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

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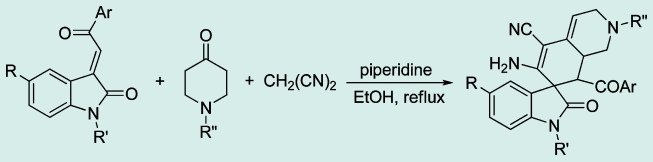
Supporting Information

**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 $^1$H 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 $\gamma$-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 malononitirle,[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-phenacyclidedenoxindoles. 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-phenacylidineoxindole 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*-

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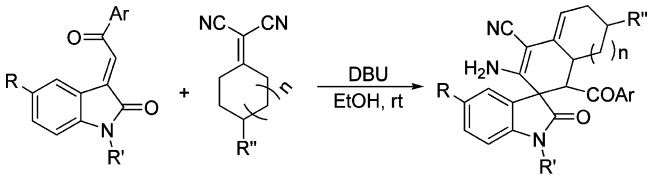
**Table 1. Synthesis of Spirocyclic Oxindoles 3a−3h**[a]




2 1 3a-3h

| entry | compd | R | R′ | Ar | R″ | *n* | yield (%)[b] |
|---|---|---|---|---|---|---|---|
| 1 | **3a** | F | Bn | *p*-$CH_3C_6H_4$ | H | 1 | 89 |
| 2 | **3b** | Cl | Bn | *p*-$CH_3C_6H_4$ | H | 1 | 74 |
| 3 | **3c** | F | *n*-$C_4H_9$ | *p*-$CH_3OC_6H_4$ | *t*-Bu | 1 | 85 |
| 4 | **3d** | H | Bn | *p*-$CH_3OC_6H_4$ | *t*-Bu | 1 | 92 |
| 5 | **3e** | H | Bn | *p*-$ClC_6H_4$ | *t*-Bu | 1 | 83 |
| 6 | **3f** | $CH_3$ | *n*-$C_4H_9$ | *p*-$ClC_6H_4$ | H | 2 | 80 |
| 7 | **3g** | H | Bn | *p*-$ClC_6H_4$ | H | 2 | 82 |
| 8 | **3h** | $CH_3$ | Bn | *p*-$ClC_6H_4$ | H | 2 | 87 |

[a]Reaction condition: 3-phenacylidieneoxindole (1.0 mmol), vinyl malononitrile (1.0 mmol), DBU (0.1 mmol) in ethanol (10.0 mL), rt, 30 min. [b]Isolated 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. $^1$H 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.

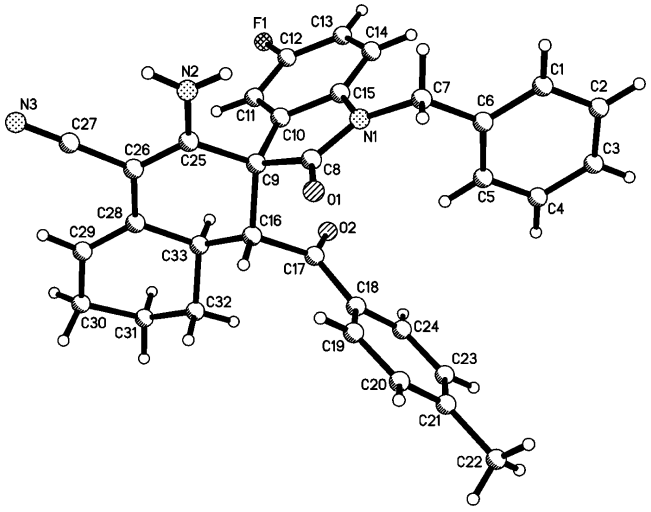



**Figure 1.** Molecular structure of compound **3a**.

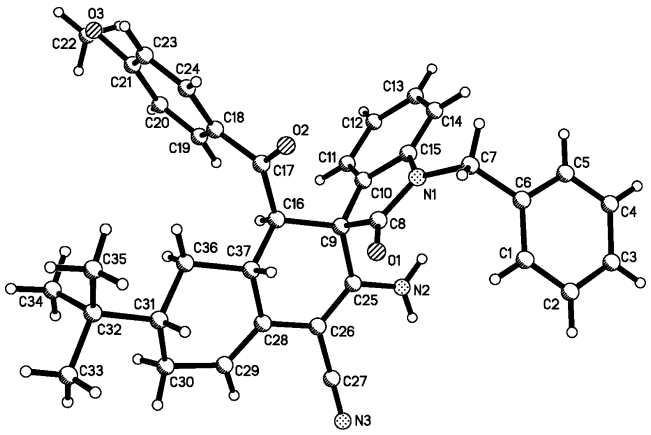
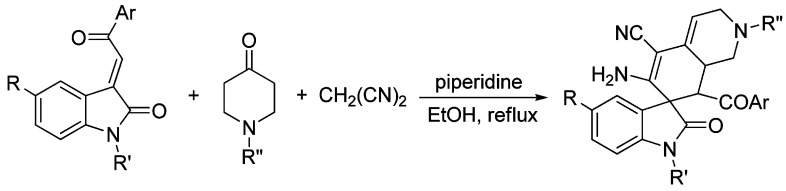



**Figure 2.** Molecular structure of compound **3d**.

**Table 2. Synthesis Spiro[indoline-3,7′-isoquinolines] 4a−4j**[a]




**4a-4j**

| entry | compd | R | R′ | Ar | R″ | yield (%)[b] |
|---|---|---|---|---|---|---|
| 1 | **4a** | H | Bn | *p*-$CH_3C_6H_4$ | $CH_3$ | 83 |
| 2 | **4b** | H | Bn | *p*-$ClC_6H_4$ | $CH_3$ | 96 |
| 3 | **4c** | F | Bn | *p*-$CH_3OC_6H_4$ | $CH_3$ | 92 |
| 4 | **4d** | Cl | Bn | $C_6H_5$ | $CH_3$ | 88 |
| 5 | **4e** | Cl | Bn | *p*-$CH_3C_6H_4$ | $CH_3$ | 89 |
| 6 | **4f** | H | Bn | *p*-$CH_3OC_6H_4$ | Bn | 92 |
| 7 | **4g** | F | Bn | $C_6H_5$ | Bn | 95 |
| 8 | **4h** | F | Bn | *p*-$CH_3OC_6H_4$ | Bn | 94 |
| 9 | **4i** | Cl | Bn | *p*-$CH_3OC_6H_4$ | Bn | 93 |
| 10 | **4j** | Cl | Bn | *p*-$CH_3C_6H_4$ | Bn | 90 |

[a]Reaction condition: piperdinone (1.0 mmol), malononitrile (1.0 mmol), piperidine (0.1 mmol) in ethanol (15.0 mL), reflux, 5 min. 3-phenacylidieneoxindole (1.0 mmol), reflux, one hour. [b]Isolated yield.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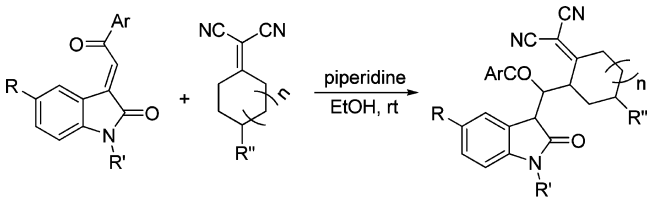
But it is clear to see that the phenyl group of oxindole moiety and the benzoyl are in trans-configuration in molecular structure of **3d**. Thus, the single crystal structures of the four compounds demonstrate that two kinds of stereoisomers exist in the prepared spiro compounds, which also reveals that it is difficult to elucidate the stereochemistry of these complex spirocyclic oxindoles with $^1$H NMR spectra.

It has been mentioned above that the piperidine promoted reaction of vinyl malononitrile with 3-phenacyclideneoxindole 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 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.

**Table 3. Synthesis of the Michael Addition Products 5a−5f**[a]




**5a-5f**

| entry | compd | R | R′ | Ar | R″ | *n* | yield (%)[b] |
|---|---|---|---|---|---|---|---|
| 1 | **5a** | Cl | *n*-$C_4H_9$ | *p*-$CH_3OC_6H_4$ | H | 1 | 81 |
| 2 | **5b** | H | Bn | *p*-$CH_3OC_6H_4$ | *t*-Bu | 1 | 85 |
| 3 | **5c** | F | Bn | *p*-$CH_3C_6H_4$ | *t*-Bu | 1 | 88 |
| 4 | **5d** | Cl | Bn | *p*-$CH_3C_6H_4$ | *t*-Bu | 1 | 87 |
| 5 | **5e** | H | Bn | *p*-$CH_3OC_6H_4$ | H | 2 | 78 |
| 6 | **5f** | H | n-$C_4H_9$ | *p*-$CH_3C_6H_4$ | H | 2 | 90 |

[a]Reaction condition: 3-phenacylidieneoxindole (1.0 mmol), vinyl malononitrile (1.0 mmol), piperidine (0.1 mmol) in ethanol (10.0 mL), rt, one hour. [b]Isolated yield.

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-phenacyldieneoxindoles 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.

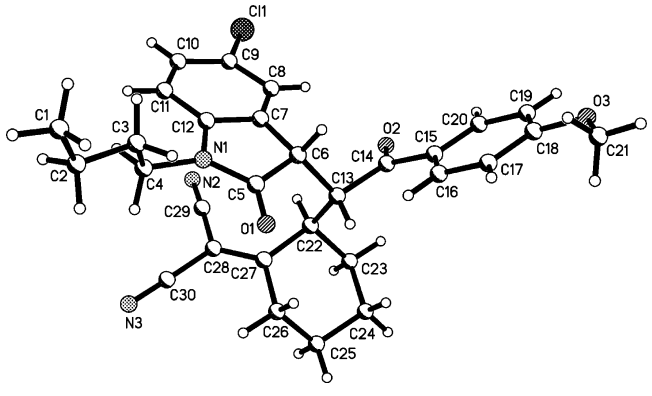



**Figure 3.** Molecular structure of compound **5a**.

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 carbanium (**A**) is generated by deprotonation of vinyl malononitrile **1** with base, which in turn attacked the exocyclic carbon atom of the 3-phenacyclideneoxindole to give a new carbanium 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 temeprature. 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-phenacyclideneoxindole 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; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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, $NH_2$), 5.64 (s, 1H, CH), 4.94 (d, $J$ = 16.2 Hz, 1H, CH), 4.25 (d, $J$ = 15.6 Hz, 1H, CH),


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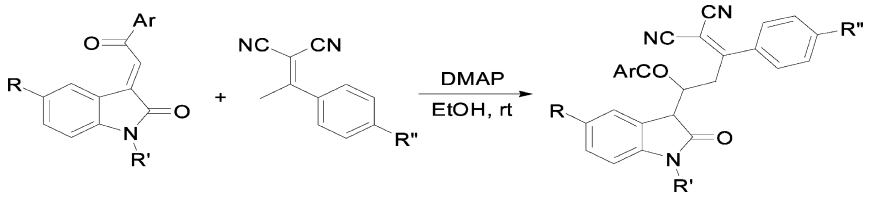
**Table 4. Synthesis of the Michael addition products 5g−5j**[a]

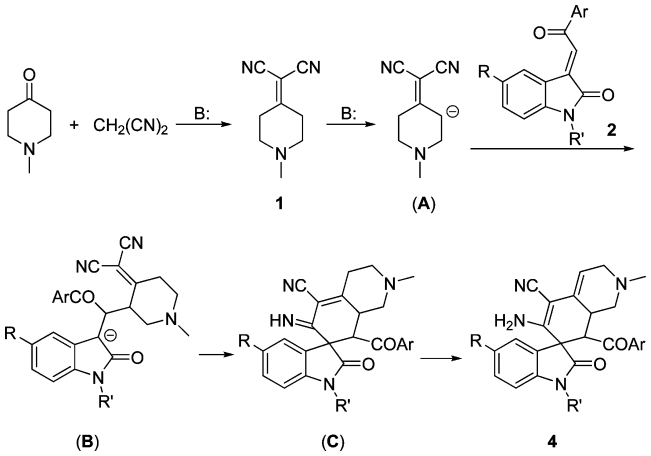



**5g-5l**

| entry | compd | R | R′ | R″ | Ar | yield (%)[b] |
|---|---|---|---|---|---|---|
| 1 | **5g** | Cl | Bn | $CH_3$ | $p$-$CH_3C_6H_4$ | 92 |
| 2 | **5h** | F | Bn | $CH_3$ | $p$-$CH_3C_6H_4$ | 90 |
| 3 | **5i** | H | Bn | $CH_3$ | $p$-$ClC_6H_4$ | 89 |
| 4 | **5j** | Cl | n-$C_4H_9$ | $CH_3$ | $p$-$CH_3C_6H_4$ | 86 |
| 5 | **5k** | Cl | Bn | Cl | $p$-$CH_3C_6H_4$ | 85 |
| 6 | **5l** | H | Bn | $OCH_3$ | $p$-$CH_3OC_6H_4$ | 88 |

[a]Reaction condition: 3-phenacylidieneoxindole (1.0 mmol), vinyl malononitrile (1.0 mmol), DMAP (1.0 mmol) in ethanol (10.0 mL), rt, 30 min. [b]Isolated 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, $CH_3$), 2.20−2.12 (m, 2H, $CH_2$), 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); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 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) $\upsilon$ 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 $C_{33}H_{29}FN_3O_2$ ([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; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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, $NH_2$), 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, $CH_3$), 2.17−2.11 (m, 2H, $CH_2$), 1.68 (s, 1H, CH), 1.36 (brs, 1H, CH), 1.25 (brs, 1H, CH), 0.98 (brs, 1H, CH); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 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) $\upsilon$ 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 $C_{33}H_{28}ClN_3NaO_2$ ([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; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$: 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, $NH_2$), 4.40 (d, $J$ = 12.0 Hz, 1H, CH), 3.79 (s, 3H, $OCH_3$), 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, $CH_2$), 1.40−1.34 (m, 2H, $CH_2$), 1.30−1.24 (m, 2H, $CH_2$), 0.95 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 0.74−0.68 (m, 1H, CH), 0.66 (s, 9H, $CH_3$); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 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) $\upsilon$ 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 $C_{34}H_{38}FN_3NaO_3$ ([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; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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, $NH_2$), 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, $OCH_3$), 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, $CH_2$), 0.77 (q, $J$ = 12.0 Hz, 1H, $CH_2$), 0.66 (s, 9H, $CH_3$); $^{13}$C NMR (150 MHz,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DMSO-$d_6$) $\delta$ 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) $\upsilon$ 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 $C_{37}H_{37}N_3NaO_3$ ([M + 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 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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, $CDCl_3$) $\delta$ 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) $\upsilon$ 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 $C_{36}H_{34}ClN_3NaO_2$ ([M + 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 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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-$d_6$) $\delta$ 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) $\upsilon$ 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 $C_{31}H_{32}ClN_3NaO_2$ ([M + 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 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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-$d_6$) $\delta$ 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) $\upsilon$ 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 $C_{33}H_{29}ClN_3O_2$ ([M + 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 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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-$d_6$) $\delta$ 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) $\upsilon$ 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 $C_{34}H_{31}ClN_3O_2$ ([M + H]$^+$) 548.2099; Found 548.2085.

**General Procedure for the Synthesis of Spirocyclic Oxindoles 4a−4j.** A mixture of *N*-methyl or *N*-benzylpiperidinone (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 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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-$d_6$) $\delta$ 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) $\upsilon$ 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 $C_{33}H_{31}N_4O_2$ ([M + 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


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°C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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-$d_6$) $\delta$ 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) $\upsilon$ 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 $C_{32}H_{28}ClN_4O_2$ ([M + 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; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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-$d_6$) $\delta$ 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) $\upsilon$ 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 $C_{33}H_{30}FN_4O_3$ ([M + 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; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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-$d_6$) $\delta$ 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., 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) $\upsilon$: 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 $C_{32}H_{28}ClN_4O_2$ ([M + 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; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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-$d_6$) $\delta$ 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) $\upsilon$ 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 $C_{33}H_{30}ClN_4O_2$ ([M + 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; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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-$d_6$) $\delta$: 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) $\upsilon$ 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 $C_{39}H_{35}N_4O_3$ ([M + 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; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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-$d_6$) $\delta$: 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) $\upsilon$ 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 $C_{38}H_{32}FN_4O_2$ ([M + H]$^+$) 595.2504; Found 595.2508.


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*6′-Amino-1,2′-dibenzyl-5-fluoro-8′-(4-methoxybenzoyl)-2-oxo-2′,3′,8′,8a′-tetrahydro-1′H-spiro[indoline-3,7′-isoquinoline]-5′-carbonitrile* ***4h:*** yellow solid, 94%, 0.587 g, mp 186.6−188.3 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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, DMSO-$d_6$) $\delta$ 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) $\upsilon$ 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 $C_{39}H_{34}FN_4O_3$ ([M + H]$^+$) 625.2609; Found 625.2611.

*6′-Amino-1,2′-dibenzyl-5-chloro-8′-(4-methoxybenzoyl)-2-oxo-2′,3′,8′,8a′-tetrahydro-1′H-spiro[indoline-3,7′-isoquinoline]-5′-carbonitrile* ***4i:*** yellow solid, 93%, 0.595g, mp 194.4−196.4 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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, DMSO-$d_6$) $\delta$ 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) $\upsilon$ 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 $C_{39}H_{34}ClN_4O_3$ ([M + H]$^+$) 641.2314; Found 641.2313.

*6′-Amino-1,2′-dibenzyl-5-chloro-8′-(4-methylbenzoyl)-2-oxo-2′,3′,8′,8a′-tetrahydro-1′H-spiro[indoline-3,7′-isoquinoline]-5′-carbonitrile* ***4j:*** yellow solid, 90%, 0.562 g, mp 188.6−190.4 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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, DMSO-$d_6$) $\delta$ 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) $\upsilon$ 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 $C_{39}H_{34}ClN_4O_2$ ([M + 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; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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, DMSO-$d_6$) $\delta$ 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) $\upsilon$ 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 $C_{30}H_{31}ClN_3O_3$ ([M + 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; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 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, $CDCl_3$) $\delta$ 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) $\upsilon$ 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 $C_{37}H_{37}N_3NaO_3$ ([M + 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; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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, DMSO-$d_6$) $\delta$ 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) $\upsilon$ 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


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(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-tolylethyl)-4-tert-butylcyclohexylidene)malononitrile (**5d**):* white solid, 87%, 0.512 g, mp 172.9−173.1 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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, $CH_2$), 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, $CH_3$), 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, $CH_2$), 0.52 (s, 9H, $CH_3$); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 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) $\upsilon$ 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; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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, $CH_2$), 4.83 (d, $J$ = 7.8 Hz, 1H, CH), 4.09 (brs, 1H, CH), 4.04 (s, 1H, CH), 3.82 (s, 3H, $OCH_3$), 2.90−2.86 (m, 1H, CH), 2.26 (brs, 1H, CH), 1.80−1.71 (m, 3H, $CH_2$, 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-$d_6$) $\delta$ 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) $\upsilon$ 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-tolylethyl)-cycloheptylidene)malononitrile (**6f**):* white solid, 90%, 0.431 g, mp 223.7−224.5 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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, $CH_2$), 2.84 (brs, 1H, CH), 2.50 (brs, 1H, CH), 2.34 (s, 3H, $CH_3$), 2.19 (brs, 1H, CH), 2.06 (brs, 1H, CH), 1.79 (brs, 2H, $CH_2$), 1.71−1.70 (m, 1H, CH), 1.62−1.61 (m, 2H, $CH_2$), 1.40−1.39 (m, 2H, $CH_2$), 1.32−1.31 (m, 1H, CH), 1.21−1.19 (m, 1H, CH), 0.94 (brs, 4H, CH, $CH_3$); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 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) $\upsilon$: 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; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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, $CH_2$), 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, $CH_3$), 2.36 (s, 3H, $CH_3$); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 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) $\upsilon$: 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; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 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, $CH_3$), 2.38 (s, 3H, $CH_3$); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$: 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) $\upsilon$: 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; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 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, $CH_3$); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 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) $\upsilon$ 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; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 7.53


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(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, $CH_3$), 2.35 (s, 3H, $CH_3$), 1.59−1.54 (m, 2H, $CH_2$), 1.36−1.32 (m, 2H, $CH_2$), 0.92 (t, $J$ = 7.8 Hz, 3H, $CH_3$); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 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) $\upsilon$ 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 $C_{33}H_{31}ClN_3O_2$ ([M + H]$^+$) 536.2105; Found 536.2103.

*2-(3-(1-benzyl-5-chloro-2-oxoindolin-3-yl)-4-(4-methylphenyl)-4-oxo-1-p-chlorophenylbutylidene)malononitrile* ***5k***. white solid, 85%, 0.501g, mp 154.2−156.6 °C; $^1$H NMR (600 MHz, DMSO) $\delta$: 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, $CH_3$); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$: 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) $\upsilon$: 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 $C_{35}H_{26}Cl_2N_3O_2$ ([M+H]$^+$): 590.1402. Found: 590.1393.

*2-(3-(1-Benzyl-2-oxoindolin-3-yl)-4-oxo-1,4-di(p-methoxyphenyl)butylidene)malononitrile* ***5l:*** white solid, 88%, 0.499 g, mp 140.8−142.6 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 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, $OCH_3$), 3.82 (s, 3H, $OCH_3$), 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); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 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) $\upsilon$ 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 $C_{36}H_{30}N_3O_4$ ([M + H]$^+$) 568.2236; Found 568.2228.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

$^1$H NMR and $^{13}$C 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.

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