, α-keto ester **1a** (36 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2k** (88 mg, 0.21 mmol) were employed to yield product **3k** (115 mg, 99% yield, 5:1 dr) as a light yellow solid; mp 160−162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 8.6 Hz, 2H), 7.66 (t, J = 7.4 Hz, 1H), 7.56 (t, J = 7.4 Hz, 2H), 7.38−7.27 (m, 6H), 7.21 (t, J = 7.4 Hz, 2H), 7.06 (d, J = 7.6 Hz, 2H), 6.96−6.90 (m, 2H), 6.46 (d, J = 8.6 Hz, 1H), 5.11 (d, J = 15.8 Hz, 1H), 4.88 (d, J = 15.8 Hz, 1H), 6.49 (s, 1H), 4.27−4.13 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.5, 173.1, 168.7, 144.7, 138.1, 135.1, 133.8, 131.6, 129.9, 129.3, 128.9, 128.8, 128.5, 128.2, 127.9, 127.1, 124.3, 121.9, 120.8, 112.1, 62.3, 52.2, 44.3, 43.1, 42.0, 13.9; HRMS−ESI $[M + H]^+$ Calcd for $C_{33}H_{27}BrNO_4$ 580.1118, found 580.1121.

*Ethyl 3-Benzoyl-1′-benzyl-7′-chloro-2′-oxo-2-phenylspiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3l**).* Following the general procedure, α-keto ester **1a** (36 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2l** (79 mg, 0.21 mmol) were employed to give product **3l** (66 mg, 62% yield, 11:1 dr) as a light yellow solid; mp 155−156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 8.6 Hz, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.54 (t, J = 7.4 Hz, 2H), 7.34−7.20 (m, 8H), 7.10 (t, J = 8.0 Hz, 3H), 6.71 (t, J = 7.9 Hz, 1H), 6.46 (d, J = 7.7 Hz, 1H), 5.55 (d, J = 16.3 Hz, 1H), 5.44 (d, J = 16.3 Hz, 1H), 4.51 (s, 1H), 4.21−4.10 (m, 2H), 1.19 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.1, 173.9, 168.7, 139.5, 138.1, 137.4, 133.8, 131.7, 130.6, 129.2, 128.9, 128.8, 128.6, 128.2, 127.2, 127.1, 126.4, 124.7, 122.1, 115.2, 62.3, 52.6, 45.6, 42.8, 42.5, 13.8; HRMS−ESI $[M + H]^+$ Calcd for $C_{33}H_{27}ClNO_4$ 536.1623, found 536.1623.

*Ethyl 1′-Allyl-3-benzoyl-2′-oxo-2-phenylspiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3m**).* Following the general procedure, α-keto ester **1a** (36 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2m** (58 mg, 0.21 mmol) were employed to obtain product **3m** (56 mg, 62% yield, 5:1 dr) as a white solid; mp 182−183 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 7.4 Hz, 2H), 7.63 (t, J = 7.4 Hz, 1H), 7.54 (t, J = 7.4 Hz, 2H), 7.29 (t, J = 7.4 Hz, 1H), 7.23−7.17 (m, 3H), 7.07 (d, J = 7.4 Hz, 2H), 6.90 (d, J = 7.8 Hz, 1H), 6.83 (t, J = 7.6 Hz, 1H), 6.63 (d, J = 7.5 Hz, 1H), 5.94−5.84 (m, 1H), 5.32−5.22 (m, 2H), 4.53−4.37 (m, 2H), 4.46 (s, 1H), 4.25−4.12 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.5, 172.7, 168.9, 143.6, 138.3, 133.6, 131.7, 131.2, 129.6, 128.8, 128.7, 128.6, 128.5, 128.1, 127.9, 121.7, 121.3, 117.4, 108.6, 62.1, 51.9, 43.4, 42.7, 41.8, 13.9; HRMS−ESI $[M + H]^+$ Calcd for $C_{29}H_{26}NO_4$ 452.1856, found 452.1861.

*Ethyl 3-Benzoyl-1′-methyl-2′-oxo-2-phenylspiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3n**).* Following the general procedure, α-keto ester **1a** (36 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2n** (56 mg, 0.21 mmol) were employed to yield product **3n** (81 mg, 95% yield, 14:1 dr) as a pale yellow solid; mp

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146−148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29−8.23 (m, 2H), 7.66−7.59 (m, 1H), 7.53 (t, J = 7.8 Hz, 2H), 7.34−7.25 (m, 2H), 7.20 (t, J = 7.8 Hz, 2H), 7.12−7.03 (m, 2H), 6.91 (d, J = 7.7 Hz, 1H), 6.85 (td, J = 7.7, 1.0 Hz, 1H), 6.63 (dd, J = 7.7, 0.8 Hz, 1H), 4.43 (s, 1H), 4.26−4.16 (m, 2H), 3.33 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.5, 172.9, 169.0, 144.5, 138.4, 133.5, 131.6, 129.7, 128.8, 128.7, 128.6, 128.5, 128.1, 121.7, 121.3, 107.9, 62.1, 51.8, 43.5, 41.8, 26.8, 13.9; HRMS−ESI $[M + H]^+$ Calcd for $C_{27}H_{24}NO_4$ 426.1700, found 426.1701.

*Ethyl 3-Benzoyl-1′-benzyl-2′-oxo-2-(p-tolyl)spiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3o**).* Following the general procedure, α-keto ester **1b** (39 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2a** (71 mg, 0.21 mmol) were employed to yield product **3o** (95 mg, 92% yield, 20:1 dr) as a white solid; mp 153−154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 7.3 Hz, 2H), 7.63 (t, J = 7.3 Hz, 1H), 7.54 (t, J = 7.8 Hz, 2H), 7.37−7.26 (m, 5H), 7.15 (t, J = 7.8 Hz, 1H), 7.01 (d, J = 8.1 Hz, 2H), 6.96 (d, J = 8.1 Hz, 2H), 6.85−6.77 (m, 2H), 6.67 (d, J = 7.6 Hz, 1H), 5.12 (d, J = 15.8 Hz, 1H), 4.93 (d, J = 15.8 Hz, 1H), 4.48 (s, 1H), 4.26−4.13 (m, 2H), 2.30 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.7, 173.3, 169.2, 143.5, 138.5, 138.4, 135.8, 133.6, 131.6, 128.9, 128.8, 128.6, 127.9, 127.7, 127.2, 126.5, 121.9, 121.4, 108.8, 62.1, 51.9, 44.2, 43.5, 42.1, 21.3, 13.9; HRMS−ESI $[M + H]^+$ Calcd for $C_{34}H_{30}NO_4$ 516.2169, found 516.2172.

*Ethyl 3-Benzoyl-1′-benzyl-2-(4-fluorophenyl)-2′-oxospiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3p**).* Following the general procedure, α-keto ester **1c** (40 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2a** (71 mg, 0.21 mmol) were employed to give product **3p** (94 mg, 91% yield, 11:1 dr) as a white solid; mp 124−125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J = 7.4 Hz, 2H), 7.63 (t, J = 7.4 Hz, 1H), 7.53 (t, J = 7.8 Hz, 2H), 7.36−7.27 (m, 5H), 7.16 (td, J = 7.7, 0.9 Hz, 1H), 7.10−7.03 (m, 2H), 6.91 (t, J = 8.7 Hz, 2H), 6.82 (t, J = 7.8 Hz, 2H), 6.64 (d, J = 7.6 Hz, 1H), 5.13 (d, J = 15.7 Hz, 1H), 4.93 (d, J = 15.7 Hz, 1H), 4.51 (s, 1H), 4.26−4.15 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.3, 172.9, 168.8, 162.7 (d, J = 248.6 Hz), 143.5, 138.2, 135.7, 133.7, 133.6 (d, J = 8.4 Hz), 128.9, 128.8, 128.5, 128.1, 127.7, 127.2, 125.4 (d, J = 3.5 Hz), 121.5, 115.1 (d, J = 21.6 Hz), 108.9, 62.2, 51.0, 44.2, 434, 41.7, 13.9; HRMS−ESI $[M + H]^+$ Calcd for $C_{33}H_{27}FNO_4$ 520.1919, found 520.1927.

*Ethyl 3-Benzoyl-1′-benzyl-2-(4-chlorophenyl)-2′-oxospiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3q**).* Following the general procedure, α-keto ester **1d** (43 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2a** (71 mg, 0.21 mmol) were employed to give product **3q** (98 mg, 92% yield, 14:1 dr) as a white solid; mp 136−138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 7.3 Hz, 2H), 7.66 (t, J = 7.3 Hz, 1H), 7.56 (t, J = 7.8 Hz, 2H), 7.37 (d, J = 4.5 Hz, 4H), 7.33−7.28 (m, 1H), 7.24 (d, J = 8.5 Hz, 2H), 7.19 (t, J = 7.7 Hz, 1H), 7.08 (d, J = 8.5 Hz, 2H), 6.90−6.83 (m, 2H), 6.72 (d, J = 7.5 Hz, 1H), 5.17 (d, J = 15.7 Hz, 1H), 4.97 (d, J = 15.7 Hz, 1H), 4.56 (s, 1H), 4.30−4.19 (m, 2H), 1.27 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.1, 172.9, 168.6, 143.5, 138.1, 135.6, 134.7, 133.7, 133.1, 128.9, 128.8, 128.4, 128.3, 128.2, 128.1, 127.7, 127.1, 121.6, 121.4, 108.9, 62.3, 51.0, 44.2, 43.3, 41.6, 13.9; HRMS−ESI $[M + H]^+$ Calcd for $C_{33}H_{27}ClNO_4$ 536.1623, found 536.1623.

*Ethyl 3-Benzoyl-1′-benzyl-2-(4-bromophenyl)-2′-oxospiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3r**).* Following the general procedure, α-keto ester **1e** (52 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2a** (71 mg, 0.21 mmol) were employed to yield product **3r** (110 mg, 95% yield, 14:1 dr) as a white solid; mp 132−134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 7.8 Hz, 2H), 7.63 (t, J = 7.3 Hz, 1H), 7.52 (t, J = 7.7 Hz, 2H), 7.39−7.26 (m, 7H), 7.16 (t, J = 7.7 Hz, 1H), 6.97 (d, J = 8.2 Hz, 2H), 6.88−6.78 (m, 2H), 6.68 (d, J = 7.7 Hz, 1H), 5.12 (d, J = 15.7 Hz, 1H), 4.93 (d, J = 15.7 Hz, 1H), 4.51 (s, 1H), 4.26−4.11 (m, 2H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.2, 172.9, 168.5, 143.5, 138.1, 135.6, 133.7, 133.4, 131.3, 128.9, 128.8, 128.6, 128.44, 128.42, 128.2, 127.7, 127.2, 123.1, 121.6, 121.4, 108.9, 62.3, 51.1, 44.3, 43.3, 41.6, 13.9; HRMS−ESI $[M + H]^+$ Calcd for $C_{33}H_{27}BrNO_4$ 580.1118, found 580.1125.

*Ethyl 3-Benzoyl-1′-benzyl-2-(naphthalen-2-yl)-2′-oxospiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3s**).* Following the general procedure, α-keto ester **1f** (46 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2a** (71 mg, 0.21 mmol) were employed to obtain product **3s** (44 mg, 40% yield, 10:1 dr) as a light yellow solid; mp 109−110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 7.5 Hz, 2H), 7.78 (d, J = 8.0 Hz, 1H), 7.71−7.62 (m, 2H), 7.56 (t, J = 7.9 Hz, 4H), 7.46 (t, J = 7.3 Hz, 1H), 7.43−7.27 (m, 6H), 7.22−7.10 (m, 2H), 6.83 (d, J = 7.8 Hz, 1H), 6.72 (t, J = 7.6 Hz, 1H), 6.59 (d, J = 7.6 Hz, 1H), 5.15 (d, J = 15.7 Hz, 1H), 4.98 (d, J = 15.7 Hz, 1H), 4.58 (s, 1H), 4.29−4.11 (m, 2H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.2, 173.2, 168.9, 143.6, 138.4, 135.8, 133.6, 133.0, 132.7, 131.3, 129.0, 128.9, 128.8, 128.6, 128.5, 128.1, 128.0, 127.7, 127.6, 127.5, 127.2, 127.1, 126.6, 126.0, 121.8, 121.5, 108.9, 62.2, 51.9, 44.3, 43.3, 42.0, 13.9; HRMS−ESI $[M + H]^+$ Calcd for $C_{37}H_{30}NO_4$ 552.2169, found 552.2172.

*Ethyl 3-Benzoyl-1′-benzyl-5′-methoxy-2′-oxo-2-(thiophen-2-yl)-spiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3t**).* Following the general procedure, α-keto ester **1g** (34 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2i** (77 mg, 0.21 mmol) were employed to obtain product **3t** (91 mg, 85% yield, 5:1 dr) as a light yellow solid; mp 153−154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, J = 7.4 Hz, 2H), 7.66 (t, J = 7.4 Hz, 1H), 7.57 (t, J = 7.4 Hz, 2H), 7.36−7.25 (m, 5H), 7.23 (d, J = 5.1 Hz, 1H), 6.85 (dd, J = 5.1, 3.6 Hz, 1H), 6.77 (d, J = 3.6 Hz, 1H), 6.71 (dd, J = 8.6, 2.5 Hz, 1H), 6.66 (d, J = 8.5 Hz, 1H), 6.18 (d, J = 2.4 Hz, 1H), 5.09 (d, J = 15.8 Hz, 1H), 4.88 (d, J = 15.8 Hz, 1H), 4.50 (s, 1H), 4.26 (q, J = 7.1 Hz, 2H), 3.51 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.5, 172.3, 168.0, 154.6, 137.8, 137.0, 135.7, 133.9, 131.7, 130.7, 128.9, 128.8, 128.7, 127.6, 127.1, 126.3, 122.8, 114.0, 113.7, 109.2, 62.4, 55.6, 46.9, 44.3, 44.0, 42.3, 13.9; HRMS−ESI $[M + H]^+$ Calcd for $C_{32}H_{28}NO_5S$ 538.1683, found 538.1687.

*(E)-Methyl 3-Benzoyl-1′-benzyl-2′-oxo-2-styrylspiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3u**).* Following the general procedure, benzylidenepyruvate ester **1i** (38 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2a** (71 mg, 0.21 mmol) were employed to obtain product **3u** (67 mg, 65% yield, 16:1 dr) as a light yellow solid; mp 84−86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21−8.16 (m, 2H), 7.61−7.56 (m, 1H), 7.54−7.45 (m, 3H), 7.34−7.30 (m, 4H), 7.28−7.22 (m, 6H), 7.19 (td, J = 7.8, 1.1 Hz, 1H), 7.02 (td, J = 7.7, 0.9 Hz, 1H), 6.82 (d, J = 7.7 Hz, 1H), 6.59 (d, J = 16.5 Hz, 1H), 6.63 (d, J = 16.5 Hz, 1H), 5.12 (d, J = 15.7 Hz, 1H), 4.89 (d, J = 15.7 Hz, 1H), 4.38 (s, 1H), 3.85 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.2, 172.8, 168.8, 143.6, 137.5, 136.9, 136.0, 135.6, 133.7, 128.8, 128.7, 128.6, 128.5, 128.3, 128.1, 127.6, 127.1, 126.8, 126.5, 122.2, 118.3, 109.3, 53.0, 48.2, 44.2, 43.4, 41.5; HRMS−ESI $[M + H]^+$ Calcd for $C_{34}H_{28}NO_4$ 514.2013, found 514.2018.

*(E)-Methyl 1′-Benzyl-3-(4-bromobenzoyl)-2′-oxo-2-styrylspiro[cyclopropane-1,3′-indoline]-2-carboxylate (**3v**).* Following the general procedure, benzylidenepyruvate ester **1i** (38 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2d** (88 mg, 0.21 mmol) were employed to yield product **3v** (58 mg, 49% yield, 14:1 dr) as a light yellow solid; mp 118−119 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.6 Hz, 2H), 7.63 (d, J = 8.6 Hz, 2H), 7.49 (d, J = 7.6 Hz, 1H), 7.36−7.29 (m, 5H), 7.29−7.26 (m, 4H), 7.24−7.21 (m, 1H), 7.19 (dd, J = 7.7, 1.1 Hz, 1H), 7.02 (td, J = 7.7, 0.9 Hz, 1H), 6.83 (d, J = 7.7 Hz, 1H), 6.61 (d, J = 16.3 Hz, 1H), 6.54 (d, J = 16.3 Hz, 1H), 5.12 (d, J = 15.7 Hz, 1H), 4.88 (d, J = 15.7 Hz, 1H), 4.30 (s, 1H), 3.84 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.3, 172.6, 168.7, 143.6, 137.1, 136.2, 135.9, 135.6, 132.2, 130.1, 129.2, 128.8, 128.6, 128.4, 128.2, 127.7, 127.2, 126.8, 126.5, 122.2, 121.9, 118.0, 109.4, 53.1, 48.2, 44.3, 43.4, 41.4; HRMS−ESI $[M + H]^+$ Calcd for $C_{34}H_{27}BrNO_4$ 592.1118, found 592.1114.

*Bis-spirooxindole Compound **3w**.* Following the general procedure, *N*-Bn isatin **1j** (48 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2j** (75 mg, 0.21 mmol) were employed to give product **3w** (110 mg, 96% yield, 7:1 dr) as a white solid; mp 193−195 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 7.4 Hz, 1H), 7.89 (d, J = 7.3 Hz, 2H), 7.66 (s, 1H), 7.57 (t, J = 7.4 Hz, 1H), 7.39 (t, J = 7.7 Hz, 2H), 7.22 (d, J = 7.7 Hz, 1H), 7.17−7.08 (m, 5H), 7.07−6.97 (m,

5H), 6.75 (d, J = 7.3 Hz, 2H), 6.69 (d, J = 7.7 Hz, 1H), 6.62 (d, J = 7.9 Hz, 1H), 5.00 (d, J = 15.7 Hz, 1H), 4.91 (d, J = 15.7 Hz, 1H), 4.78 (d, J = 15.7 Hz, 1H), 4.45 (d, J = 15.7 Hz, 1H), 4.43 (s, 1H), 2.33 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.6, 170.9, 169.2, 143.1, 140.9, 136.5, 135.5, 135.3, 133.3, 131.4, 129.2, 128.8, 128.7, 128.6, 128.5, 128.2, 127.4, 127.3, 127.0, 126.9, 125.1, 123.0, 122.2, 121.1, 108.8, 108.1, 47.1, 46.4, 44.2, 43.7, 40.8, 21.4; HRMS−ESI $[M + H]^+$ Calcd for $C_{39}H_{31}N_2O_3$ 575.2329, found 575.2336.

Bis-spirooxindole Compound ***3x***. Following the general procedure, *N*-Bn isatin **1k** (55 mg, 0.2 mmol) and isatin-derived electron-deficient alkene **2a** (71 mg, 0.21 mmol) were employed to give product **3x** (42 mg, 35% yield, 20:1 dr) as a white solid; mp 195−197 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 7.7 Hz, 1H), 7.93 (d, J = 7.2 Hz, 2H), 7.78 (d, J = 7.7 Hz, 1H), 7.61 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.8 Hz, 2H), 7.27−7.16 (m, 5H), 7.14−7.02 (m, 5H), 6.96 (t, J = 7.8 Hz, 2H), 6.79 (d, J = 7.7 Hz, 1H), 6.65 (d, J = 7.5 Hz, 2H), 5.17 (d, J = 16.2 Hz, 1H), 5.12 (d, J = 16.2 Hz, 1H), 5.07 (d, J = 15.7 Hz, 1H), 4.81 (d, J = 15.7 Hz, 1H), 4.50 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.2, 170.3, 169.7, 143.3, 139.2, 136.7, 136.3, 135.4, 133.6, 131.4, 128.9, 128.7, 128.6, 128.2, 128.1, 127.6, 127.0, 126.8, 126.2, 125.4, 123.5, 122.9, 122.1, 120.6, 115.2, 108.6, 47.4, 47.1, 44.9, 44.2, 40.5; HRMS−ESI $[M + H]^+$ Calcd for $C_{38}H_{28}ClN_2O_3$ 595.1783, found 595.1783.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of NMR (^{1}H, ^{13}C) spectra of new compounds **3**; X-ray crystallographic data (CIF files) for compounds **3a** and **3x**. 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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