

Domino Reactions of Vinyl Malononitriles with 3-Phenacylideneoxindoles for Efficient Synthesis of Functionalized Spirocyclic Oxindoles

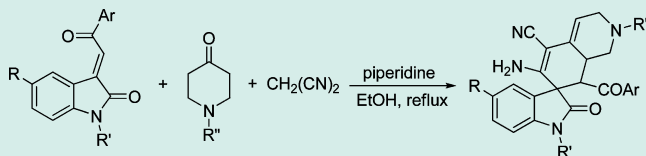
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S Supporting Information

ABSTRACT: The reactions of vinyl malononitriles with 3-phenacylideneoxindoles in ethanol in the presence of DBU as base resulted in the functionalized spirocyclic oxindoles through the domino Michael addition and intramolecular nucleophilic addition to cyano group. On the other hand, the similar reaction in the presence of piperidine as base afforded the simple Michael addition products in good yields. The stereochemistry of the spirooxindoles was established with ^1H NMR data and single crystal structures.

KEYWORDS: spirooxindole, vinyl malononitrile, domino reaction, Michael addition, cycloaddition



1. INTRODUCTION

In recent years, spirocyclic 2-oxindoles have drawn tremendous interests in synthetic and medicinal chemistry because they occur in many natural products and have been reported to have various types of bioactivity.^{1,2} Isatin and its C-3 derivatives are the most employed starting materials in the architecture of various spirocyclic 2-oxindoles.^{3,4} In this respect, 3-methylene-2-oxindoles are one of the most important reagents because of their easy synthesis and versatile reactivity.⁵ They have been used as active electron-deficient alkenes in many synthetic reactions, such as 1,3-dipolar cycloaddition, Diels–Alder reaction, Michael addition and versatile multicomponent reactions for the design of the fused cyclic and spirocyclic frameworks.^{6–10} In recent years, we have developed several efficient procedures for the synthesis spirocyclic oxindoles by using 3-phenacylideneoxindoles as key substrates.^{11–13} In continuation of our interest on the construction of complex spirooxindole skeletons with domino reaction, herein we wish to report the domino reactions of vinyl malononitriles with 3-phenacylideneoxindoles for the efficient synthesis of a series of the functionalized spiro[indoline-3,2'-naphthalene], spiro[benzo[7]annulene-2,3'-indoline], and spiro[indoline-3,7'-isoquinoline] derivatives.

2. RESULTS AND DISCUSSION

Since the γ -C–H of vinyl malononitriles are easily deuterated in the presence of organic bases, they can act as versatile, direct vinylogous donors in Michael addition reactions and behave as good hydride acceptors in conjugate reduction reactions.^{14–16} According to the previously reported reaction of vinyl malononitrile with isatylidene malononitrile,¹⁷ the reaction of equimolecular cyclohexylidene malononitrile (**1a**) and 3-phenacylideneoxindole (**2a**) in ethanol was carried out with different base catalysts at room temperature. It is interesting to

find out that the base appears to be a crucial factor for the reaction. No reaction was observed when pyridine was used as base. When piperidine was used as base, the reaction gave the simple Michael addition product at room temperature. Prolonging the reaction time or heating the reaction mixture affords the expected cyclized product **3a** in 83% yield. The reaction also proceeded smoothly to afford a mixture of products when triethylamine, diethylamine was used as the base. When DBU was used, the reaction was complete in less than half an hour at room temperature affording the spirocyclic oxindole **3a** in 89% yields. Thus, DBU was chosen as the best base for the reaction of various vinyl malononitriles with 3-phenacylideneoxindoles. The results are summarized in Table 1. It can be seen that the reactions usually gave the functionalized spiro[indoline-3,2'-naphthalenes] **3a–3e** and spiro[benzo[7]annulene-2,3'-indolines] **3f–3h** in satisfactory yields. It should be pointed out that very pure products are obtained only by filtration of the resulting precipitates and washing with a little ethanol. There was not need for further purification.

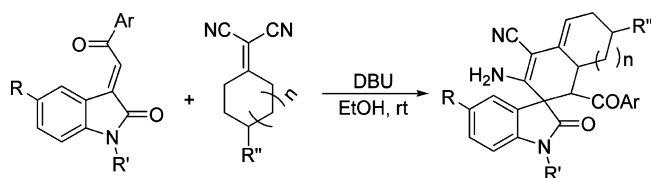
To demonstrate the utility and generality of this reaction, a one-pot domino reaction procedure was developed for the reactions containing 4-alkylpiperidinones. First, an ethanol solution of *N*-methylpiperidinone and malononitrile in the presence of piperidine was heated for five minutes. Then 3-phenacylideneoxindole was added and the resulting mixture was refluxed for about one hour. The expected functionalized spiro[indoline-3,7'-isoquinolines] **4a–4e** were obtained in satisfactory yields (Table 2, entries 1–5). By using this one-pot domino reaction procedure, the reactions containing *N*-

Received: January 15, 2014

Revised: February 15, 2014

Published: February 20, 2014



Table 1. Synthesis of Spirocyclic Oxindoles 3a–3h^a


entry	compd	R	R'	Ar	R''	n	yield (%) ^b
1	3a	F	Bn	<i>p</i> -CH ₃ C ₆ H ₄	H	1	89
2	3b	Cl	Bn	<i>p</i> -CH ₃ C ₆ H ₄	H	1	74
3	3c	F	<i>n</i> -C ₄ H ₉	<i>p</i> -CH ₃ OC ₆ H ₄	<i>t</i> -Bu	1	85
4	3d	H	Bn	<i>p</i> -CH ₃ OC ₆ H ₄	<i>t</i> -Bu	1	92
5	3e	H	Bn	<i>p</i> -ClC ₆ H ₄	<i>t</i> -Bu	1	83
6	3f	CH ₃	<i>n</i> -C ₄ H ₉	<i>p</i> -ClC ₆ H ₄	H	2	80
7	3g	H	Bn	<i>p</i> -ClC ₆ H ₄	H	2	82
8	3h	CH ₃	Bn	<i>p</i> -ClC ₆ H ₄	H	2	87

^aReaction condition: 3-phenacylideneoxindole (1.0 mmol), vinyl malononitrile (1.0 mmol), DBU (0.1 mmol) in ethanol (10.0 mL), rt, 30 min. ^bIsolated yield.

benzylpiperidinone also afforded the corresponding spiro[indoline-3,7'-isoquinolines] 4f–4e in high yields (Table 2, entries 6–10).

The structures of the above obtained spirocyclic oxindoles 3a–3h and 4a–4j were characterized by spectroscopic methods. The single crystal structures of 3a (Figure 1), 3d (Figure 2), 3h and 4e were successfully determined by X-ray diffraction method. ¹H NMR spectra of 3a–3h and 4a–4j usually display one set of absorptions for the characteristic groups in each spirooxindole, which indicated there is only one stereoisomer. In the molecular structures of 3a, 3h, and 4e, the phenyl group of oxindole moiety and the benzoyl group exist in a *cis*-configuration. Furthermore, the benzoyl group also exists in *trans*-position to the methylene unit of the annulated cycle.

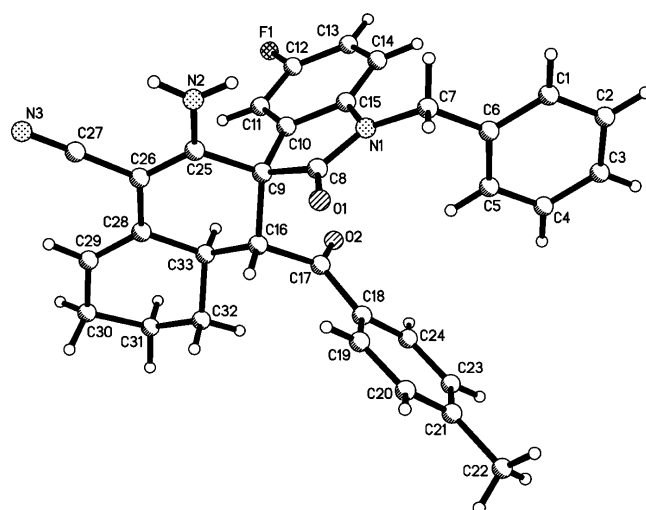


Figure 1. Molecular structure of compound 3a.

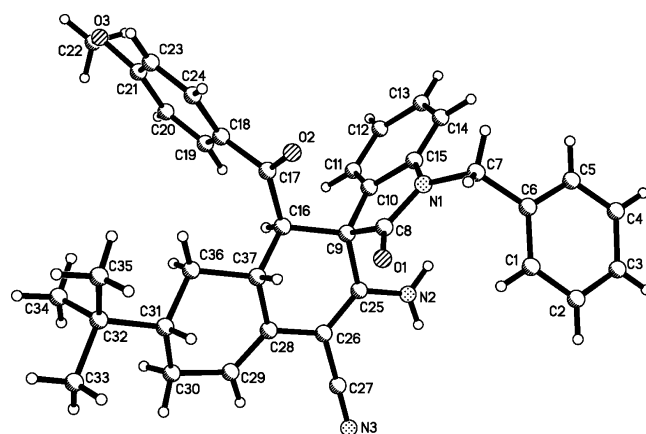
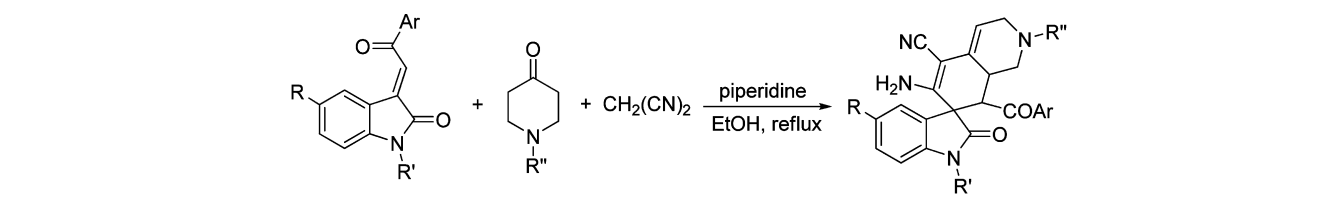


Figure 2. Molecular structure of compound 3d.

Table 2. Synthesis Spiro[indoline-3,7'-isoquinolines] 4a–4j^a


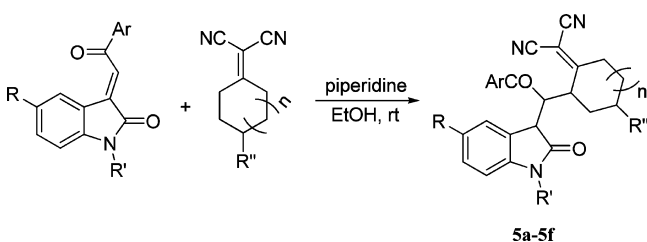
entry	compd	R	R'	Ar	R''	yield (%) ^b
1	4a	H	Bn	<i>p</i> -CH ₃ C ₆ H ₄	CH ₃	83
2	4b	H	Bn	<i>p</i> -ClC ₆ H ₄	CH ₃	96
3	4c	F	Bn	<i>p</i> -CH ₃ OC ₆ H ₄	CH ₃	92
4	4d	Cl	Bn	C ₆ H ₅	CH ₃	88
5	4e	Cl	Bn	<i>p</i> -CH ₃ C ₆ H ₄	CH ₃	89
6	4f	H	Bn	<i>p</i> -CH ₃ OC ₆ H ₄	Bn	92
7	4g	F	Bn	C ₆ H ₅	Bn	95
8	4h	F	Bn	<i>p</i> -CH ₃ OC ₆ H ₄	Bn	94
9	4i	Cl	Bn	<i>p</i> -CH ₃ OC ₆ H ₄	Bn	93
10	4j	Cl	Bn	<i>p</i> -CH ₃ C ₆ H ₄	Bn	90

^aReaction condition: piperidinone (1.0 mmol), malononitrile (1.0 mmol), piperidine (0.1 mmol) in ethanol (15.0 mL), reflux, 5 min. 3-phenacylideneoxindole (1.0 mmol), reflux, one hour. ^bIsolated yield.

But it is clear to see that the phenyl group of oxindole moiety and the benzoyl are in trans-configuration in molecular structure of **3d**. Thus, the single crystal structures of the four compounds demonstrate that two kinds of stereoisomers exist in the prepared spiro compounds, which also reveals that it is difficult to elucidate the stereochemistry of these complex spirocyclic oxindoles with ^1H NMR spectra.

It has been mentioned above that the piperidine promoted reaction of vinyl malononitrile with 3-phenacylideneoxindole can afford the simple Michael addition product at room temperature. Thus, we also extended this strategy to the reactions of *p*-*tert*-butylcyclohexylidene malononitrile and cycloheptylidene malononitrile. The simple Michael addition products **5a–5f** were successfully prepared in good yields (Table 3). This reaction not only provides an efficient

Table 3. Synthesis of the Michael Addition Products **5a–5f**^a



entry	compd	R	R'	Ar	R''	n	yield (%) ^b
1	5a	Cl	<i>n</i> -C ₄ H ₉	<i>p</i> -CH ₃ OC ₆ H ₄	H	1	81
2	5b	H	Bn	<i>p</i> -CH ₃ OC ₆ H ₄	<i>t</i> -Bu	1	85
3	5c	F	Bn	<i>p</i> -CH ₃ C ₆ H ₄	<i>t</i> -Bu	1	88
4	5d	Cl	Bn	<i>p</i> -CH ₃ C ₆ H ₄	<i>t</i> -Bu	1	87
5	5e	H	Bn	<i>p</i> -CH ₃ OC ₆ H ₄	H	2	78
6	5f	H	<i>n</i> -C ₄ H ₉	<i>p</i> -CH ₃ C ₆ H ₄	H	2	90

^aReaction condition: 3-phenacylideneoxindole (1.0 mmol), vinyl malononitrile (1.0 mmol), piperidine (0.1 mmol) in ethanol (10.0 mL), rt, one hour. ^bIsolated yield.

procedure for the preparation of functionalized 3-substituted oxindoles, but also provides practical facts for the reaction mechanism for the formation of spirocyclic oxindoles. The single crystal structures of the compounds **5a** (Figure 3) and **5e** were determined by X-ray diffraction method.

The acyclic vinyl malononitrile displayed different reactivity to the above used cyclic vinyl malononitriles in the reaction. Under similar conditions, treatment of 2-(1-*p*-tolylethylidene)-malononitrile with 3-phenacylideneoxindoles in ethanol with

piperidine as base gave a complicated mixture of products. When 4-dimethylaminopyridine was used as the base, the simple adducts **5g–5l** were obtained in very high yields (Table 4). On the other hand, the trying to produce cycloaddition products continuously failed despite many attempts. The simple Michael adduct **5a–5l** in ethanol in the presence of DBU did not afford the cyclized product. The single crystal structure of the compound **5i** was determined by X-ray diffraction method.

On the basis of the above experimental results, together with the related reports of the vinyl malononitrile,¹⁴ a plausible mechanism for the formation of the spirooxindoles is illustrated in Scheme 1 by using *N*-methylpiperidinone as an example. At first, the base catalyzed condensation of *N*-methylpiperidinone with malononitrile afforded the vinyl malononitrile **1**. Second, a carbanion (**A**) is generated by deprotonation of vinyl malononitrile **1** with base, which in turn attacked the exocyclic carbon atom of the 3-phenacylideneoxindole to give a new carbanion intermediate (**B**). Then the intramolecular addition of carbanion to one cyano group resulted in the cyclized product with a imino group (**C**). At last, the spirocyclic oxindole **4** was formed by imino-enamine tautomerization. Depending on the reaction conditions and structures of the substrates, the sequential reactions can stop at the middle step to give the separated product. The simple Michael addition product can be separated in case of using weak base or carrying out the reaction at room temperature. In the proposed reaction mechanism, it is clear to be seen that each reaction step is thermodynamically controlled reaction and a mixture of the diastereoisomers is formed in this domino reaction.

CONCLUSION

In conclusion, we systematically investigated the domino reactions of 3-phenacylideneoxindole with a series of vinyl malononitriles and successfully developed an efficient protocol for the synthesis of novel functionalized spirocyclic oxindoles. Significantly, the stereochemistry of the reaction was clearly elucidated mainly by determination of seven single crystal structures. The reaction mechanism is also rationally proposed on the basis of capture of the reaction intermediates. The advantages of the reactions are using readily available starting materials, mild reaction conditions, short reaction times, operational simplicity by avoiding column chromatography and good to high yields. The potential uses of the reaction in synthetic and medicinal chemistry may be significant.

EXPERIMENTAL PROCEDURES

General Procedure for the Synthesis of Spirocyclic Oxindoles **3a–3h.** A mixture of vinyl malononitrile (1.0 mmol) and 3-phenacylideneoxindole (1.0 mmol) and DBU (0.1 mmol) in ethanol (10.0 mL) was stirred at room temperature for about 20–30 min. The resulting precipitate was collected by filtration and washed with cold alcohol to give the pure product for analysis.

3'-Amino-1-benzyl-5-fluoro-1'-(4-methylbenzoyl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile **3a:** white solid, 89%, 0.460 g, mp 213.6–214.0 °C; ^1H NMR (600 MHz, DMSO-*d*₆) δ 7.77 (d, *J* = 7.8 Hz, 2H, ArH), 7.30 (d, *J* = 7.8 Hz, 2H, ArH), 7.27 (d, *J* = 7.8 Hz, 1H, ArH), 7.11–7.07 (m, 2H, ArH), 6.94 (t, *J* = 7.2 Hz, 2H, ArH), 6.71–6.68 (m, 3H, ArH), 6.17 (s, 2H, NH₂), 5.64 (s, 1H, CH), 4.94 (d, *J* = 16.2 Hz, 1H, CH), 4.25 (d, *J* = 15.6 Hz, 1H, CH),

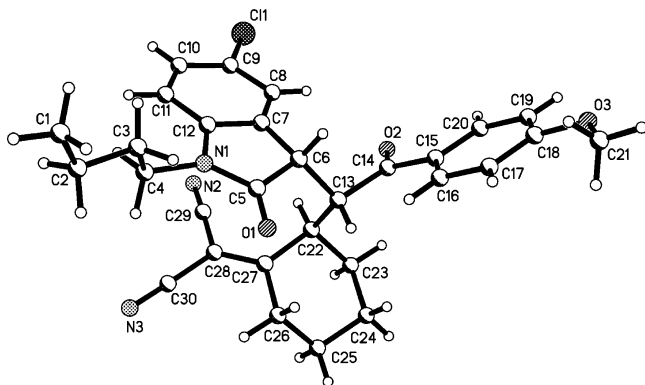
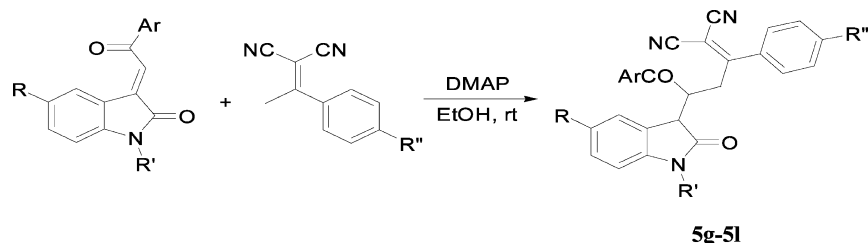
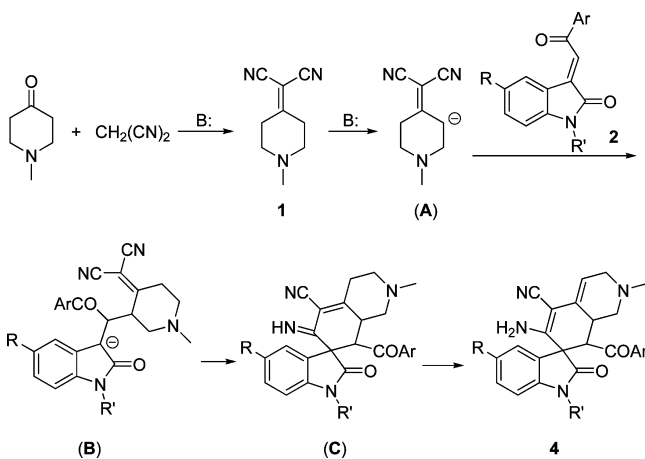


Figure 3. Molecular structure of compound **5a**.

Table 4. Synthesis of the Michael addition products 5g–5j^a

entry	compd	R	R'	R''	Ar	yield (%) ^b
1	5g	Cl	Bn	CH ₃	<i>p</i> -CH ₃ C ₆ H ₄	92
2	5h	F	Bn	CH ₃	<i>p</i> -CH ₃ C ₆ H ₄	90
3	5i	H	Bn	CH ₃	<i>p</i> -ClC ₆ H ₄	89
4	5j	Cl	<i>n</i> -C ₄ H ₉	CH ₃	<i>p</i> -CH ₃ C ₆ H ₄	86
5	5k	Cl	Bn	Cl	<i>p</i> -CH ₃ C ₆ H ₄	85
6	5l	H	Bn	OCH ₃	<i>p</i> -CH ₃ OC ₆ H ₄	88

^aReaction condition: 3-phenacylideneoxindole (1.0 mmol), vinyl malononitrile (1.0 mmol), DMAP (1.0 mmol) in ethanol (10.0 mL), rt, 30 min.^bIsolated yield.**Scheme 1. Formation Mechanism for the Spirocyclic Oxindoles**

4.18 (d, *J* = 12.0 Hz, 1H, CH), 2.93 (brs, 1H, CH), 2.37 (s, 3H, CH₃), 2.20–2.12 (m, 2H, CH₂), 1.67–1.65 (m, 1H, CH), 1.50–1.47 (m, 1H, CH), 1.36–1.34 (m, 1H, CH), 1.06–1.01 (m, 1H, CH); ¹³C NMR (150 MHz, DMSO-*d*₆) δ 197.0, 174.1, 153.3, 144.6, 139.3, 135.2, 134.5, 130.2, 129.4, 128.7, 128.2, 127.0, 126.9, 117.6, 117.1, 114.9, 114.8, 112.7, 112.5, 110.4, 110.3, 79.9, 55.3, 49.9, 44.1, 34.1, 27.0, 24.8, 21.3, 21.1, 18.5; IR (KBr) ν 3460, 3320, 3234, 3078, 2948, 2887, 2203, 1708, 1667, 1607, 1572, 1498, 1433, 1396, 1350, 1201, 1177, 1131, 1087, 1030, 985, 845, 818, 792 cm⁻¹; MS (*m/z*) HRMS (ESI) Calcd for C₃₃H₂₉FN₃O₂ ([*M* + H]⁺) 518.2238; Found 518.2242.

3'-Amino-1-benzyl-5-chloro-1'-(4-methylbenzoyl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile 3b: white solid, 74%, 0.394 g, mp 118.1–118.4 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ 7.78 (s, 2H, ArH), 7.67 (s, 1H, ArH), 7.45 (brs, 2H, ArH), 7.35 (brs, 2H, ArH), 7.28–7.21 (m, 3H, ArH), 7.09 (s, 1H, ArH), 6.61 (s, 1H, ArH), 5.75 (s, 2H, NH₂), 5.61 (s, 1H, CH), 4.96 (brs, 1H, CH), 4.77 (brs, 1H, CH), 4.54 (brs, 1H, CH), 3.42 (brs, 1H, CH), 2.30 (s, 3H, CH₃), 2.17–2.11 (m, 2H, CH₂), 1.68 (s, 1H, CH), 1.36 (brs, 1H, CH), 1.25 (brs, 1H, CH), 0.98 (brs, 1H, CH); ¹³C NMR (150 MHz, CDCl₃) δ 199.2, 177.4, 150.1, 144.8, 142.5, 135.3, 130.1, 129.4, 128.9, 128.2, 128.1, 127.9, 127.5, 124.2, 121.8,

117.0, 110.9, 95.3, 86.9, 53.8, 53.2, 44.6, 33.0, 27.9, 25.3, 21.7, 21.6; IR (KBr) ν 3456, 3330, 3235, 3070, 2928, 2862, 2824, 2206, 1709, 1669, 1627, 1607, 1570, 1489, 1456, 1429, 1397, 1336, 1272, 1208, 1178, 1124, 1082, 1030, 991, 913, 848, 810, 776 cm⁻¹; MS (*m/z*) HRMS (ESI) Calcd for C₃₃H₂₈ClN₃NaO₂ ([*M* + Na]⁺) 556.1762; Found 556.1756.

3'-Amino-7'-tert-butyl-1-butyl-5-fluoro-1'-(4-methoxybenzoyl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile 3c: white solid, 85%, 0.472 g, mp 228.1–230.5 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ: 7.81 (d, *J* = 9.0 Hz, 2H, ArH), 7.41 (dd, *J*₁ = 8.2 Hz, *J*₂ = 2.0 Hz, 1H, ArH), 6.96–6.92 (m, 1H, ArH), 6.90 (d, *J* = 8.4 Hz, 2H, ArH), 6.88–6.86 (m, 1H, ArH), 5.60 (brs, 1H, CH), 5.57 (s, 2H, NH₂), 4.40 (d, *J* = 12.0 Hz, 1H, CH), 3.79 (s, 3H, OCH₃), 3.68–3.64 (m, 1H, CH), 3.57–3.52 (m, 1H, CH), 3.39 (t, *J* = 11.4 Hz, 1H, CH), 2.91 (d, *J* = 18.0 Hz, 1H, CH), 1.91–1.86 (m, 1H, CH), 1.63–1.58 (m, 2H, CH₂), 1.40–1.34 (m, 2H, CH₂), 1.30–1.24 (m, 2H, CH₂), 0.95 (t, *J* = 7.2 Hz, 3H, CH₃), 0.74–0.68 (m, 1H, CH), 0.66 (s, 9H, CH₃); ¹³C NMR (150 MHz, DMSO-*d*₆) δ 197.9, 173.8, 163.3, 158.8, 157.2, 153.7, 140.5, 131.4, 130.7, 130.4, 128.4 (d, *J* = 8.2 Hz), 117.9, 116.6, 115.6 (d, *J* = 23.5 Hz), 113.7, 112.6 (d, *J* = 25.2 Hz), 109.7 (d, *J* = 7.7 Hz), 80.7, 55.4, 53.7, 51.7, 43.1, 33.5, 31.8, 28.9, 28.7, 26.6, 26.5, 19.6, 13.8; IR (KBr) ν 3685, 3469, 3352, 3236, 2958, 2907, 2871, 2202, 1705, 1667, 1624, 1600, 1574, 1494, 1452, 1421, 1398, 1354, 1268, 1207, 1177, 1139, 1090, 1028, 987, 845, 819, 803 cm⁻¹; MS (*m/z*) HRMS (ESI) Calcd for C₃₄H₃₈FN₃NaO₃ ([*M* + Na]⁺) 578.2789; Found 578.2782.

3'-Amino-1-benzyl-7'-tert-butyl-1'-(4-methoxybenzoyl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile 3d: white solid, 92%, 0.525 g, mp 232.2–233.9 °C; ¹H NMR (600 MHz, DMSO-*d*₆) δ 7.85 (d, *J* = 9.0 Hz, 2H, ArH), 7.48–7.45 (m, 3H, ArH), 7.35 (t, *J* = 7.8 Hz, 2H, ArH), 7.29–7.27 (m, 1H, ArH), 7.04 (t, *J* = 7.8 Hz, 1H, ArH), 6.89 (d, *J* = 8.4 Hz, 2H, ArH), 6.81 (t, *J* = 7.8 Hz, 1H, ArH), 6.62 (d, *J* = 8.4 Hz, 1H, ArH), 5.63 (s, 1H, CH), 5.47 (s, 2H, NH₂), 4.97 (d, *J* = 15.6 Hz, 1H, CH), 4.79 (d, *J* = 16.2 Hz, 1H, CH), 4.48 (d, *J* = 12.0 Hz, 1H, CH), 3.78 (s, 3H, OCH₃), 3.48–3.45 (m, 1H, CH), 2.21 (d, *J* = 18.0 Hz, 1H, CH), 1.93–1.88 (m, 1H, CH), 1.32–1.26 (m, 2H, CH₂), 0.77 (q, *J* = 12.0 Hz, 1H, CH₂), 0.66 (s, 9H, CH₃); ¹³C NMR (150 MHz,

DMSO- d_6) δ 198.4, 174.5, 163.3, 154.1, 143.8, 136.2, 131.4, 130.7, 130.6, 129.3, 128.4, 127.2, 126.7, 124.6, 122.2, 117.9, 116.8, 113.7, 109.4, 81.0, 55.4, 53.6, 51.7, 43.6, 43.1, 33.8, 31.8, 28.7, 26.6, 26.5; IR (KBr) ν 3656, 3464, 3347, 3237, 3194, 3057, 2948, 2903, 2203, 1707, 1666, 1625, 1598, 1573, 1509, 1489, 1467, 1420, 1398, 1350, 1327, 1267, 1249, 1205, 1174, 1110, 1077, 1027, 981, 846, 803 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd for $\text{C}_{37}\text{H}_{37}\text{N}_3\text{NaO}_3$ ($[\text{M} + \text{Na}]^+$) 594.2727; Found 594.2724.

3'-Amino-1-benzyl-7'-tert-butyl-1'-(4-chlorobenzoyl)-2-oxo-6',7',8',8a'-tetrahydro-1'H-spiro[indoline-3,2'-naphthalene]-4'-carbonitrile 3e: white solid, 83%, 0.477 g, mp 164.8–165.3 $^\circ\text{C}$; ^1H NMR (600 MHz, DMSO- d_6) δ 7.85 (d, J = 6.6 Hz, 2H, ArH), 7.55 (d, J = 6.0 Hz, 2H, ArH), 7.36 (d, J = 6.0 Hz, 1H, ArH), 7.25 (brs, 1H, ArH), 7.12–7.08 (m, 2H, ArH), 6.99 (brs, 2H, ArH), 6.79 (d, J = 6.0 Hz, 1H, ArH), 6.73 (d, J = 4.2 Hz, 2H, ArH), 6.18 (s, 2H, NH_2), 5.65 (s, 1H, CH), 4.90 (d, J = 16.2 Hz, 1H, CH), 4.29 (d, J = 15.0 Hz, 1H, CH), 4.18 (d, J = 10.8 Hz, 1H, CH), 2.97 (brs, 1H, CH), 2.20 (d, J = 14.4 Hz, 1H, CH), 1.96–1.91 (m, 1H, CH), 1.38–1.33 (m, 2H, CH_2), 0.83–0.80 (m, 1H, CH), 0.69 (s, 9H, CH_3); ^{13}C NMR (150 MHz, CDCl_3) δ 197.1, 174.8, 151.1, 142.3, 140.3, 135.9, 134.9, 130.0, 129.5, 129.0, 128.8, 126.6, 127.8, 127.3, 125.6, 123.5, 122.4, 116.8, 109.7, 86.1, 55.6, 51.2, 44.3, 43.7, 35.6, 32.3, 28.8, 27.7, 27.2, 27.0; IR (KBr) ν 3419, 3327, 3230, 3060, 2925, 2852, 2235, 1701, 1655, 1580, 1484, 1453, 1429, 1367, 1300, 1287, 1202, 1173, 1027, 1003, 990, 919, 826, 764 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd for $\text{C}_{36}\text{H}_{34}\text{ClN}_3\text{NaO}_2$ ($[\text{M} + \text{Na}]^+$) 598.2232; Found 598.2228.

3-Amino-1'-butyl-1-(4-chlorobenzoyl)-5'-methyl-2'-oxo-1,6,7,8,9,9a-hexahydrospiro[benzo[7]annulene-2,3'-indoline]-4-carbonitrile 3f: white solid, 80%, 0.513 g, mp 222.7–223.9 $^\circ\text{C}$; ^1H NMR (600 MHz, DMSO- d_6) δ 7.88 (d, J = 8.4 Hz, 2H, ArH), 7.54 (d, J = 7.8 Hz, 2H, ArH), 7.11 (d, J = 7.8 Hz, 1H, ArH), 6.92 (s, 1H, ArH), 6.84 (d, J = 7.8 Hz, 1H, ArH), 6.01 (s, 2H, NH_2), 5.84 (s, 1H, CH), 4.31 (d, J = 12.0 Hz, 1H, CH), 3.51–3.46 (m, 1H, CH), 3.17–3.14 (m, 1H, CH), 3.08–3.04 (m, 1H, CH), 2.29 (s, 3H, CH_3), 1.72–1.70 (m, 2H, CH_2), 1.55–1.49 (m, 1H, CH), 1.41–1.35 (m, 1H, CH), 1.31–1.27 (m, 1H, CH), 1.16 (d, J = 13.2 Hz, 1H, CH), 0.98–0.94 (m, 1H, CH), 0.91–0.87 (m, 2H, CH_2), 0.74–0.70 (m, 1H, CH), 0.61 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO- d_6) δ 197.0, 172.4, 155.5, 140.8, 139.0, 136.6, 135.6, 131.0, 129.1, 128.6, 128.5, 124.8, 120.7, 118.4, 108.8, 79.5, 55.0, 50.6, 37.7, 32.9, 30.2, 28.6, 27.8, 25.4, 20.9, 19.3, 13.5; IR (KBr) ν 3461, 3330, 3241, 3031, 2957, 2916, 2853, 2207, 1710, 1675, 1650, 1618, 1587, 1491, 1441, 1400, 1400, 1283, 1254, 1234, 1203, 1093, 1041, 1012, 990, 931, 849, 803, 769, 751 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd for $\text{C}_{31}\text{H}_{32}\text{ClN}_3\text{NaO}_2$ ($[\text{M} + \text{Na}]^+$) 536.2075; Found 536.2076.

3-Amino-1'-benzyl-1-(4-chlorobenzoyl)-2'-oxo-1,6,7,8,9,9a-hexahydrospiro[benzo[7]annulene-2,3'-indoline]-4-carbonitrile 3g: white solid, 82%, 0.437 g, mp 234.6–236.2 $^\circ\text{C}$; ^1H NMR (600 MHz, DMSO- d_6) δ 7.95 (d, J = 8.4 Hz, 2H, ArH), 7.55 (d, J = 8.4 Hz, 2H, ArH), 7.24 (t, J = 7.8 Hz, 1H, ArH), 7.18–7.15 (m, 2H, ArH), 7.09–7.06 (m, 3H, ArH), 6.82–6.79 (m, 3H, ArH), 6.23 (s, 2H, NH_2), 5.86 (t, J = 6.0 Hz, 1H, CH), 4.91 (d, J = 15.6 Hz, 1H, CH), 4.45 (d, J = 12.0 Hz, 1H, CH), 4.29 (d, J = 16.2 Hz, 1H, CH), 3.14 (t, J = 10.2 Hz, 1H, CH), 2.35–2.30 (m, 1H, CH), 2.25–2.20 (m, 1H, CH), 1.76–1.74 (m, 1H, CH), 1.68–1.67 (m, 1H, CH), 1.53–1.47 (m, 1H, CH), 1.37–1.31 (m, 1H, CH), 1.27–1.23 (m, 1H, CH), 1.19 (d, J = 10.2 Hz, 1H, CH); ^{13}C NMR (150 MHz,

DMSO- d_6) δ 197.4, 73.1, 155.9, 142.8, 139.2, 136.7, 135.5, 130.8, 128.7, 128.2, 127.1, 127.0, 124.3, 122.6, 121.0, 118.3, 109.5, 79.4, 56.1, 55.1, 50.0, 43.9, 32.7, 30.5, 27.9, 25.4, 18.5; IR (KBr) ν 3457, 3326, 3225, 3059, 2921, 2846, 2201, 1708, 1676, 1649, 1609, 1588, 1483, 1462, 1437, 1400, 1356, 1295, 1236, 1201, 1176, 1087, 1041, 1006, 986, 928, 882, 850, 833, 811, 781 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd for $\text{C}_{33}\text{H}_{29}\text{ClN}_3\text{O}_2$ ($[\text{M} + \text{H}]^+$) 534.1943; Found 534.1931.

3-Amino-1'-benzyl-1-(4-chlorobenzoyl)-5'-methyl-2'-oxo-1,6,7,8,9,9a-hexahydrospiro[benzo[7]annulene-2,3'-indoline]-4-carbonitrile 3h: white solid, 87%, 0.476 g, mp 224.3–226.1 $^\circ\text{C}$; ^1H NMR (600 MHz, DMSO- d_6) δ 7.95 (d, J = 8.4 Hz, 2H, ArH), 7.55 (d, J = 8.4 Hz, 2H, ArH), 7.16–7.14 (m, 1H, ArH), 7.08–7.04 (m, 3H, ArH), 6.97 (s, 1H, ArH), 6.78 (d, J = 7.8 Hz, 2H, ArH), 6.69 (d, J = 7.8 Hz, 1H, ArH), 6.20 (s, 2H, NH_2), 5.86 (t, J = 6.0 Hz, 1H, CH), 4.89 (d, J = 16.2 Hz, 1H, CH), 4.43 (d, J = 12.0 Hz, 1H, CH), 4.26 (d, J = 16.2 Hz, 1H, CH), 3.15 (t, J = 10.8 Hz, 1H, CH), 2.35–2.31 (m, 1H, CH), 2.27 (s, 3H, CH_3), 2.25–2.20 (m, 1H, CH), 1.75–1.73 (m, 1H, CH), 1.69–1.68 (m, 1H, CH), 1.53–1.47 (m, 1H, CH), 1.39–1.33 (m, 1H, CH), 1.28–1.25 (m, 1H, CH), 1.19 (d, J = 13.2 Hz, 1H, CH); ^{13}C NMR (150 MHz, DMSO- d_6) δ 197.4, 172.9, 156.0, 140.5, 139.1, 136.8, 135.6, 135.5, 131.4, 130.8, 129.0, 128.7, 128.2, 127.1, 127.0, 124.8, 120.8, 118.4, 109.3, 79.2, 55.1, 50.0, 43.9, 32.7, 30.4, 27.8, 25.4, 20.9, 14.1; IR (KBr) ν 3731, 3454, 3329, 3240, 3030, 2919, 2848, 2207, 1708, 1673, 1650, 1616, 1588, 1490, 1454, 1436, 1400, 1347, 1283, 1250, 1231, 1197, 1137, 1090, 1042, 1012, 987, 951, 849, 836, 808, 771 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd for $\text{C}_{34}\text{H}_{31}\text{ClN}_3\text{O}_2$ ($[\text{M} + \text{H}]^+$) 548.2099; Found 548.2085.

General Procedure for the Synthesis of Spirocyclic Oxindoles 4a–4j. A mixture of *N*-methyl or *N*-benzylpiperidine (1.0 mmol), malononitrile (1.0 mmol), and piperidine (0.1 mmol) in ethanol (15.0 mL) was refluxed for 5 min. Then 3-phenacylideneoxindole (1.0 mmol) was added, and the mixture was refluxed for about one hour. After it was cooled, the resulting precipitate was collected by filtration and washed with cold alcohol to give the pure product for analysis.

6'-Amino-1-benzyl-2'-methyl-8'-(4-methylbenzoyl)-2-oxo-2',3',8',8a'-tetrahydro-1'H-spiro[indoline-3,7'-isoquinoline]-5'-carbonitrile 4a: yellow solid, 83%, 0.427 g, mp 118.1–118.4 $^\circ\text{C}$; ^1H NMR (600 MHz, DMSO- d_6) δ 7.75 (d, J = 7.8 Hz, 2H, ArH), 7.49 (d, J = 7.2 Hz, 1H, ArH), 7.46 (d, J = 7.2 Hz, 2H, ArH), 7.35 (t, J = 7.8 Hz, 2H, ArH), 7.29–7.27 (m, 1H, ArH), 7.17 (d, J = 8.4 Hz, 2H, ArH), 7.04 (t, J = 7.8 Hz, 1H, ArH), 6.80 (t, J = 7.2 Hz, 1H, ArH), 6.63 (d, J = 7.8 Hz, 1H, ArH), 5.68 (s, 2H, NH_2), 5.53–5.52 (m, 1H, CH), 4.98 (d, J = 15.6 Hz, 1H, CH), 4.78 (d, J = 16.2 Hz, 1H, CH), 4.53 (d, J = 12.6 Hz, 1H, CH), 3.77–3.73 (m, 1H, CH), 3.30 (brs, 1H, CH), 2.68 (d, J = 18.0 Hz, 1H, CH), 2.29 (s, 3H, CH_3), 2.22 (dd, J_1 = 10.2 Hz, J_2 = 4.4 Hz, 1H, CH), 2.08 (s, 3H, CH_3), 1.76 (t, J = 10.2 Hz, 1H, CH); ^{13}C NMR (150 MHz, DMSO- d_6) δ 199.3, 174.7, 155.1, 144.7, 144.2, 136.7, 135.1, 130.5, 129.9, 129.8, 129.7, 129.1, 128.9, 127.8, 127.7, 127.6, 125.2, 122.8, 118.0, 109.9, 55.6, 55.3, 54.8, 54.0, 49.8, 44.1, 33.4, 21.5; IR (KBr) ν 3424, 3317, 3204, 2944, 2849, 2780, 2209, 1713, 1678, 1638, 1608, 1587, 1488, 1423, 1398, 1352, 1279, 1258, 1190, 1171, 1085, 985, 936, 846, 815, 796, 755 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd for $\text{C}_{33}\text{H}_{31}\text{N}_4\text{O}_2$ ($[\text{M} + \text{H}]^+$) 515.2442; Found 515.2424.

6'-Amino-1-benzyl-8'-(4-chlorobenzoyl)-2'-methyl-2-oxo-2',3',8',8a'-tetrahydro-1'H-spiro[indoline-3,7'-isoquinoline]-5'-carbonitrile 4b: yellow solid, 96%, 0.513 g, mp 190.3–192.1

°C; ^1H NMR (600 MHz, DMSO- d_6) δ 7.83 (d, J = 8.4 Hz, 2H, ArH), 7.47–7.42 (m, 5H, ArH), 7.36 (t, J = 7.8 Hz, 2H, ArH), 7.29 (t, J = 7.2 Hz, 1H, ArH), 7.04 (t, J = 7.2 Hz, 1H, ArH), 6.80 (t, J = 7.8 Hz, 1H, ArH), 6.65 (d, J = 7.8 Hz, 1H, ArH), 5.73 (s, 2H, NH_2), 5.54–5.53 (m, 1H, CH), 4.97 (d, J = 16.2 Hz, 1H, CH), 4.77 (d, J = 15.6 Hz, 1H, CH), 4.57 (d, J = 12.0 Hz, 1H, CH), 3.75 (brs, 1H, CH), 3.38 (m, 1H, CH), 2.70 (d, J = 16.8 Hz, 1H, CH), 2.25 (dd, J_1 = 10.2 Hz, J_2 = 4.8 Hz, 1H, CH), 2.10 (s, 3H, CH_3), 1.78 (t, J = 10.2 Hz, 1H, CH); ^{13}C NMR (150 MHz, DMSO- d_6) δ 198.7, 174.0, 154.3, 143.6, 138.8, 136.1, 135.6, 130.1, 129.7, 129.5, 128.7, 128.4, 127.3, 126.1, 124.8, 122.4, 117.6, 114.1, 109.5, 79.9, 55.0, 54.4, 53.5, 49.4, 45.2, 43.6, 32.9; IR (KBr) ν 3460, 3327, 3234, 3061, 2940, 2779, 2205, 1716, 1676, 1637, 1609, 1586, 1489, 1468, 1400, 1380, 1352, 1282, 1239, 1202, 1177, 1091, 982, 848, 794, 754 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd for $\text{C}_{32}\text{H}_{28}\text{ClN}_4\text{O}_2$ ($[\text{M} + \text{H}]^+$) 535.1895. Found 535.1906.

6'-Amino-1-benzyl-5-fluoro-8'-(4-methoxybenzoyl)-2'-methyl-2-oxo-2',3',8',8a'-tetrahydro-1'H-spiro[indoline-3,7'-isoquinoline]-5'-carbonitrile 4c: yellow solid, 92%, 0.504 g, mp 200.8–202.2 °C; ^1H NMR (600 MHz, DMSO- d_6) δ 7.87 (d, J = 7.8 Hz, 2H, ArH), 7.50 (d, J = 7.8 Hz, 1H, ArH), 7.46–7.45 (m, 2H, ArH), 7.35 (t, J = 6.6 Hz, 2H, ArH), 7.29–7.28 (m, 1H, ArH), 6.91–6.86 (m, 3H, ArH), 6.60 (brs, 1H, ArH), 5.86 (s, 2H, NH_2), 5.52 (s, 1H, CH), 4.97 (d, J = 15.6 Hz, 1H, CH), 4.76 (d, J = 15.6 Hz, 1H, CH), 4.52 (d, J = 12.0 Hz, 1H, CH), 3.80 (s, 3H, OCH_3), 3.73 (brs, 1H, CH), 3.37 (brs, 1H, CH), 2.68 (d, J = 16.8 Hz, 1H, CH), 2.23 (d, J = 6.0 Hz, 1H, CH), 2.09 (s, 3H, CH_3), 1.73 (t, J = 10.2 Hz, 1H, CH); ^{13}C NMR (150 MHz, DMSO- d_6) δ 197.3, 174.1, 163.6, 159.0, 157.4, 154.2, 140.1, 136.0, 130.8, 129.9 (d, J = 16.5 Hz), 128.4, 128.1 (d, J = 5.1 Hz), 127.3, 117.6, 115.8, 115.6, 113.8, 113.0, 112.8, 110.3 (d, J = 8.4 Hz), 79.9, 55.5, 55.3, 54.5, 53.9, 49.0, 45.3, 43.7, 32.9, 18.5; IR (KBr) ν 3398, 3313, 3084, 2940, 2845, 2790, 2204, 1716, 1643, 1599, 1575, 1496, 1455, 1422, 1399, 1382, 1344, 1258, 1241, 1205, 1177, 1081, 1024, 984, 964, 845, 818, 792 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd. for $\text{C}_{33}\text{H}_{30}\text{FN}_4\text{O}_3$ ($[\text{M} + \text{H}]^+$) 549.2296; Found 549.2313.

6'-Amino-8'-benzoyl-1-benzyl-5-chloro-2'-methyl-2-oxo-2',3',8',8a'-tetrahydro-1'H-spiro[indoline-3,7'-isoquinoline]-5'-carbonitrile 4d: yellow solid, 88%, 0.470 g, mp 180.6–182.4 °C; ^1H NMR (600 MHz, DMSO- d_6) δ 7.88 (d, J = 7.8 Hz, 2H, ArH), 7.68 (t, J = 7.2 Hz, 1H, ArH), 7.52 (t, J = 7.8 Hz, 2H, ArH), 7.35–7.34 (m, 2H, ArH), 7.09 (t, J = 7.2 Hz, 1H, ArH), 6.94 (t, J = 7.8 Hz, 2H, ArH), 6.76 (d, J = 9.0 Hz, 1H, ArH), 6.66 (d, J = 7.8 Hz, 2H, ArH), 6.41 (s, 2H, NH_2), 5.58 (brs, 1H, CH), 4.92 (d, J = 16.2 Hz, 1H, CH), 4.37 (t, J = 4.8 Hz, 1H, CH), 4.26 (d, J = 3.6 Hz, 1H, CH), 4.24 (d, J = 7.8 Hz, 1H, CH), 3.37 (brs, 1H, CH), 2.72 (d, J = 17.4 Hz, 1H, CH), 2.30 (dd, J_1 = 10.2 Hz, J_2 = 4.6 Hz, 1H, CH), 2.11 (s, 3H, CH_3), 1.81 (t, J = 10.2 Hz, 1H, CH); ^{13}C NMR (150 MHz, DMSO- d_6) δ 196.9, 173.7, 153.6, 142.1, 136.3, 135.0, 134.3, 131.1, 128.9, 128.7, 128.6, 128.3, 128.2, 127.1, 126.9, 126.6, 124.4, 117.4, 114.7, 111.2, 78.7, 56.0, 55.0, 54.6, 54.3, 47.6, 45.1, 44.2, 34.9, 18.5; IR (KBr) ν : 3468, 3316, 3195, 2967, 2863, 2788, 2206, 1712, 1671, 1639, 1590, 1481, 1448, 1428, 1395, 1335, 1281, 1256, 1239, 1202, 1170, 1124, 1081, 1047, 983, 932, 886, 851, 819, 756 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd. for $\text{C}_{32}\text{H}_{28}\text{ClN}_4\text{O}_2$ ($[\text{M} + \text{H}]^+$) 535.1895; Found 535.1903.

6'-Amino-1-benzyl-5-chloro-2'-methyl-8'-(4-methylbenzoyl)-2-oxo-2',3',8',8a'-tetrahydro-1'H-spiro[indoline-3,7'-isoquinoline]-5'-carbonitrile 4e: yellow solid, 89%, 0.488 g, mp 188.1–190.0 °C; ^1H NMR (600 MHz, DMSO- d_6) δ 7.78

(d, J = 8.4 Hz, 2H, ArH), 7.34–7.30 (m, 4H, ArH), 7.11 (t, J = 7.2 Hz, 1H, ArH), 6.95 (t, J = 7.8 Hz, 2H, ArH), 6.74 (d, J = 7.8 Hz, 1H, ArH), 6.66 (d, J = 7.8 Hz, 2H, ArH), 6.40 (s, 2H, NH_2), 5.57 (s, 1H, CH), 4.93 (d, J = 16.2 Hz, 1H, CH), 4.37 (t, J = 4.8 Hz, 1H, CH), 4.25–4.19 (m, 2H, CH), 3.37 (brs, 1H, CH), 2.71 (d, J = 17.4 Hz, 1H, CH), 2.37 (s, 3H, CH_3), 2.29 (dd, J_1 = 10.1 Hz, J_2 = 4.2 Hz, 1H, CH), 2.11 (s, 3H, CH_3), 1.79 (t, J = 10.2 Hz, 1H, CH); ^{13}C NMR (150 MHz, DMSO- d_6) δ 196.2, 173.7, 153.8, 145.1, 142.0, 135.0, 133.8, 131.1, 129.5, 128.8, 128.7, 128.4, 128.2, 127.1, 126.9, 126.5, 124.4, 117.3, 111.2, 78.6, 56.0, 55.0, 54.2, 47.4, 44.9, 44.2, 34.6, 21.1, 18.5; IR (KBr) ν 3462, 3317, 3202, 2956, 2922, 2858, 2785, 2207, 1714, 1668, 1639, 1607, 1586, 1481, 1428, 1396, 1331, 1280, 1258, 1188, 1169, 1123, 1080, 1050, 983, 934, 887, 854, 837, 815, 777, 755 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd for $\text{C}_{33}\text{H}_{30}\text{ClN}_4\text{O}_2$ ($[\text{M} + \text{H}]^+$) 549.2052; Found 549.2069.

6'-Amino-1,2'-dibenzyl-8'-(4-methoxybenzoyl)-2-oxo-2',3',8',8a'-tetrahydro-1'H-spiro[indoline-3,7'-isoquinoline]-5'-carbonitrile 4f: yellow solid, 92%, 0.582 g, mp 192.5–194.1 °C; ^1H NMR (600 MHz, DMSO- d_6) δ 7.79 (d, J = 8.4 Hz, 2H, ArH), 7.50 (d, J = 7.8 Hz, 1H, ArH), 7.46 (d, J = 7.8 Hz, 2H, ArH), 7.35 (t, J = 7.2 Hz, 2H, ArH), 7.28 (d, J = 7.2 Hz, 1H, ArH), 7.26–7.20 (m, 3H, ArH), 7.11 (d, J = 7.2 Hz, 2H, ArH), 7.04 (t, J = 7.8 Hz, 1H, ArH), 6.88 (d, J = 9.0 Hz, 2H, ArH), 6.81 (t, J = 7.8 Hz, 1H, ArH), 6.61 (d, J = 7.8 Hz, 1H, ArH), 5.67 (s, 2H, NH_2), 5.52 (s, 1H, CH), 4.97 (d, J = 15.6 Hz, 1H, CH), 4.78 (d, J = 16.2 Hz, 1H, CH), 4.52 (d, J = 12.0 Hz, 1H, CH), 3.80 (s, 3H, OCH_3), 3.72 (brs, 1H, CH), 3.38 (s, 2H, CH_2), 3.29 (d, J = 15.0 Hz, 1H, CH), 2.79 (d, J = 17.4 Hz, 1H, CH), 2.36 (dd, J_1 = 10.4 Hz, J_2 = 4.6 Hz, 1H, CH), 1.83 (t, J = 10.6 Hz, 1H, CH); ^{13}C NMR (150 MHz, DMSO- d_6) δ : 197.6, 174.4, 163.4, 154.7, 143.8, 137.8, 136.2, 130.7, 130.3, 130.1, 129.4, 128.7, 128.4, 128.1, 127.3, 126.9, 126.5, 124.7, 122.3, 117.6, 113.8, 113.7, 109.4, 79.8, 61.6, 55.5, 53.5, 53.4, 52.4, 49.3, 43.6, 33.0; IR (KBr) ν 3458, 3333, 3238, 3197, 3028, 2937, 2867, 2801, 2756, 2205, 1703, 1661, 1629, 1599, 1576, 1511, 1493, 1468, 1398, 1360, 134, 1311, 1269, 1247, 1173, 1080, 1030, 984, 847, 804 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd for $\text{C}_{39}\text{H}_{35}\text{N}_4\text{O}_3$ ($[\text{M} + \text{H}]^+$) 607.2704; Found 607.2706.

6'-Amino-8'-benzoyl-1,2'-dibenzyl-5-fluoro-2-oxo-2',3',8',8a'-tetrahydro-1'H-spiro[indoline-3,7'-isoquinoline]-5'-carbonitrile 4g: yellow solid, 95%, 0.564 g, mp 196.8–198.3 °C; ^1H NMR (600 MHz, DMSO- d_6) δ 7.76 (d, J = 7.8 Hz, 2H, ArH), 7.56 (t, J = 7.2 Hz, 1H, ArH), 7.50 (dd, J_1 = 8.4 Hz, J_2 = 2.5 Hz, 1H, ArH), 7.45 (d, J = 7.2 Hz, 2H, ArH), 7.40–7.35 (m, 4H, ArH), 7.30–7.27 (m, 1H, ArH), 7.25–7.20 (m, 3H, ArH), 7.09 (d, J = 6.6 Hz, 2H, ArH), 6.86 (td, J_1 = 9.0 Hz, J_2 = 2.4 Hz, 1H, ArH), 6.61 (dd, J_1 = 8.6 Hz, J_2 = 4.2 Hz, 1H, ArH), 5.89 (s, 2H, NH_2), 5.53–5.52 (m, 1H, CH), 4.95 (d, J = 15.6 Hz, 1H, CH), 4.77 (d, J = 16.2 Hz, 1H, CH), 4.58 (d, J = 12.0 Hz, 1H, CH), 3.71 (t, J = 10.8 Hz, 1H, CH), 3.42–3.37 (m, 2H, CH_2), 3.32–3.30 (m, 1H, CH), 2.81–2.78 (m, 1H, CH), 2.38 (dd, J_1 = 10.4 Hz, J_2 = 4.7 Hz, 1H, CH), 1.79 (t, J = 10.2 Hz, 1H, CH); ^{13}C NMR (150 MHz, DMSO- d_6) δ : 199.7, 174.1, 159.0, 157.5, 154.1, 140.1, 137.7, 137.2, 136.0, 133.7, 130.0, 128.7, 128.6, 128.5, 128.1, 128.0, 127.3, 126.9, 117.6, 115.8 (d, J = 23.0 Hz), 114.0, 112.9 (d, J = 26.0 Hz), 110.4 (d, J = 8.4 Hz), 79.8, 61.5, 53.8, 53.2, 52.3, 49.7, 43.7, 32.9; IR (KBr) ν 3457, 3330, 3240, 3200, 3028, 2917, 2868, 2800, 2753, 2206, 1703, 1671, 1630, 1580, 1494, 1451, 1394, 1359, 1337, 1271, 1241, 1202, 1172, 1143, 1081, 1028, 987, 969, 899, 858, 801 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd for $\text{C}_{38}\text{H}_{32}\text{FN}_4\text{O}_2$ ($[\text{M} + \text{H}]^+$) 595.2504; Found 595.2508.

6'-Amino-1,2'-dibenzyl-5-fluoro-8'-(4-methoxybenzoyl)-2-oxo-2',3',8'a'-tetrahydro-1'H-spiro[indoline-3,7'-isoquinoline]-5'-carbonitrile 4h: yellow solid, 94%, 0.587 g, mp 186.6–188.3 °C; ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ 7.81 (s, 2H, ArH), 7.51–7.45 (m, 3H, ArH), 7.35 (s, 2H, ArH), 7.28–7.24 (m, 4H, ArH), 7.12 (s, 2H, ArH), 6.90 (s, 3H, ArH), 6.59 (s, 1H, ArH), 5.86 (s, 2H, NH_2), 5.52 (s, 1H, CH), 4.96 (d, J = 14.4 Hz, 1H, CH), 4.77 (d, J = 16.2 Hz, 1H, CH), 4.52 (d, J = 9.6 Hz, 1H, CH), 3.81 (s, 3H, OCH_3), 3.71 (s, 1H, CH), 3.39 (s, 2H, CH_2), 3.30 (d, J = 16.2 Hz, 1H, CH), 2.79 (d, J = 15.0 Hz, 1H, CH), 2.38 (s, 1H, CH), 1.81 (s, 1H, CH); ^{13}C NMR (150 MHz, $\text{DMSO}-d_6$) δ 197.5, 174.2, 163.6, 159.0, 157.4, 154.3, 140.1, 137.8, 136.0, 130.7, 130.1(25.5), 128.6(33.1), 128.1, 127.3, 126.9, 117.6, 115.8(20.0), 113.8, 112.8(26.2), 110.3, 79.9, 61.6, 55.5, 53.9, 53.4, 52.4, 49.3, 43.7, 33.0; IR (KBr) ν 3458, 3339, 3240, 3026, 2915, 2867, 2803, 2754, 2206, 1704, 1660, 1629, 1595, 1493, 1453, 1396, 1358, 1336, 1316, 1267, 1245, 1203, 1169, 1079, 1023, 989, 898, 838, 791 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd. for $\text{C}_{39}\text{H}_{34}\text{FN}_4\text{O}_3$ ($[\text{M} + \text{H}]^+$) 625.2609; Found 625.2611.

6'-Amino-1,2'-dibenzyl-5-chloro-8'-(4-methoxybenzoyl)-2-oxo-2',3',8'a'-tetrahydro-1'H-spiro[indoline-3,7'-isoquinoline]-5'-carbonitrile 4i: yellow solid, 93%, 0.595 g, mp 194.4–196.4 °C; ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ 7.80 (d, J = 8.4 Hz, 2H, ArH), 7.66 (s, 1H, ArH), 7.44–7.43 (m, 2H, ArH), 7.36–7.34 (m, 2H, ArH), 7.28 (t, J = 7.2 Hz, 1H, ArH), 7.24–7.21 (m, 3H, ArH), 7.11 (d, J = 6.6 Hz, 2H, ArH), 7.08 (d, J = 7.2 Hz, 1H, ArH), 6.90 (d, J = 7.8 Hz, 2H, ArH), 6.59 (d, J = 8.4 Hz, 1H, ArH), 5.90 (s, 2H, NH_2), 5.51 (s, 1H, CH), 4.97 (d, J = 16.2 Hz, 1H, CH), 4.75 (d, J = 15.6 Hz, 1H, CH), 4.54 (d, J = 11.4 Hz, 1H, CH), 3.81 (s, 3H, OCH_3), 3.68 (s, 1H, CH), 3.39 (s, 2H, CH_2), 3.29 (d, J = 16.8 Hz, 1H, CH), 2.78 (d, J = 16.2 Hz, 1H, CH), 2.37–2.36 (m, 1H, CH), 1.80 (t, J = 16.2 Hz, 1H, CH); ^{13}C NMR (150 MHz, $\text{DMSO}-d_6$) δ 197.5, 174.1, 163.6, 154.1, 142.7, 137.7, 135.8, 130.7, 130.1, 130.0, 129.2, 128.7, 128.4, 128.1, 127.3, 127.2, 126.9, 126.4, 125.2, 117.6, 113.8, 110.8, 79.8, 61.6, 55.6, 53.7, 53.3, 52.4, 49.3, 43.7, 32.9; IR (KBr) ν 3455, 3325, 3240, 3198, 3027, 2939, 2800, 2753, 2207, 1706, 1661, 1630, 1598, 1576, 1510, 1489, 1456, 1428, 1397, 1335, 1267, 1246, 1172, 1081, 1031, 985, 884, 844, 805 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd for $\text{C}_{39}\text{H}_{34}\text{ClN}_4\text{O}_3$ ($[\text{M} + \text{H}]^+$) 641.2314; Found 641.2313.

6'-Amino-1,2'-dibenzyl-5-chloro-8'-(4-methylbenzoyl)-2-oxo-2',3',8'a'-tetrahydro-1'H-spiro[indoline-3,7'-isoquinoline]-5'-carbonitrile 4j: yellow solid, 90%, 0.562 g, mp 188.6–190.4 °C; ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ 7.69–7.66 (m, 3H, ArH), 7.43 (s, 2H, ArH), 7.35 (s, 2H, ArH), 7.28–7.20 (m, 6H, ArH), 7.11 (brs, 3H, ArH), 6.60 (d, J = 6.0 Hz, 1H, ArH), 5.90 (s, 2H, NH_2), 5.52 (s, 1H, CH), 4.97 (d, J = 15.0 Hz, 1H, CH), 4.76 (d, J = 15.6 Hz, 1H, CH), 4.55 (d, J = 11.4 Hz, 1H, CH), 3.68 (s, 1H, CH), 3.38 (s, 2H, CH_2), 3.30 (d, J = 16.2 Hz, 1H, CH), 2.78 (d, J = 16.2 Hz, 1H, CH), 2.35–2.32 (m, 4H, CH, CH_3), 1.80 (brs, 1H, CH); ^{13}C NMR (150 MHz, $\text{DMSO}-d_6$) δ 199.0, 174.0, 154.0, 144.3, 142.7, 137.7, 135.8, 134.6, 130.1, 129.2, 128.7, 128.4, 128.3, 128.1, 127.3, 126.9, 126.5, 125.2, 117.6, 13.9, 110.8, 79.8, 61.6, 53.6, 53.2, 52.3, 49.6, 43.7, 32.9, 21.1; IR (KBr) ν 3454, 3324, 3239, 3198, 3028, 2917, 2867, 2799, 2752, 2207, 1705, 1666, 1631, 1607, 1576, 1489, 1455, 1430, 1399, 1335, 1273, 1246, 1176, 1081, 1032, 985, 884, 804, 784 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd. for $\text{C}_{39}\text{H}_{34}\text{ClN}_4\text{O}_2$ ($[\text{M} + \text{H}]^+$) 625.2365; Found: 625.2359.

General Procedure for the Synthesis of Compound 5a–5l. A mixture of vinyl malononitrile (1.0 mmol) and 3-

phenacylideneoxindole (1.0 mmol) and piperidine (0.1 mmol) in ethanol (10.0 mL) was stirred at room temperature for about one hour. The resulting precipitate was collected by filtration and washed with cold alcohol to give the pure product for analysis.

2-(2-(1-(1-Butyl-5-chloro-2-oxoindolin-3-yl)-2-(4-methoxyphenyl)-2-oxoethyl)cyclohexylidene)malononitrile (5a): white solid, 81%, 0.458 g, mp 164.8–168.2 °C; ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ 8.14 (d, J = 9.0 Hz, 2H, ArH), 7.57 (brs, 1H, ArH), 7.29 (d, J = 7.8 Hz, 1H, ArH), 7.11 (d, J = 9.0 Hz, 2H, ArH), 7.02 (d, J = 8.4 Hz, 1H, ArH), 4.96 (dd, J_1 = 11.2 Hz, J_2 = 1.7 Hz, 1H, CH), 3.87 (s, 3H, OCH_3), 3.79 (brs, 1H, CH), 3.67–3.56 (m, 3H, CH_2 , CH), 2.94–2.90 (m, 1H, CH), 2.65 (d, J = 12.6 Hz, 1H, CH), 2.12 (d, J = 12.0 Hz, 1H, CH), 1.76–1.71 (m, 1H, CH), 1.59–1.57 (m, 1H, CH), 1.54–1.46 (m, 3H, CH), 1.45–1.42 (m, 1H, CH), 1.40–1.36 (m, 1H, CH), 1.35–1.31 (m, 2H, CH_2), 0.92 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (150 MHz, $\text{DMSO}-d_6$) δ 197.7, 173.7, 164.0, 142.6, 131.3, 131.0, 128.3, 125.4, 114.5, 114.3, 109.8, 82.8, 55.7, 44.8, 42.0, 34.2, 32.1, 32.0, 30.2, 29.2, 27.3, 24.2, 19.6, 19.5, 13.6; IR (KBr) ν 2960, 2934, 2866, 2228, 1713, 1667, 1599, 1510, 1480, 1425, 1353, 1312, 1266, 1210, 1175, 1114, 1026, 996, 958, 845, 815 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd for $\text{C}_{30}\text{H}_{31}\text{ClN}_3\text{O}_3$ ($[\text{M} + \text{H}]^+$) 516.2054; Found 516.2048.

2-(2-(1-(1-Benzyl-2-oxoindolin-3-yl)-2-(4-methoxyphenyl)-2-oxoethyl)-4-tert-butylcyclohexylidene)malononitrile (5b): white solid, 85%, 0.485 g, mp 193.1–193.7 °C; ^1H NMR (600 MHz, CDCl_3) δ 8.24 (d, J = 8.4 Hz, 2H, ArH), 7.54 (d, J = 7.2 Hz, 1H, ArH), 7.33–7.27 (m, 5H, ArH), 7.26 (brs, 1H, ArH), 7.20 (t, J = 7.8 Hz, 1H, ArH), 7.05 (d, J = 9.0 Hz, 2H, ArH), 6.80 (d, J = 7.8 Hz, 1H, ArH), 5.30 (d, J = 15.6 Hz, 1H, CH), 4.98 (d, J = 10.8 Hz, 1H, CH), 4.51 (d, J = 15.0 Hz, 1H, CH), 3.92 (s, 3H, OCH_3), 3.75 (d, J = 10.2 Hz, 1H, CH), 3.71 (s, 1H, CH), 2.91–2.82 (m, 2H, CH_2), 2.15 (d, J = 12.0 Hz, 1H, CH), 1.94 (d, J = 12.6 Hz, 1H, CH), 1.56–1.51 (m, 1H, CH), 1.24–1.11 (m, 2H, CH_2), 0.65 (s, 9H, CH_3); ^{13}C NMR (150 MHz, CDCl_3) δ 197.3, 184.3, 175.1, 164.5, 143.6, 135.2, 131.1, 129.4, 128.9, 128.6, 127.9, 127.4, 126.5, 124.5, 123.0, 114.5, 111.6, 109.6, 109.5, 83.2, 55.6, 46.2, 44.2, 43.4, 41.8, 41.6, 33.8, 32.4, 32.1, 31.4, 27.2; IR (KBr) ν 3064, 3024, 2963, 2870, 2230, 1701, 1679, 1600, 1575, 1511, 1483, 1463, 1440, 1421, 1371, 1351, 1295, 1262, 1212, 1180, 1111, 1079, 1029, 991, 898, 858, 840, 762 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd for $\text{C}_{37}\text{H}_{37}\text{N}_3\text{NaO}_3$ ($[\text{M} + \text{Na}]^+$) 594.2727; Found 594.2725.

2-(2-(1-(1-Benzyl-5-fluoro-2-oxoindolin-3-yl)-2-oxo-2-p-tolylethyl)-4-tert-butylcyclohexylidene)malononitrile (5c): white solid, 88%, 0.504 g, mp 189.5–190.5 °C; ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ 8.05 (d, J = 7.8 Hz, 2H, ArH), 7.59 (d, J = 7.2 Hz, 1H, ArH), 7.38–7.35 (m, 4H, ArH), 7.33–7.31 (m, 2H, ArH), 7.26–7.24 (m, 1H, ArH), 6.94 (t, J = 7.8 Hz, 1H, ArH), 6.71 (brs, 1H, ArH), 5.08 (d, J = 10.8 Hz, 1H, CH), 4.92–4.89 (m, 1H, CH), 4.83–4.80 (m, 1H, CH), 3.88 (s, 2H, CH_2), 3.11–3.07 (m, 1H, CH), 2.77 (d, J = 12.6 Hz, 1H, CH), 2.38 (s, 3H, CH_3), 2.18 (d, J = 10.8 Hz, 1H, CH), 1.78 (t, J = 12.6 Hz, 1H, CH), 1.58 (d, J = 13.2 Hz, 1H, CH), 1.33–1.23 (m, 2H, CH_2), 0.53 (s, 9H, CH_3); ^{13}C NMR (150 MHz, $\text{DMSO}-d_6$) δ 199.6, 185.6, 174.2, 144.9, 139.5, 134.5, 129.5, 129.4, 128.8, 128.7, 128.5, 128.3, 127.3, 127.2, 126.8, 114.5, 113.1, 112.3, 112.1, 111.1, 109.5, 83.0, 44.8, 42.8, 42.4, 34.1, 32.7, 31.8, 31.7, 31.2, 28.1, 27.2, 26.9, 26.8, 21.1; IR (KBr) ν 3036, 2968, 2871, 2229, 1707, 1682, 1606, 1488, 1452, 1411, 1366, 1345, 1287, 1259, 1223, 1185, 1138, 1023, 995, 969, 941, 898, 877, 854, 829, 813, 783, 768 cm^{-1} ; MS (m/z) HRMS

(ESI) Calcd for $C_{37}H_{36}FN_3NaO_2$ ($[M + Na]^+$) 596.2684; Found 596.2684.

2-(2-(1-(1-Benzyl-5-chloro-2-oxoindolin-3-yl)-2-oxo-2-p-tolylolethyl)-4-tert-butylcyclohexylidene)malononitrile (5d): white solid, 87%, 0.512 g, mp 172.9–173.1 °C; 1H NMR (600 MHz, DMSO- d_6) δ 8.00 (d, J = 8.4 Hz, 2H, ArH), 7.83 (s, 1H, ArH), 7.37–7.31 (m, 6H, ArH), 7.27–7.24 (m, 1H, ArH), 7.13 (d, J = 8.4 Hz, 1H, ArH), 6.69 (d, J = 8.4 Hz, 1H, ArH), 5.11 (dd, J_1 = 11.7 Hz, J_2 = 2.4 Hz, 1H, CH), 4.86 (s, 2H, CH₂), 3.92 (m, J = 9.0 Hz, 1H, CH), 3.85 (s, 1H, CH), 3.16–3.11 (m, 1H, CH), 2.78 (d, J = 12.6 Hz, 1H, CH), 2.37 (s, 3H, CH₃), 2.19–2.17 (m, 1H, CH), 1.83–1.79 (d, J = 12.6 Hz, 1H, CH), 1.56 (d, J = 13.8 Hz, 1H, CH), 1.34–1.25 (m, 2H, CH₂), 0.52 (s, 9H, CH₃); ^{13}C NMR (150 MHz, DMSO- d_6) δ 199.6, 187.1, 174.0, 166.7, 144.9, 143.6, 142.0, 135.8, 135.7, 134.4, 132.0, 129.7, 129.4, 128.9, 128.8, 128.7, 128.5, 128.3, 127.3, 127.2, 126.8, 126.1, 125.4, 120.9, 112.1, 111.2, 110.0, 83.1, 80.5, 45.5, 43.0, 42.7, 42.5, 43.0, 42.7, 42.5, 34.0, 32.7, 32.1, 31.8, 31.7, 31.3, 28.1, 27.2, 26.9, 26.7, 21.3, 21.1; IR (KBr) ν 3072, 3024, 2968, 2253, 1708, 1681, 1606, 1582, 1484, 1454, 1431, 1344, 1283, 1175, 1101, 1079, 994, 910, 812, 784 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd for $C_{37}H_{36}ClN_3NaO_2$ ($[M + Na]^+$) 612.2388; Found 612.2390.

2-(2-(1-(1-Benzyl-2-oxoindolin-3-yl)-2-(4-methoxyphenyl)-2-oxoethyl)cycloheptylidene)malononitrile (5e): white solid, 78%, 0.412 g, mp 192.6–193.4 °C; 1H NMR (600 MHz, DMSO- d_6) δ 7.84 (d, J = 7.8 Hz, 2H, ArH), 7.50–7.46 (m, 3H, ArH), 7.35–7.33 (m, 2H, ArH), 7.28–7.26 (m, 1H, ArH), 7.06–7.03 (m, 1H, ArH), 7.01 (d, J = 7.8 Hz, 2H, ArH), 6.85–6.82 (m, 1H, ArH), 6.71 (d, J = 7.8 Hz, 1H, ArH), 4.98–4.91 (m, 2H, CH₂), 4.83 (d, J = 7.8 Hz, 1H, CH), 4.09 (brs, 1H, CH), 4.04 (s, 1H, CH), 3.82 (s, 3H, OCH₃), 2.90–2.86 (m, 1H, CH), 2.26 (brs, 1H, CH), 1.80–1.71 (m, 3H, CH₂, CH), 1.35–1.32 (m, 1H, CH), 1.23–1.21 (m, 1H, CH), 0.95–0.93 (m, 1H, CH); ^{13}C NMR (150 MHz, DMSO- d_6) δ 197.6, 175.4, 163.5, 143.3, 136.5, 130.3, 128.4, 127.8, 127.4, 127.2, 123.4, 121.5, 114.1, 111.5, 111.3, 108.7, 86.7, 55.6, 49.5, 45.6, 42.7, 32.1, 30.0, 29.0, 28.8, 24.2; IR (KBr) ν 3466, 3033, 2926, 2855, 2227, 1699, 1674, 1598, 1513, 1488, 1467, 1351, 1310, 1264, 1232, 1212, 1172, 1105, 1020, 997, 952, 922, 892, 847, 782, 753 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd for $C_{34}H_{31}N_3NaO_3$ ($[M + Na]^+$) 552.2258; Found 552.2258.

2-(2-(1-(1-Butyl-2-oxoindolin-3-yl)-2-oxo-2-p-tolylolethyl)-cycloheptylidene)malononitrile (6f): white solid, 90%, 0.431 g, mp 223.7–224.5 °C; 1H NMR (600 MHz, DMSO- d_6) δ 7.71 (d, J = 4.2 Hz, 2H, ArH), 7.48 (brs, 1H, ArH), 7.29 (d, J = 4.8 Hz, 2H, ArH), 7.13 (brs, 1H, ArH), 6.92 (d, J = 4.8 Hz, 1H, ArH), 6.84 (brs, 1H, ArH), 4.79 (d, J = 6.0 Hz, 1H, CH), 4.04 (s, 1H, CH), 3.88 (s, 1H, CH), 3.70 (d, J = 17.4 Hz, 2H, CH₂), 2.84 (brs, 1H, CH), 2.50 (brs, 1H, CH), 2.34 (s, 3H, CH₃), 2.19 (brs, 1H, CH), 2.06 (brs, 1H, CH), 1.79 (brs, 2H, CH₂), 1.71–1.70 (m, 1H, CH), 1.62–1.61 (m, 2H, CH₂), 1.40–1.39 (m, 2H, CH₂), 1.32–1.31 (m, 1H, CH), 1.21–1.19 (m, 1H, CH), 0.94 (brs, 4H, CH, CH₃); ^{13}C NMR (150 MHz, DMSO- d_6) δ 198.8, 188.4, 175.1, 144.2, 143.8, 134.9, 129.4, 127.9, 127.0, 123.4, 121.2, 111.4, 111.3, 108.1, 86.8, 49.7, 45.5, 41.9, 32.1, 29.9, 29.0, 28.8, 24.2, 21.1, 19.5, 13.7; IR (KBr) ν 2931, 2826, 2228, 1701, 1678, 1608, 1486, 1466, 1352, 1273, 1231, 1205, 1185, 1135, 1096, 1024, 956, 921, 831, 793, 772 cm^{-1} ; MS (m/z): HRMS (ESI) Calcd for $C_{31}H_{33}N_3NaO_2$ ($[M + Na]^+$) 502.2465. Found 502.2467.

General Procedure for the Synthesis of Compounds 5g–5l. A mixture of vinyl malononitrile (1.0 mmol) and 3-

phenacylideneoxindole (1.0 mmol) and *p*-dimethylaminopyridine (1.0 mmol) in ethanol (10.0 mL) was stirred at room temperature for about 30 min. The resulting precipitate was collected by filtration and washed with cold alcohol to give the pure product for analysis.

2-(3-(1-Benzyl-5-chloro-2-oxoindolin-3-yl)-4-oxo-1,4-di(*p*-tolyl)butylidene)malononitrile (5g): white solid, 92%, 0.523 g, mp 152.3–154.6 °C; 1H NMR (600 MHz, DMSO- d_6) δ 7.54 (d, J = 8.4 Hz, 2H, ArH), 7.38–7.37 (m, 2H, ArH), 7.35–7.32 (m, 6H, ArH), 7.29–7.26 (m, 3H, ArH), 7.20–7.18 (m, 2H, ArH), 6.79 (d, J = 8.4 Hz, 1H, ArH), 4.96–4.87 (m, 2H, CH₂), 4.32–4.30 (m, 1H, CH), 3.96 (d, J = 3.0 Hz, 1H, CH), 3.58 (dd, J_1 = 14.8 Hz, J_2 = 8.4 Hz, 1H, CH), 3.39 (dd, J_1 = 14.8 Hz, J_2 = 5.8 Hz, 1H, CH), 2.38 (s, 3H, CH₃), 2.36 (s, 3H, CH₃); ^{13}C NMR (150 MHz, DMSO- d_6) δ 198.6, 177.5, 174.6, 144.5, 142.6, 142.2, 135.9, 132.7, 130.7, 129.5, 129.3, 128.6, 128.3, 128.0, 127.6, 127.4, 127.2, 126.1, 124.2, 113.2, 112.5, 110.4, 84.6, 45.4, 44.7, 43.0, 35.2, 21.1, 21.0; IR (KBr) ν : 3062, 2028, 2922, 2230, 1725, 1679, 1609, 1584, 1484, 1436, 1375, 1343, 1289, 1245, 1215, 1166, 1120, 1080, 1014, 973, 939, 917, 890, 826, 809, 779 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd for $C_{36}H_{29}ClN_3O_2$ ($[M + H]^+$) 570.1948; Found 570.1946.

2-(3-(1-Benzyl-5-fluoro-2-oxoindolin-3-yl)-4-oxo-1,4-di(*p*-tolyl)butylidene)malononitrile (5h): white solid, 90%, 0.498 g, mp 135.8–138.6 °C; 1H NMR (600 MHz, CDCl₃) δ 7.71 (d, J = 8.4 Hz, 2H, ArH), 7.35–7.29 (m, 5H, ArH), 7.24–7.20 (m, 6H, ArH), 6.92–6.89 (m, 1H, ArH), 6.85 (d, J = 7.8 Hz, 1H, ArH), 6.69 (dd, J_1 = 8.5 Hz, J_2 = 4.6 Hz, 1H, ArH), 5.11 (d, J = 15.6 Hz, 1H, CH), 4.79 (d, J = 15.6 Hz, 1H, CH), 4.31–4.29 (m, 1H, CH), 3.80 (brs, 1H, CH), 3.45 (dd, J_1 = 15.0 Hz, J_2 = 8.3 Hz, 1H, CH), 2.69 (dd, J_1 = 15.0 Hz, J_2 = 4.7 Hz, 1H, CH), 2.40 (s, 3H, CH₃), 2.38 (s, 3H, CH₃); ^{13}C NMR (150 MHz, CDCl₃) δ : 198.2, 175.7 (d, J = 313.5 Hz), 172.7 (d, J = 240.4 Hz), 145.2, 143.2, 139.6, 135.4, 132.2, 130.7, 129.9 (d, J = 12.6 Hz), 128.6, 128.0, 127.9, 127.4, 125.5 (d, J = 8.4 Hz), 115.5 (d, J = 23.5 Hz), 113.2 (d, J = 25.2 Hz), 112.9, 112.3, 110.2 (d, J = 7.8 Hz), 85.6, 47.1, 45.2, 44.4, 33.5, 21.6 (d, J = 20.1 Hz); IR (KBr) ν : 3044, 2911, 1130, 1718, 1682, 1608, 1578, 1492, 1451, 1348, 1268, 1228, 1181, 1136, 1019, 966, 929, 882, 820 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd for $C_{36}H_{29}FN_3O_2$ ($[M + H]^+$) 554.2244; Found 554.2236.

2-(3-(1-Benzyl-2-oxoindolin-3-yl)-4-(4-chlorophenyl)-4-oxo-1-p-tolylbutylidene)malononitrile (5i): white solid, 89%, 0.494 g, mp 136–138 °C; 1H NMR (600 MHz, DMSO- d_6) δ 7.62 (d, J = 8.4 Hz, 2H, ArH), 7.52 (d, J = 7.8 Hz, 2H, ArH), 7.38–7.31 (m, 2H, ArH), 7.35–7.32 (m, 4H, ArH), 7.31–7.26 (m, 3H, ArH), 7.15 (t, J = 7.8 Hz, 1H, ArH), 7.07 (d, J = 7.8 Hz, 1H, ArH), 6.91 (t, J = 7.8 Hz, 1H, ArH), 6.82 (t, J = 7.8 Hz, 1H, ArH), 4.96 (d, J = 15.6 Hz, 1H, CH), 4.87 (d, J = 15.6 Hz, 1H, CH), 4.26–4.23 (m, 1H, CH), 3.98 (d, J = 3.0 Hz, 1H, CH), 3.54 (dd, J_1 = 14.9 Hz, J_2 = 8.8 Hz, 1H, CH), 3.30 (dd, J_1 = 14.9 Hz, J_2 = 5.2 Hz, 1H, CH), 2.37 (s, 3H, CH₃); ^{13}C NMR (150 MHz, CDCl₃) δ 197.6, 176.5, 174.8, 143.5, 143.2, 140.5, 135.6, 133.1, 130.7, 130.1, 130.0, 129.8, 129.7, 129.5, 129.2, 129.0, 128.9, 128.0, 127.9, 127.8, 127.5, 127.4, 124.9, 123.6, 123.2, 122.8, 112.9, 112.3, 109.7, 109.6, 85.8, 46.8, 46.6, 46.4, 45.5, 44.3, 43.9, 36.6, 33.4, 21.6; IR (KBr) ν 3060, 3026, 2230, 1715, 1690, 1591, 1490, 1446, 1358, 1263, 1204, 1169, 1093, 1012, 966, 937, 821, 747 cm^{-1} ; MS (m/z) HRMS (ESI) Calcd for $C_{35}H_{27}ClN_3O_2$ ($[M + H]^+$) 556.1792; Found 556.1792.

2-(3-(1-Butyl-5-chloro-2-oxoindolin-3-yl)-4-oxo-1,4-di(*p*-tolyl)butylidene)malononitrile (5j): white solid, 86%, 0.460 g, mp 139.9–141.1 °C; 1H NMR (600 MHz, DMSO- d_6) δ 7.53

(d, $J = 8.4$ Hz, 2H, ArH), 7.34–7.30 (m, 4H, ArH), 7.28 (dd, $J_1 = 8.4$ Hz, $J_2 = 1.8$ Hz, 1H, ArH), 7.26 (d, $J = 8.4$ Hz, 2H, ArH), 7.13 (brs, 1H, ArH), 7.02 (d, $J = 8.4$ Hz, 1H, ArH), 4.24–4.21 (m, 1H, CH), 3.80 (d, $J = 3.0$ Hz, 1H, CH), 3.66 (t, $J = 7.8$ Hz, 2H, CH), 3.49 (dd, $J_1 = 14.8$ Hz, $J_2 = 8.2$ Hz, 1H, CH), 3.26 (dd, $J_1 = 14.8$ Hz, $J_2 = 5.8$ Hz, 1H, CH), 2.38 (s, 3H, CH₃), 2.35 (s, 3H, CH₃), 1.59–1.54 (m, 2H, CH₂), 1.36–1.32 (m, 2H, CH₂), 0.92 (t, $J = 7.8$ Hz, 3H, CH₃); ¹³C NMR (150 MHz, CDCl₃) δ 198.2, 176.8, 174.2, 145.1, 143.1, 142.5, 132.1, 130.7, 129.9, 129.8, 129.0, 128.5, 128.2, 127.8, 125.8, 125.4, 112.9, 112.2, 109.8, 85.5, 46.8, 45.1, 40.4, 33.5, 29.4, 21.7, 21.6, 20.2, 13.7; IR (KBr) ν 2961, 2928, 2871, 2223, 1709, 1673, 1607, 1557, 1484, 1432, 1353, 1311, 1268, 1180, 1114, 930, 824, 781 cm⁻¹; MS (m/z) HRMS (ESI) Calcd for C₃₃H₃₁ClN₃O₂ ([M + H]⁺) 536.2105; Found 536.2103.

2-(3-(1-Benzyl-5-chloro-2-oxindolin-3-yl)-4-(4-methylphenyl)-4-oxo-1-*p*-chlorophenylbutylidene)malononitrile 5k. white solid, 85%, 0.501g, mp 154.2–156.6 °C; ¹H NMR (600 MHz, DMSO) δ : 7.62 (d, $J = 8.4$ Hz, 2H, ArH), 7.59 (d, $J = 7.8$ Hz, 2H, ArH), 7.50 (d, $J = 8.4$ Hz, 2H, ArH), 7.39 (d, $J = 7.2$ Hz, 2H, ArH), 7.34 (t, $J = 7.2$ Hz, 2H, ArH), 7.28 (d, $J = 7.8$ Hz, 3H, ArH), 7.25 (s, 1H, ArH), 7.19 (d, $J = 7.8$ Hz, 1H, ArH), 6.78 (d, $J = 8.4$ Hz, 1H, ArH), 4.96–4.89 (m, 2H, CH), 4.36–4.33 (m, 1H, CH), 3.97 (d, $J = 2.4$ Hz, 1H, CH), 3.62 (dd, $J_1 = 14.8$ Hz, $J_2 = 8.1$ Hz, 1H, CH), 3.47 (dd, $J_1 = 14.8$ Hz, $J_2 = 6.1$ Hz, 1H, CH), 2.37 (s, 3H, CH₃); ¹³C NMR (150 MHz, CDCl₃) δ : 197.8, 175.5, 174.5, 145.5, 142.1, 138.6, 135.1, 131.9, 130.0, 129.7, 129.6, 129.4, 129.2, 129.0, 128.6, 128.4, 128.1, 127.4, 127.3, 125.4, 112.3, 111.8, 110.6, 86.9, 47.0, 46.3, 46.0, 45.0, 44.4, 33.6, 21.8; IR (KBr) ν : 3063, 3030, 2925, 2231, 2015, 1723, 1679, 1609, 1587, 1486, 1436, 1405, 1344, 1269, 1244, 1218, 1168, 1120, 1091, 1012, 938, 918, 891, 838, 814, 799 cm⁻¹; MS (m/z): HRMS (ESI) Calcd. for C₃₅H₂₆Cl₂N₃O₂ ([M+H]⁺): 590.1402. Found: 590.1393.

2-(3-(1-Benzyl-2-oxindolin-3-yl)-4-oxo-1,4-di(*p*-methoxyphenyl)butylidene)malononitrile 5l: white solid, 88%, 0.499 g, mp 140.8–142.6 °C; ¹H NMR (600 MHz, CDCl₃) δ 7.67 (d, $J = 8.4$ Hz, 2H, ArH), 7.43 (d, $J = 7.8$ Hz, 2H, ArH), 7.39 (d, $J = 7.8$ Hz, 2H, ArH), 7.34 (t, $J = 7.2$ Hz, 2H, ArH), 7.27 (t, $J = 7.2$ Hz, 1H, ArH), 7.14 (t, $J = 7.2$ Hz, 1H, ArH), 7.08–7.06 (m, 3H, ArH), 6.99 (d, $J = 7.8$ Hz, 2H, ArH), 6.91 (t, $J = 7.2$ Hz, 1H, ArH), 6.82 (d, $J = 7.8$ Hz, 1H, ArH), 4.98 (d, $J = 15.6$ Hz, 1H, CH), 4.88 (d, $J = 15.6$ Hz, 1H, CH), 4.26–4.25 (m, 1H, CH), 3.94 (s, 1H, CH), 3.84 (s, 3H, OCH₃), 3.82 (s, 3H, OCH₃), 3.51 (dd, $J_1 = 14.7$ Hz, $J_2 = 9.0$ Hz, 1H, CH), 3.26 (dd, $J_1 = 14.7$ Hz, $J_2 = 4.8$ Hz, 1H, CH); ¹³C NMR (150 MHz, CDCl₃) δ 197.0, 176.1, 175.1, 164.1, 162.8, 143.5, 135.7, 130.8, 130.0, 129.0, 128.9, 127.9, 127.7, 127.5, 125.6, 125.1, 123.9, 123.1, 114.6, 114.3, 113.5, 112.7, 109.5, 84.1, 55.6, 55.5, 47.2, 45.2, 44.3, 33.2; IR (KBr) ν 3016, 2935, 2841, 2225, 1699, 1672, 1604, 1574, 1542, 1510, 1488, 1466, 1434, 1365, 1341, 1301, 1267, 1231, 1196, 1176, 1120, 1074, 1025, 949, 861, 830, 762 cm⁻¹; MS (m/z) HRMS (ESI) Calcd for C₃₆H₃₀N₃O₄ ([M + H]⁺) 568.2236; Found 568.2228.

■ ASSOCIATED CONTENT

■ Supporting Information

¹H NMR and ¹³C NMR spectra for all compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>. Crystallographic data **3a** (CCDC 971475), **3d** (CCDC 971476), **3h** (CCDC 971477), **4e** (CCDC 971478), **5a** (CCDC 971472), **5e** (CCDC 971473), **5i** (CCDC 971474)

have been deposited at the Cambridge Crystallographic Database Centre.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was financially supported by the National Natural Science Foundation of China (Grant No. 21172189) and the Priority Academic Program Development of Jiangsu Higher Education Institutions.

■ REFERENCES

- (1) (a) Abdel-Rahman, A. H.; Keshk, E. M.; Hanna, M. A.; El-Bady, Sh. M. Synthesis and Evaluation of Some New Spiro Indoline-Based Heterocycles As Potentially Active Antimicrobial Agents. *Bioorg. Med. Chem.* **2004**, *12*, 2483–2488. (b) Marti, C.; Carreira, E. M. Construction of Spiro[pyrrolidine-3,3'-oxindoles]—Recent Applications to the Synthesis of Oxindole Alkaloids. *Eur. J. Org. Chem.* **2003**, 2209–2214. (c) Sebahar, P. R.; Williams, R. M. The Asymmetric Total Synthesis of (+)- and (–)-Spirotryprostatin B. *J. Am. Chem. Soc.* **2000**, *122*, 5666–5667.
- (2) (a) Vintonyak, V. V.; Warburg, K.; Kruse, H.; Grimme, S.; Hubel, K.; Rauth, D.; Waldmann, H. Identification of Thiazolidinones Spiro-Fused to Indolin-2-ones as Potent and Selective Inhibitors of the *Mycobacterium tuberculosis* Protein Tyrosine Phosphatase B. *Angew. Chem., Int. Ed.* **2010**, *49*, 5902. (b) Ding, K.; Lu, Y.; Nikolovska-Coleska, Z.; Wang, G.; Qiu, S.; Shangary, S.; Gao, W.; Qin, D.; Stuke, J.; Krajewski, K.; Roller, P. P.; Wang, S. Structure-Based Design of Spiro-oxindoles as Potent, Specific Small-Molecule Inhibitors of the MDM2–p53 Interaction. *J. Med. Chem.* **2006**, *49*, 3432.
- (3) (a) Kotha, S. B.; Deb, A. C.; Lahiri, K.; Manivannan, E. Selected Synthetic Strategies to Spirocyclics. *Synthesis* **2009**, 165–193. (b) Trost, B. M.; Brennan, M. K. Asymmetric Syntheses of Oxindole and Indole Spirocyclic Alkaloid Natural Products. *Synthesis* **2009**, 3003–3025. (c) Chauhan, P.; Chimni, S. S. Organocatalytic Asymmetric Synthesis of 3-Amino-2-oxindole Derivatives Bearing a Tetra-Substituted Stereocenter. *Tetrahedron: Asymmetry* **2013**, *24*, 343–356.
- (4) (a) Singh, G. S.; Desta, Z. Y. Isatins As Privileged Molecules in Design and Synthesis of Spiro-Fused Cyclic Frameworks. *Chem. Rev.* **2012**, *112*, 6104–6155. (b) Ball-Jones, N. R.; Badillo, J. J.; Franz, A. K. Strategies for the Enantioselective Synthesis of Spirooxindoles. *Org. Biomol. Chem.* **2012**, *10*, 5165–5181.
- (5) (a) Hong, L.; Wang, R. Recent Advances in Asymmetric Organocatalytic Construction of 3,3'-Spirocyclic Oxindoles. *Adv. Synth. Catal.* **2013**, *355*, 1023–1030. (b) Liu, Y. Y.; Wang, H.; Wan, J. P. Recent Advances in Diversity Oriented Synthesis through Isatin-based Multicomponent Reactions. *Asian J. Org. Chem.* **2013**, *2*, 374–386.
- (6) (a) Tsuda, M.; Kasai, Y.; Komatsu, K.; Sone, T.; Tanaka, M. Y.; Kobayashi, J. Citrinadin A, a Novel Pentacyclic Alkaloid from Marine-Derived Fungus *Penicillium citrinum*. *Org. Lett.* **2004**, *6*, 3087–3089. (b) Mugishima, T.; Tsuda, M.; Kasai, Y.; Ishiyama, H.; Fukushi, E.; Kawabata, J.; Watanabe, M.; Akao, K.; Kobayashi, J. Absolute Stereochemistry of Citrinadins A and B from Marine-Derived Fungus. *J. Org. Chem.* **2005**, *70*, 9430–9435. (c) Greshock, T. J.; Grubbs, A. W.; Jiao, P.; Wicklow, D. T.; Gloer, J. B.; Williams, R. M. Isolation, Structure Elucidation, and Biomimetic Total Synthesis of Versicolamide B, and the Isolation of Antipodal (–)-Stephacidin A and (+)-Notoamide B from *Aspergillus versicolor* NRRL 35600. *Angew. Chem., Int. Ed.* **2008**, *47*, 3573–3575.
- (7) (a) Babu, A. B. S.; Raghunathan, R. Synthesis of ferrocenyl monospirooxindolopyrrolidines—A facile [3 + 2]-cycloaddition of

azomethine ylides. *Tetrahedron Lett.* **2008**, 49, 4487–4490. (b) Liu, J.; Sun, H.; Liu, X.; Ouyang, L.; Kang, T.; Xie, Y.; Wang, X. Direct Construction of Novel Exo'-Selective Spiropyrrolidine Bisoxindoles via a Three-Component 1,3-Dipolar Cycloaddition Reaction. *Tetrahedron Lett.* **2012**, 53, 2336–2340.

(8) (a) Tan, B.; Hernandez-Torres, G.; Barbas, C. F., III Highly Efficient Hydrogen-Bonding Catalysis of the Diels–Alder Reaction of 3-Vinylindoles and Methyleneindolinones Provides Carbazolespirooxindole Skeletons. *J. Am. Chem. Soc.* **2011**, 128, 12354–12357. (b) Li, J.; Wang, N.; Li, C.; Jia, X. Construction of Naphtho-Fused Oxindoles via the Aryne Diels–Alder Reaction with Methyleneindolinones. *Org. Lett.* **2012**, 14, 4994–4997.

(9) (a) Gomez, C.; Gicquel, M.; Carry, J. C.; Schio, L.; Retaillieu, P.; Voituriez, A.; Marinetti, A. Phosphine-Catalyzed Synthesis of 3,3-Spirocyclopenteneoxindoles from γ -Substituted Allenates: Systematic Studies and Targeted Applications. *J. Org. Chem.* **2013**, 78, 1488–1496. (b) Yang, W.; Du, D. M. Cinchona-Based Squaramide-Catalysed Cascade Aza-Michael–Michael Addition: Enantioselective Construction of Functionalized Spirooxindole Tetrahydroquinolines. *Chem-Comm* **2013**, 49, 8842–8844. (c) Tian, X.; Melchiorre, P. Control of Remote Stereochemistry in the Synthesis of Spirocyclic Oxindoles: Vinylogous Organocascade Catalysis. *Angew. Chem., Int. Ed.* **2013**, 52, 5360–5363.

(10) (a) Ribeiro, C.; Kumar, S. P.; Moreira, R.; Santos, M. Efficient Synthesis of Spiroisoxazoline oxindoles. *Tetrahedron Lett.* **2012**, 53, 281–284. (b) Sirisha, N.; Raghunathan, R. Facile Synthesis of Novel Glycosyl Oxindoles through 1,3-Dipolar Cycloaddition. *Synlett* **2013**, 1973–1977. (c) Hao, L.; Chuen, C. W.; Ganguly, R.; Chi, R. B. NHC-Catalyzed Ester Activation: Access to Sterically Congested Spirocyclic Oxindoles via Reaction of α -Aryl Esters and Unsaturated Imines. *Synlett* **2013**, 24, 1197–1200. (d) Dai, C. H.; Liang, B.; Stephenson, C. Expanding the Chemical Diversity of Spirooxindoles via Alkylative Pyridine Dearomatization. *Beilstein J. Org. Chem.* **2012**, 8, 986–993.

(11) (a) Zhang, L. J.; Wu, Q.; Sun, J.; Yan, C. G. Synthesis of Functionalized Spiro[Indoline-3,4'-pyridines] and Spiro[Indoline-3,4'-pyridinones] via One-Pot Four-Component Reactions. *Beilstein J. Org. Chem.* **2013**, 9, 846–851. (b) Sun, J.; Sun, Y.; Gao, H.; Yan, C. G. Synthesis of Spiro[indoline-3,2'-quinoline] Derivatives through a Four-Component Reaction. *Eur. J. Org. Chem.* **2012**, 1976–1983. (c) Han, Y.; Wu, Q.; Sun, J.; Yan, C. G. Synthesis of the functionalized spiro[indoline-3,5'-pyrroline]-2,2'-diones via three-component reactions of arylamines, acetylenedicarboxylates, and isatins. *Tetrahedron* **2012**, 68, 8539–8544. (d) Sun, J.; Sun, Y.; Yan, C. G. Synthesis of 1'-aryl-2'-(2-oxindolin-3-yl)spiro[indoline-3,5'-pyrroline]-2,3'-dione via One-Pot Reaction of Arylamines, Acetone, and Isatins. *Tetrahedron Lett.* **2012**, 53, 3647–3649.

(12) (a) Wu, L.; Sun, J.; Yan, C. G. Facile Synthesis of Spiro[Indoline-3,3'-pyrrolo[1,2-*a*]quinolines] and Spiro[Indoline-3,1'-pyrrolo[2,1-*a*]isoquinolines] via 1,3-Dipolar Cycloaddition Reactions of Heteroaromatic Ammonium Salts with 3-Phenacylideneoxindoles. *Org. Biomol. Chem.* **2012**, 10, 9452–9463. (b) Hui, L.; Li, H. Y.; Yan, C. G. Molecular Diversity of Three-Component Reactions of *N*-Benzylbenzimidazolium Salts, Isatin, and Malononitrile or Ethyl Cyanoacetate. *Eur. J. Org. Chem.* **2012**, 3157–3164. (c) Fu, Q.; Yan, C. G. Molecular Diversity of Cycloaddition Reactions of the Functionalized Pyridinium Salts with 3-Phenacylideneoxindoles. *Tetrahedron* **2013**, 69, 5842–5849.

(13) (a) Sun, J.; Sun, Y.; Gong, H.; Xie, Y. J.; Yan, C. G. Facile Synthesis of Dispirooxindole-Fused Heterocycles via Domino 1,4-Dipolar Addition and Diels–Alder Reaction of in Situ Generated Huisgen 1,4-Dipoles. *Org. Lett.* **2012**, 14, 5172–5175. (b) Han, Y.; Sun, J.; Sun, Y.; Yan, C. G. Efficient Synthesis of Pentasubstituted Pyrroles via One-Pot Reactions of Arylamines, Acetylenedicarboxylates, and 3-Phenacylideneoxindoles. *Tetrahedron* **2012**, 68, 8256–8260. (c) Sun, J.; Zhu, D.; Gong, H.; Yan, C. G. Diastereoselective Synthesis of Dispirooxindoline Fused [1,3]Oxazines via Diels–Alder Reaction of Functionalized 1,2-Dihydropyridines with (*E*)-1,3-Dihydro-3-phenacylidene-2*H*-indol-2-ones. *Tetrahedron* **2013**, 69, 10235–10244. (d) Sun, J.; Xie, Y. J.; Yan, C. G. Construction of

Dispirocyclopentanebisoxindoles via Self-Domino Michael–Aldol Reactions of 3-Phenacylideneoxindoles. *J. Org. Chem.* **2013**, 78, 8354–8365.

(14) Freeman, F. Properties and Reactions of Ylidenemalononitriles. *Chem. Rev.* **1980**, 80, 329–350.

(15) (a) Chen, Y. C.; Xue, D.; Deng, J. G.; Cui, X.; Zhu, J.; Jiang, Y. Z. Efficient Asymmetric Transfer Hydrogenation of Activated Olefins Catalyzed by Ruthenium Amido Complexes. *Tetrahedron Lett.* **2004**, 45, 1555. (b) Xue, D.; Chen, Y. C.; Cui, X.; Wang, Q. W.; Zhu, J.; Deng, J. G. Transfer Hydrogenation of Activated C=C Bonds Catalyzed by Ruthenium Amido Complexes: Reaction Scope, Limitation, and Enantioselectivity. *J. Org. Chem.* **2005**, 70, 3584. (c) Liu, T. Y.; Cui, H. L.; Long, J.; Li, B. J.; Wu, Y.; Ding, L. S.; Chen, Y. C. Organocatalytic and Highly Stereoselective Direct Vinylogous Mannich Reaction. *J. Am. Chem. Soc.* **2007**, 129, 1878–1879. (g) Cui, H. L.; Chen, Y. C. α,α -Dicyanoalkenes: Versatile vinylogous nucleophiles for organic synthesis. *Chem. Commun.* **2009**, 4479–4486.

(16) (a) Peng, J.; Huang, X.; Cui, H. L.; Chen, Y. C. Organocatalytic and Electrophilic Approach to Oxindoles with C3-Quaternary Stereocenters. *Org. Lett.* **2010**, 12, 4260–4263. (b) Li, P.; Luo, L. L.; Li, X. S.; Xie, J. W. A Simple Method for the Synthesis of Functionalized 6-Aryl-6*H*-dibenzo[*b,d*]pyran Derivatives from 3-Nitro-2*H* Chromenes. *Tetrahedron* **2010**, 66, 7590–7594. (c) Zhang, X. N.; Shi, M. Phosphine-Catalyzed [3 + 2] Cycloaddition of 4,4-Dicyano-2-methylenebut-3-enates with Benzyl Buta-2,3-dienoate and Penta-3,4-dien-2-one. *ACS Catal.* **2013**, 3, 507–512.

(17) (a) Babu, T. H.; Joseph, A. A.; Muralidharan, D.; Perumal, P. T. A Novel Method for the Synthesis of Functionalized Spirocyclic Oxindoles by One-Pot Tandem Reaction of Vinyl Malononitriles with Isatylidene malononitrile. *Tetrahedron Lett.* **2010**, 51, 994–996. (b) Babu, T. H.; Karthik, K.; Perumal, P. T. A Facile, One-Pot Synthesis of Functionalized Spiro-Oxindoles via Vinylogous Aldol Reaction of Vinyl Malononitriles with Isatin Derivatives in Aqueous Media. *Synlett* **2010**, 1128–1132. (c) Lakshmi, N. V.; Josephine, G. A. S.; Perumal, P. T. Novel Route to Spiropiperidines Using *N*-Methyl-4-piperidone, Malononitrile and Electrophiles. *Tetrahedron Lett.* **2012**, 53, 1282–1286. (d) Elinson, M. N.; Ilvovskiy, A. I.; Merkulova, V. M.; Barba, F.; Batanero, B. General Approach to Spiroacenaphthylene Pentacyclic Systems: Direct Multicomponent Assembling of Acenaphthenequinone and Cyclic Carbonyl Compounds with Two Molecules of Malononitrile. *Tetrahedron* **2013**, 69, 7125–7130.