Diastereoselective synthesis of cyclopentanone-fused spirooxindoles by N-heterocyclic carbene-catalyzed homoenolate annulation with isatilidenes

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1. General Information

Unless otherwise specified, all reactions were carried out under an atmosphere of argon in flame-dried reaction vessels with Teflon screw cap. 30 °C corresponds to the room temperature of the lab when experiments were performed. Dry THF was purchased from commercial sources and stored under argon over 4 Å molecular sieves. The isatin derivatives and aldehydes were purchased from commercial sources, and used without any further purification. The α,β-unsaturated aldehydes¹ and isatilidenes² were synthesized from corresponding aldehydes following the literature procedure. KOt-Bu was purchased from Sigma Aldrich and was handled inside glove box. The imidazolium salt 4 was synthesized following the literature procedure.³

Analytical thin layer chromatography was performed on TLC Silica gel 60 F₂₅₄. Visualization was accomplished with short wave UV light or KMnO₄ staining solutions followed by heating. Flash chromatography was performed on silica gel (230-400 mesh) by standard techniques eluting with solvents as indicated.

All compounds were fully characterized. ¹H, ¹³C and ¹⁹F NMR spectra were recorded on Bruker AV 400 in solvents as indicated. Chemical shifts (δ) are given in ppm. The residual solvent signals were used as references and the chemical shifts converted to the TMS scale (CDCl₃: δH = 7.26 ppm, δC = 77.16 ppm). Infrared spectra were recorded on a Perkin-Elmer 1615 FT Infrared Spectrophotometer Model 60B. The wave numbers (n) of recorded IR-signals are quoted in cm⁻¹. HRMS mass spectra were recorded on a Thermo Scientific Q-Exactive, Accela 1250 pump. HPLC analysis was performed on either a Shimadzu Class-VP V6.12 SP5 with UV detector or Agilent Technologies 1260 Infinity with UV detector.

2. General Procedure for the Optimization of Reaction Conditions

To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the azolium salt NHC.HX (0.025 mmol) and tert-butyl (E)-3-benzylidene-2-oxoindoline-1-carboxylate 1a (80 mg, 0.25 mmol). Then the screw-capped tube was evacuated and backfilled with argon. The mixture was dissolved in THF (1.0 mL) under argon atmosphere. The resultant reaction mixture was kept stirring at 30 °C. To this mixture was added the trans cinnamaldehyde 2a (33 mg, 31 μL, 0.25 mmol) followed by the addition of KOt-Bu (8.5 mg, 0.05 mmol). After 40 hours stirring, the solvent was evaporated and the crude residue was purified by flash column chromatography on silica gel to afford the corresponding cyclopentanone-fused spirooxindoles. The diastereoselectivity was determined by 1H NMR of crude products (obtained by filtration of the crude reaction mixture through a pad of silica gel and eluting using EtOAc).

3. Optimization Studies

Our optimization study commenced with treatment of tert-butyl (E)-3-benzylidene-2-oxoindoline-1-carboxylate 1a with trans cinnamaldehyde 2a. Treatment of 1a with 2a in the presence of the carbene generated from 4 by deprotonation using KOt-Bu resulted in the formation of cyclopentanone-fused spirooxindoles derivative 3a in 51% yield (isolated yield). Notably, in contrast to this NHC, other common NHCs derived from precursors 5-7 are less effective (entries 2-4). NHC derived from precursor 8 resulted with increasing reactivity but dr decreased (entry 5). With increase in temperature to 50 °C instead of 30 °C reactivity decreases, resulted 41% yield (entry 6). Other bases such as DBU, K2CO3, NEt3, Cs2CO3, KOAc, DMAP, and K3PO4 furnished the desired product in reduced yields (Table 1, entries 7-13). Among the various solvents screened, DME, 1,4-dioxane, DCM, and Toluene resulted in very less reactivity (entries 14-17). Gratifyingly, when the reaction was performed using 15 mol % of 4 and 30 mol
% of KOt-Bu, the yield of 3a was improved to 59% maintaining the excellent diastereoselectivity (entry 18). Interestingly, use of 1.5 equiv of enal 2a afforded 3a in 71% yield and >20:1 diastereoselectivity (entry 19). Additionally, use of Lewis acids and Bronstead acids to improve the yield of 3a were unsuccessful (entries 20-23).

![Chemical reaction](image)

<table>
<thead>
<tr>
<th>entry</th>
<th>variation of the standard conditions</th>
<th>yield of 3a (%)&lt;sup&gt;b,c&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>51</td>
</tr>
<tr>
<td>2</td>
<td>5 instead of 4</td>
<td>&lt;5</td>
</tr>
<tr>
<td>3</td>
<td>6 instead of 4</td>
<td>21</td>
</tr>
<tr>
<td>4</td>
<td>7 instead of 4</td>
<td>&lt;5</td>
</tr>
<tr>
<td>5</td>
<td>8 instead of 4</td>
<td>59&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>6</td>
<td>50 °C instead of 30 °C</td>
<td>41</td>
</tr>
<tr>
<td>7</td>
<td>DBU instead of KOt-Bu</td>
<td>29</td>
</tr>
<tr>
<td>8</td>
<td>K&lt;sub&gt;2&lt;/sub&gt;CO&lt;sub&gt;3&lt;/sub&gt; instead of KOt-Bu</td>
<td>23</td>
</tr>
<tr>
<td>9</td>
<td>Et&lt;sub&gt;3&lt;/sub&gt;N instead of KOt-Bu</td>
<td>&lt;5</td>
</tr>
<tr>
<td>10</td>
<td>Cs&lt;sub&gt;2&lt;/sub&gt;CO&lt;sub&gt;3&lt;/sub&gt; instead of KOt-Bu</td>
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</tr>
<tr>
<td>11</td>
<td>KOAc instead of KOt-Bu</td>
<td>&lt;5</td>
</tr>
<tr>
<td>12</td>
<td>DMAP instead of KOt-Bu</td>
<td>&lt;5</td>
</tr>
<tr>
<td>13</td>
<td>K&lt;sub&gt;3&lt;/sub&gt;PO&lt;sub&gt;4&lt;/sub&gt; instead of KOt-Bu</td>
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</tr>
<tr>
<td>14</td>
<td>DME instead of THF</td>
<td>&lt;5</td>
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<tr>
<td>15</td>
<td>1,4-dioxane instead of THF</td>
<td>11</td>
</tr>
<tr>
<td>16</td>
<td>CH&lt;sub&gt;2&lt;/sub&gt;Cl&lt;sub&gt;2&lt;/sub&gt; instead of THF</td>
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<tr>
<td>17</td>
<td>toluene instead of THF</td>
<td>26</td>
</tr>
<tr>
<td>18</td>
<td>15 mol % of 4 and 30 mol % of KOt-Bu</td>
<td>59</td>
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<tr>
<td>19</td>
<td>15 mol % of 4, 30 mol % of KOt-Bu and 1.5 equiv of 2a</td>
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<tr>
<td>20</td>
<td>AcOH as a additive</td>
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21 Benzoic acid as a additive 48
22 LiCl as a additive 62
23 LiOt-Bu as a additive 51

\[ a \] Standard conditions: 1a (0.25 mmol), 2a (0.25 mmol), 4 (10 mol %), KOt-Bu (20 mol %), THF (1.0 mL), 30 °C and 40 h. \[ b \] Isolated yield of the product. \[ c \] The diastereoselectivity observed by \(^1\)H NMR of crude products was >20:1 unless indicated. \[ d \] The \( dr \) of 3:1 was observed.

4. General Procedure for the NHC-Catalyzed Annulation Reaction

To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the imidazolium salt 4 (0.027 g, 0.075 mmol) and the (E)-3-benzylidene-2-oxoindoline-1-carboxylate 1 (0.5 mmol). Then the screw-capped tube was evacuated and backfilled with argon. To this mixture was added THF (2.0 mL) under argon atmosphere. The resultant reaction mixture was kept stirring at 30 °C. To this mixture was added the aldehyde 2a (0.75 mmol) (solid aldehydes were transferred to the screw-capped tube by closing the argon flow and liquid aldehydes were transferred via syringe under argon flow) and the KOt-Bu (0.017 gm, 0.15 mmol) was successively added. Then the reaction mixture was stirred at 30° C for 40 h. After 40 h the solvent was evaporated and the crude residue was purified by flash column chromatography on silica gel to afford the corresponding functionalized cyclopentanone-fused spirooxindoles derivatives.
5. Optimization Studies for the Enantioselective Synthesis of cyclopentanone-fused spirooxindole (*chiral-3a*)

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>entry</th>
<th>variation of the standard conditions&lt;sup&gt;a&lt;/sup&gt;</th>
<th>yield of <em>Chiral 3a</em> (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>ee of <em>Chiral 3a</em> (%)&lt;sup&gt;c,d&lt;/sup&gt;</th>
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<td>22</td>
<td>97</td>
</tr>
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<td>13 instead of 12</td>
<td>&lt;5</td>
<td>N.D.</td>
</tr>
<tr>
<td>3</td>
<td>DBU instead of KOt-Bu</td>
<td>&lt;5</td>
<td>N.D.</td>
</tr>
<tr>
<td>4</td>
<td>DABCO instead of KOt-Bu</td>
<td>&lt;5</td>
<td>N.D.</td>
</tr>
<tr>
<td>5</td>
<td>Et&lt;sub&gt;3&lt;/sub&gt;N instead of KOt-Bu</td>
<td>&lt;5</td>
<td>N.D.</td>
</tr>
<tr>
<td>6</td>
<td>DMAP instead of KOt-Bu</td>
<td>&lt;5</td>
<td>N.D.</td>
</tr>
<tr>
<td>7</td>
<td>K&lt;sub&gt;2&lt;/sub&gt;CO&lt;sub&gt;3&lt;/sub&gt; instead of KOt-Bu</td>
<td>&lt;5</td>
<td>N.D.</td>
</tr>
<tr>
<td>8</td>
<td>Cs&lt;sub&gt;2&lt;/sub&gt;CO&lt;sub&gt;3&lt;/sub&gt; instead of KOt-Bu</td>
<td>&lt;5</td>
<td>N.D.</td>
</tr>
</tbody>
</table>

<sup>a</sup> Standard conditions: 1a (0.25 mmol), 2a (0.38 mmol), 12 (10 mol %), KOt-Bu (20 mol %), THF (1.0 mL), 50 °C and 36 h. <sup>b</sup>The yields were determined by <sup>1</sup>H NMR analysis of crude products using CH<sub>2</sub>Br<sub>2</sub> as the internal standard. <sup>c</sup>Determined by HPLC analysis on a chiral column. <sup>d</sup>dr > 20:1
6. Procedure for the Enantioselective Synthesis of cyclopentanone-fused spirooxindole (*chiral-3a*)

![Chemical Reaction Diagram]

To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the triazolium salt 12 (0.008 g, 0.025 mmol) and the *tert*-butyl (*E*)-3-benzylidene-2-oxoindoline-1-carboxylate 1a (0.25 mmol). Then the screw-capped tube was evacuated and backfilled with argon. To this mixture was added THF (1.0 mL) under argon atmosphere. The resultant reaction mixture was kept stirring at 30 °C. To this mixture was added the aldehyde 2a (0.375 mmol) and the KOt-Bu (0.006 gm, 0.05 mmol) was successively added. Then the reaction mixture was stirred at 50 °C for 36 h. After 36 h, the solvent was evaporated and the crude residue was purified by flash column chromatography on silica gel to afford the corresponding cyclopentanone-fused spirooxindoles in high enantioselectivity.
7. Synthesis and Characterization cyclopentanone-fused spirooxindoles

**tert-Butyl -2',5-dioxo-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3a)**

Following the general procedure, treatment of *trans* cinnamaldehyde 2a (0.099 g, 94 μL, 0.75 mmol) and *tert*-butyl (E)-3-benzylidene-2-oxoindoline-1-carboxylate 1a (0.160 g, 0.5 mmol) with imidazolium salt 4 (0.027 g, 0.075 mmol) and KOT-Bu (0.017 g, 0.15 mmol) in THF (2.0 mL) at 30 °C for 40 h followed by flash column chromatography afforded *tert*-butyl -2',5-dioxo-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate 3a as a white solid (0.161 g, 71% yield). CCDC-1413690 (3a) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

**Rf** (Pet. ether /EtOAc = 80/20): 0.61; **1H NMR** (400 MHz, CDCl₃) δ 7.66 (d, J = 8.1 Hz, 1H), 7.35-7.25 (m, 7H), 7.20-7.16 (m, 1H), 7.09-7.02 (m, 5H), 4.89-4.81 (m, 1H), 4.01 (d, J = 12.3 Hz, 1H), 3.45-3.38 (m, 1H), 2.84-2.77 (m, 1H), 1.52 (s, 9H). **13C NMR** (100 MHz, CDCl₃) δ 209.27, 170.84, 148.42, 141.00, 140.58, 134.27, 129.42, 128.93, 128.37, 127.81, 127.18, 126.76, 125.06, 123.21, 115.30, 84.50, 70.97, 60.67, 47.66, 41.06, 28.09. **HRMS** calculated [M+Na]⁺ for C₂₉H₂₇O₄NNa: 476.1832, found: 476.1833. **FTIR (cm⁻¹)** 3023, 2403, 1742, 1661, 1607, 1482, 1354, 1258, 1216, 1150, 1092, 1026, 928, 842, 767, 670.

**X-ray Crystal Structure Analysis of 3a.**

X-ray intensity data measurements of compound 3a was carried out on a Bruker SMART APEX II CCD diffractometer with graphite-monochromatized (MoKα = 0.71073 Å) radiation at 90(2) K. The X-ray generator was operated at 50 kV and 30 mA. A preliminary set of cell constants and an orientation matrix were calculated from three sets of 36 frames. Data were collected with ω scan width of 0.5° at different settings of ϕ and 2θ with a frame time of 10 secs keeping the sample-to-detector distance fixed at 5.00 cm. The X-ray data collection was
monitored by APEX2 program (Bruker, 2006). All the data were corrected for Lorentzian, polarization and absorption effects using SAINT and SADABS programs (Bruker, 2006). SHELX-97 was used for structure solution and full matrix least-squares refinement on $F^2$. All the hydrogen atoms were placed in geometrically idealized position and constrained to ride on their parent atoms. An ORTEP III view of both compounds were drawn with 50% probability displacement ellipsoids and H atoms are shown as small spheres of arbitrary radii. The crystals belong to triclinic P-1 space group containing two molecules in the asymmetric unit. The detail crystallography data is given below.

Crystal data of 3a $C_{29}H_{27}NO_4$, $M = 453.51$, colorless block, $0.47 \times 0.44 \times 0.13 \text{ mm}^3$, triclinic, space group $P-1$, $a = 10.7670(9)$ Å, $b = 11.4830(9)$ Å, $c = 19.2866(15)$ Å, $\alpha = 88.719(3)^\circ$, $\beta = 87.476(3)^\circ$, $\gamma = 80.292(3)^\circ$, $V = 2347.8(3)$ Å$^3$, $Z = 4$, $T = 90(2)$ K, $2\theta_{\text{max}} = 50.00^\circ$, $D_{\text{calc}} (\text{g cm}^{-3}) = 1.283$, $F(000) = 960$, $\mu$ (mm$^{-1}$) = 0.085, 35150 reflections collected, 9223 unique reflections ($R_{\text{int}} = 0.0300$), 8423 observed ($I > 2\sigma (I)$) reflections, multi-scan absorption correction, $T_{\text{min}} = 0.961$, $T_{\text{max}} = 0.989$, 619 refined parameters, $S = 1.031$, $R_1 = 0.0393$, $wR_2 = 0.0876$ (all data $R = 0.0357$, $wR_2 = 0.0906$), maximum and minimum residual electron densities; $\Delta \rho_{\text{max}} = 0.33$, $\Delta \rho_{\text{min}} = -0.21$ (eÅ$^{-3}$).

1'-Acetyl-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-2',5-dione (3b)

Following the general procedure, treatment of trans cinnamaldehyde 2a (0.099 g, 94 μL, 0.75 mmol) and (E)-1-acetyl-3-benzylideneindolin-2-one 1b (0.132 g, 0.5 mmol) with imidazolium salt 4 (0.027 g, 0.075 mmol) and KOT-Bu (0.017 g, 0.15 mmol) in THF (2.0 mL) at 30 °C for 40 h followed


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by flash column chromatography afforded 1'-acetyl-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-2',5-dione 3b as a white solid (0.115 g, 58%, dr determined by \(^1\)H NMR analysis of crude reaction mixture is 3:1).

\( R_f \) (Pet. ether /EtOAc = 80/20): 0.54; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.07-8.03 (m, 1H), 7.42-7.21 (m, 8H), 7.12-7.08 (m, 2H), 4.85-4.77 (m, 1H), 4.10 (d, \( J = 12.1 \) Hz, 1H), 3.45-3.38 (m, 1H), 2.89-2.82 (m, 1H), 2.38 (s, 3H). \(^1\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 209.14, 173.60, 170.03, 141.35, 140.17, 139.86, 138.35, 137.65, 134.37, 134.05, 131.06, 130.83, 130.75, 129.89, 129.63, 129.01, 128.44, 128.10, 128.06, 127.89, 127.79, 127.50, 127.31, 125.88, 122.98, 116.72, 70.85, 60.44, 48.02, 40.93, 26.32. Representative Peaks of Minor Isomer: \(^1\)H NMR \( \delta \) 7.93 (m), 6.59 (d, \( J = 7.6 \) Hz), 5.03-5.00 (m), 4.32 (d, \( J = 9.4 \) Hz), 2.72-2.65 (m), 1.52 (s), \(^1\)C NMR \( \delta \) 201.53, 174.42, 170.43, 141.10, 133.93, 129.26, 128.89, 127.96, 125.69, 122.37, 116.51, 68.04, 59.19, 26.55. HRMS calculated [M+Na]\(^+\) for C\(_{26}\)H\(_{21}\)O\(_3\)NNa: 418.1414, found: 418.1410. FTIR (cm\(^{-1}\)) 3023, 2403, 1710, 1650, 1612, 1482, 1422, 1378, 1269, 1216, 1158, 1095, 1026, 922, 767, 670.

1'-Benzyl-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-2',5-dione (3c)

Following the general procedure, treatment of \( \text{trans} \) cinnamaldehyde 2a (0.099 g, 94 \( \mu \)L, 0.75 mmol) and (\( E \))-1-benzyl-3-benzylideneindolin-2-one 1c (0.156 g, 0.5 mmol) with imidazolium salt 4 (0.027 g, 0.075 mmol) and KOT-Bu (0.017 g, 0.15 mmol) in THF (2.0 mL) at 30 °C for 40 h followed by flash column chromatography afforded 1'-benzyl-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-2',5-dione 3c as a white solid (0.133 g, 60% dr determined by \(^1\)H NMR analysis of crude reaction mixture is 3:1).

\( R_f \) (Pet. ether /EtOAc = 80/20): 0.51; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.40-7.36 (m, 4H), 7.32-7.27 (m, 4H), 7.21-7.05 (m, 12H), 6.45-6.43 (m, 2H), 5.08-4.99 (m, 2H), 4.32 (d, \( J = 16.3 \) Hz, 1H), 4.18 (d, \( J = 12.5 \) Hz, 1H), 3.47-3.40 (m, 1H), 2.87-2.79 (m, 1H). \(^1\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 210.26, 172.14, 143.88, 140.81, 134.94, 134.73, 133.98, 129.28, 129.23, 128.91, 128.81, 128.73, 128.69, 128.50, 128.14, 128.03, 127.61, 127.41, 127.27, 127.10, 126.89, 126.41, 124.81, 123.38, 123.37, 109.71, 86.87, 58.83, 48.02, 43.55, 41.00. Representative Peaks of Minor Isomer: \(^1\)H NMR \( \delta \) 6.62-6.58 (m), 6.26-6.20 (m), 3.57-3.50 (m), 3.06-3.00 (m), \(^1\)C NMR \( \delta \) 70.70, 48.47, 36.79, 31.08. HRMS calculated [M+Na]\(^+\) for C\(_{31}\)H\(_{25}\)O\(_2\)NNa: 466.1778, found:
466.1768. FTIR (cm$^{-1}$) 3023, 2926, 2334, 1745, 1687, 1648, 1609, 1483, 1459, 1368, 1216, 1142, 1103, 1026, 758, 700, 665.

**tert-Butyl-2-(4-chlorophenyl)-2',5-dioxo-3-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3d)**

Following the general procedure, treatment of trans cinnamaldehyde 2a (0.099 g, 0.75 mmol) and tert-butyl (E)-3-(4-chlorobenzylidene)-2-oxoindoline-1-carboxylate 1d (0.178 g, 0.5 mmol) with imidazolium salt 4 (0.027 g, 0.075 mmol) and KOt-Bu (0.017 g, 0.15 mmol) in THF (2.0 mL) at 30 °C for 40 h followed by flash column chromatography afforded tert-butyl-2-(4-chlorophenyl)-2',5-dioxo-3-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate 3d as a white solid (0.149 g, 61% yield).

$R_f$ (Pet. ether/EtOAc = 80/20): 0.57; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.70 (d, $J = 8.0$ Hz, 1H), 7.35-7.29 (m, 7H), 7.22-7.21 (m, 1H), 7.07-7.06 (m, 2H), 6.98-6.96 (m, 2H), 4.84-4.76 (m, 1H), 3.99 (d, $J = 12.3$ Hz, 1H), 3.45-3.38 (m, 1H), 2.85-2.77 (m, 1H), 1.55 (s, 9H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 208.69, 170.67, 148.27, 140.94, 140.30, 133.71, 132.88, 129.70, 129.59, 129.01, 128.59, 127.44, 127.35, 126.43, 125.15, 123.10, 115.40, 84.78, 70.74, 59.82, 47.90, 41.21, 28.06. HRMS calculated [M+Na]$^+$ for C$_{29}$H$_{26}$O$_4$NClNa: 510.1443, found: 510.1433. FTIR (cm$^{-1}$) 3022, 2976, 2358, 1783, 1723, 1654, 1611, 1526, 1423, 1355, 1297, 1254, 1217, 1154, 1094, 1031, 751, 670.

**tert-Butyl-2',5-dioxo-3-phenyl-2-(p-tolyl)spiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3e)**

Following the general procedure, treatment of trans cinnamaldehyde 1a (0.099 g, 0.75 mmol) and tert-butyl (E)-3-(4-methylbenzylidene)-2-oxoindoline-1-carboxylate 2e (0.168 g, 0.5 mmol) with imidazolium salt 4 (0.027 g, 0.15 mmol) and KOt-Bu (0.017 g, 0.30 mmol) in THF (2.0 mL) at 35 °C for 40 h followed by flash column chromatography afforded tert-butyl-2',5-dioxo-3-phenyl-2-(p-tolyl)spiro[cyclopentane-1,3'-indoline]-1'-carboxylate 3e as a white solid (0.131 g, 56% yield).

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$R_f$ (Pet. ether /EtOAc = 80/20): 0.48; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.70 (d, $J = 8.0$ Hz, 1H), 7.37-7.28 (m, 7H), 7.21-7.18 (m, 1H), 6.94-6.88 (m, 4H), 4.89-4.81 (m, 1H), 4.01 (d, $J = 12.3$ Hz, 1H), 3.47-3.40 (m, 1H), 2.86-2.78 (m, 1H), 2.19 (s, 3H), 1.55 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 209.47, 170.89, 148.43, 140.95, 140.64, 137.29, 131.12, 129.31, 129.03, 128.86, 128.15, 127.51, 127.09, 126.82, 125.01, 123.19, 115.25, 84.40, 70.96, 60.33, 47.68, 41.07, 28.02, 21.03. HRMS calculated [M+Na]$^+$ for C$_{30}$H$_{29}$O$_4$NNa: 490.1989, found: 490.1982. FTIR (cm$^{-1}$): 3023, 2979, 2403, 1784, 1737, 1660, 1611, 1480, 1323, 1216, 1159, 1062, 1028, 929, 842, 766, 671.

**tert-Butyl -2',5-dioxo-3-phenyl-2-(4-(trifluoromethyl)phenyl)spiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3f)**

Following the general procedure, treatment of trans cinnamaldehyde 2a (0.099 g, 94 μL, 0.75 mmol) and (E)-tert-butyl (E)-3-(4-(trifluoromethyl)benzylidene)-2-oxoindoline-1-carboxylate 1f (0.194 g, 0.5 mmol) with imidazolium salt 4 (0.027 g, 0.075 mmol) and KOt-Bu (0.017 g, 0.15 mmol) in THF (2.0 mL) at 30 °C for 40 h followed by flash column chromatography afforded tert-butyl -2',5-dioxo-3-phenyl-2-(4-(trifluoromethyl)phenyl)spiro[cyclopentane-1,3'-indoline]-1'-carboxylate 3f as a white solid (0.146 g, 56% yield).

$R_f$ (Pet. ether /EtOAc = 80/20): 0.51; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.68 (d, $J = 7.9$ Hz, 1H), 7.36-7.29 (m, 10H), 7.14 (d, $J = 8.2$ Hz, 2H), 4.88-4.80 (m, 1H), 4.07 (d, $J = 12.4$ Hz, 1H), 3.45-3.38 (m, 1H), 2.85-2.78 (m, 1H), 1.51 (s, 9H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 208.33, 170.58, 148.22, 140.99, 139.94, 138.55, 129.75, 129.13, 128.78, 127.49, 127.43, 125.35, 125.31, 125.24, 123.12, 115.47, 88.47, 70.70, 59.98, 47.59, 41.13, 28.03. $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -62.58. (HRMS calculated [M+Na]$^+$ for C$_{30}$H$_{26}$O$_4$NF$_3$Na: 544.1706, found: 544.1708. FTIR (cm$^{-1}$): 3356, 3023, 2977, 2403, 1784, 1737, 1660, 1611, 1480, 1323, 1216, 1159, 1062, 1028, 929, 842, 766, 671.

**tert-Butyl -2-(3-bromophenyl)-2',5-dioxo-3-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3g)**
Following the general procedure, treatment of trans cinnamaldehyde 2a (0.099 g, 94 μL, 0.75 mmol) and tert-butyl (E)-3-bromobenzylidene)-2-oxoindoline-1-carboxylate 1g (0.200 g, 0.5 mmol) with imidazolium salt 4 (0.027 g, 0.075 mmol) and KOt-Bu (0.017 g, 0.15 mmol) in THF (2.0 mL) at 30 °C for 40 h followed by flash column chromatography afforded tert-butyl 2-(3-bromophenyl)-2',5-dioxo-3-phenylspirop[cyclopentane-1,3'-indoline]-1'-carboxylate 3g as a white solid (0.146 g, 55% yield).

\[ \text{Rf (Pet. ether /EtOAc = 80/20): 0.59; }^{1}\text{H NMR (400 MHz, CDCl}_3\text{) } \delta 7.71 (d, J = 8.0 \text{ Hz, 1H), 7.37-7.29 (m, 7H), 7.24-7.20 (m, 3H), 6.96-6.92(m, 2H), 4.81-4.73 (m, 1H), 3.94 (d, J = 12.3 Hz, 1H), 3.45-3.38 (m, 1H), 2.84-2.76 (m, 1H), 1.55 (s, 9H). }^{13}\text{C NMR (100 MHz, CDCl}_3\text{) } \delta 208.71, 170.61, 148.41, 140.94, 140.06, 136.74, 131.21, 131.05, 129.93, 129.68, 129.07, 127.46, 127.40, 127.23, 126.24, 125.22, 123.11, 115.41, 84.78, 70.70, 60.20, 47.47, 41.16, 28.07. \text{HRMS calculated [M+Na] }^+ \text{ for C}_{29}\text{H}_{26}\text{O}_4\text{NBrNa: 554.0937, found: 554.0930. FTIR (cm}^{-1}\text{) 3024, 1781, 1718, 1154, 1090, 1026, 841, 759, 667.} \]

**tert-Butyl 2',5-dioxo-2-(perfluorophenyl)-3-phenylspirop[cyclopentane-1,3'-indoline]-1'-carboxylate (3h)**

Following the general procedure, treatment of trans cinnamaldehyde 2a (0.099 g, 94 μL, 0.75 mmol) and tert-butyl 2-oxo- (E)-3-(perfluorobenzylidene)indoline-1-carboxylate 1h (0.206 g, 0.5 mmol) with imidazolium salt 4 (0.027 g, 0.075 mmol) and KOt-Bu (0.017 g, 0.15 mmol) in THF (2.0 mL) at 30 °C for 40 h followed by flash column chromatography afforded tert-butyl 2',5-dioxo-2-(perfluorophenyl)-3-phenylspirop[cyclopentane-1,3'-indoline]-1'-carboxylate 3h as a white solid (0.152 g, 56% yield).

\[ \text{Rf (Pet. ether /EtOAc = 80/20): 0.54; }^{1}\text{H NMR (400 MHz, CDCl}_3\text{) } \delta 7.89 (d, J = 8.2 \text{ Hz, 1H), 7.51 (d, J = 7.5 \text{ Hz, 1H), 7.46-7.42 (m, 1H), 7.31-7.16 (m, 6H), 4.79-4.71 (m, 1H), 4.64 (d, J = 8.9 \text{ Hz, 1H), 3.55-3.43 (m, 1H), 3.16-3.06 (m, 1H), 1.60 (s, 9H). }^{13}\text{C NMR (100 MHz, CDCl}_3\text{) } \delta 207.89, 169.07, 148.34, 139.40, 136.77, 129.83, 128.87, 128.71, 127.75, 126.88, 125.22, 122.06, 116.03, 85.32, 66.91, 47.16, 43.06, 38.59, 28.12. \text{HRMS calculated [M+Na] }^+ \text{ for} \]
C$_{29}$H$_{22}$O$_4$NF$_5$Na: 566.1361, found: 566.1364. FTIR (cm$^{-1}$) 3023, 2403, 1791, 1743, 1659, 1606, 1510, 1424, 1305, 1216, 1147, 1096, 1012, 925, 767, 670.

**tert-Butyl-5'-methoxy-2',5-dioxo-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3i)**

Following the general procedure, treatment of trans cinnamaldehyde 2a (0.099 g, 94 μL, 0.75 mmol) and tert-butyl (E)-3-benzylidene-5-methoxy-2-oxoindoline-1-carboxylate 1i (0.176 g, 0.5 mmol) with imidazolium salt 4 (0.027 g, 0.075 mmol) and KOt-Bu (0.017 g, 0.15 mmol) in THF (2.0 mL) at 30 °C for 40 h followed by flash column chromatography afforded tert-butyl-5'-methoxy-2',5-dioxo-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate 3i as a white solid (0.152 g, 63% yield).

$R_f$ (Pet. ether /EtOAc = 80/20): 0.55; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.61 (d, $J = 8.8$ Hz, 1H), 7.34-7.26 (m, 5H), 7.11-7.05 (m, 5H), 6.90-6.85 (m, 2H), 4.90-4.82 (m, 1H), 4.00 (d, $J = 12.3$ Hz, 1H), 3.88 (s, 3H), 3.47-3.40 (m, 1H), 2.86-2.78 (m, 1H), 1.53 (s, 9H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 209.24, 170.83, 157.26, 148.46, 140.55, 134.35, 134.25, 128.91, 128.37, 127.90, 127.79, 127.53, 127.16, 116.23, 113.94, 109.60, 84.29, 71.20, 60.64, 55.88, 47.63, 41.04, 28.09. HRMS calculated [M+Na]$^+$ for C$_{30}$H$_{29}$O$_5$NNa: 506.1938, found: 506.1928. FTIR (cm$^{-1}$) 3022, 2403, 1779, 1724, 1664, 1486, 1437, 1262, 1216, 1159, 1109, 1040, 927, 766, 670.

**tert-Butyl-5'-fluoro-2',5-dioxo-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3j)**

Following the general procedure, treatment of trans cinnamaldehyde 2a (0.099 g, 94 μL, 0.75 mmol) and tert-butyl (E)-3-benzylidene-5-fluoro-2-oxoindoline-1-carboxylate 1j (0.170 g, 0.5 mmol) with imidazolium salt 4 (0.027 g, 0.075 mmol) and KOt-Bu (0.017 g, 0.15 mmol) in THF (2.0 mL) at 30 °C for 40 h followed by flash column chromatography afforded tert-butyl-5'-fluoro-2',5-dioxo-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate 3j as a white solid (0.122 g, 52% yield).
R$_f$ (Pet. ether /EtOAc = 80/20): 0.51; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.67 (dd, $J_1 = 9.0$ Hz, $J_2 = 4.6$ Hz, 1H), 7.33-7.28 (m, 4H), 7.21-7.19 (m, 1H), 7.12-7.08 (m, 4H), 7.06-7.01 (m, 3H), 4.90-4.82 (m, 1H), 3.97 (d, $J = 12.3$ Hz, 1H), 3.47-3.40 (m, 1H), 2.86-2.78 (m, 1H), 1.53 (s, 9H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 208.53, 170.41, 160.16 (d, $J_{C-F} = 244$ Hz), 148.33, 140.27, 136.93, 133.95, 132.15, 131.12, 130.92, 128.96, 128.45, 128.32, 127.97, 127.81, 127.49, 127.26, 116.68 (d, $J_{C-F} = 7.8$ Hz), 116.00 (d, $J_{C-F} = 22.8$ Hz), 110.78 (d, $J_{C-F} = 24.6$ Hz), 84.73, 71.10, 60.80, 47.47, 41.09, 28.05. HRMS calculated [M+Na]$^+$ for C$_{29}$H$_{26}$O$_4$NFNa: 494.1738, found: 494.1727.

FTIR (cm$^{-1}$) 2978, 2104, 1782, 1648, 1623, 1485, 1403, 1307, 1266, 1213, 1153, 1027, 838, 764, 667.

tert-Butyl -2',5-dioxo-3-phenyl-2-(pyridin-2-yl)spiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3k)

Following the general procedure, treatment of trans cinnamaldehyde 2a (0.099 g, 94 μL, 0.75 mmol) and tert-butyl 2-oxo (E)-3-((pyridin-2-yl)methylene)indoline-1-carboxylate 1k (0.161 g, 0.5 mmol) with imidazolium salt 4 (0.027 g, 0.075 mmol) and KOt-Bu (0.017 g, 0.15 mmol) in THF (2.0 mL) at 30 °C for 40 h followed by flash column chromatography afforded tert-butyl -2',5-dioxo-3-phenyl-2-(pyridin-2-yl)spiro[cyclopentane-1,3'-indoline]-1'-carboxylate 3k as a brownish solid (0.143 g, 63% yield).

R$_f$ (Pet. ether /EtOAc = 80/20): 0.48; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.57 (d, $J = 4.7$ Hz, 1H), 7.79 (d, $J = 8.2$ Hz, 1H), 7.27-7.18 (m, 3H), 7.09-7.08 (m, 4H), 7.04-7.01 (m, 2H), 6.76 (t, $J = 7.6$ Hz, 1H), 6.53 (d, $J = 7.7$ Hz, 1H), 6.17 (d, $J = 7.6$ Hz, 1H), 5.20-5.13 (m, 1H), 4.13 (d, $J = 7.1$ Hz, 1H), 3.88-3.81 (m, 1H), 3.09-3.02 (m, 1H), 1.68 (s, 9H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 210.28, 172.57, 158.03, 148.94, 148.70, 140.75, 139.21, 136.33, 128.97, 128.04, 127.98, 126.39, 126.33, 125.53, 124.32, 122.54, 114.58, 85.08, 69.78, 59.22, 42.75, 40.24, 28.22. HRMS calculated [M+H]$^+$ for C$_{28}$H$_{27}$O$_4$N$_2$: 455.1965, found: 455.1954. FTIR (cm$^{-1}$) 3024, 2951, 1821, 1781, 1484, 1308, 1264, 1215, 1155, 1027, 840, 761, 699.
**tert-Butyl -2-(furan-2-yl)-2',5-dioxo-3-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3l)**

Following the general procedure, treatment of *trans* cinnamaldehyde 2a (0.099 g, 94 μL, 0.75 mmol) and *tert*-butyl (*E*)-3-((furan-2-yl)methylene)-2-oxoindoline-1-carboxylate 1l (0.156 g, 0.5 mmol) with imidazolium salt 4 (0.027 g, 0.075 mmol) and KOr-Bu (0.017 g, 0.15 mmol) in THF (2.0 mL) at 30 °C for 40 h followed by flash column chromatography afforded *tert*-butyl -2-(furan-2-yl)-2',5-dioxo-3-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate 3l as a brownish solid (0.124 g, 56%, dr determined by $^1$H NMR analysis of crude reaction mixture is 1:1).

$R_f$ (Pet. ether/EtOAc = 80/20): 0.58; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.86 (d, $J = 8.2$ Hz, 1H), 7.45-7.43 (m, 2H), 7.39-7.34 (m, 7H), 7.28-7.25 (m, 5H), 7.18 (d, $J = 7.5$ Hz, 1H), 7.10-7.02 (m, 3H), 6.13-6.11 (m, 1H), 6.01-6.00 (m, 2H), 5.97-5.96 (m, 1H), 4.68-4.60 (m, 2H), 3.40-3.33 (m, 1H), 3.00-2.92 (m, 1H), 1.68 (s, 9H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 208.50, 172.99, 150.32, 149.90, 148.87, 142.09, 140.97, 140.55, 129.44, 128.97, 127.65, 127.30, 126.70, 125.06, 124.30, 123.96, 84.91, 69.33, 53.99, 47.39, 43.66, 28.18. Representative Peaks of Other Isomer: $^1$H NMR $\delta$ 7.80 (d, $J = 8.2$ Hz, 1H), 4.17-4.08 (m, 2H), 3.18-3.11 (m, 1H), 2.83-2.76 (m, 1H), 1.61 (s, 9H), $^{13}$C NMR $\delta$ 207.78, 170.45, 148.68, 140.61, 140.03, 129.08, 127.39, 123.02, 84.67, 68.97, 51.79, 46.86, 42.01, 28.13. HRMS calculated [M+Na]$^+$ for C$_{27}$H$_{25}$O$_5$NNa: 466.1625, found: 466.1620. FTIR (cm$^{-1}$) 3023, 2403, 1782, 1720, 1608, 1480, 1424, 1356, 1257, 1216, 1155, 1090, 1043, 925, 843, 766, 670.

**tert-Butyl -3-(4-methoxyphenyl)-2',5-dioxo-2-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3m)**

Following the general procedure, treatment of (*E*)-3-(4-methoxyphenyl)acrylaldehyde 2m (0.122 g, 0.75 mmol) and *tert*-butyl (*E*)-3-benzylidene-2-oxoindoline-1-carboxylate 1a (0.160 g, 0.5 mmol) with imidazolium salt 4 (0.027 g, 0.075 mmol) and KOr-Bu (0.017 g, 0.15 mmol) in THF (2.0 mL) at 30 °C for 40 h followed by flash column chromatography afforded *tert*-butyl -3-(4-
methoxyphenyl)-2',5-dioxo-2-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate 3m as a white solid (0.116 g, 51% yield).

\( R_f \) (Pet. ether / EtOAc = 80/20): 0.52; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.65 (d, \( J = 8.0 \) Hz, 1H), 7.34-7.25 (m, 2H), 7.23-7.21 (m, 2H), 7.09-7.05 (m, 3H), 7.01-6.99 (m, 2H), 6.81-6.78 (m, 2H), 4.83-4.75 (m, 1H), 3.94 (d, \( J = 12.6 \) Hz, 1H), 3.73 (s, 3H), 3.41-3.34 (m, 1H), 2.79-2.72 (m, 1H), 1.51 (s, 9H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 209.44, 170.86, 158.61, 148.42, 140.97, 134.36, 132.44, 132.15, 129.38, 128.47, 128.39, 128.34, 127.77, 126.81, 125.03, 123.19, 115.27, 114.32, 84.48, 70.99, 60.94, 55.33, 47.72, 40.31, 28.08. HRMS calculated [M+Na]\(^+\) for C\(_{30}\)H\(_{29}\)O\(_5\)NNa: 506.1938, found: 506.1940. FTIR (cm\(^{-1}\)) 3020, 1737, 1643, 1611, 1514, 1482, 1467, 1371, 1348, 1310, 1256, 1218, 1148, 1095, 1043, 1016, 835, 772, 669.

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tert-Butyl -2',5-dioxo-2-phenyl-3-(p-tolyl)spiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3n)

Following the general procedure, treatment of \((E)-3-p\)-tolylacrylaldehyde 2n (0.110 g, 0.75 mmol) and tert-butyl \((E)-3\)-benzylidene-2-oxoindoline-1-carboxylate 1a (0.160 g, 0.5 mmol) with imidazolium salt 4 (0.027 g, 0.075 mmol) and KOt-Bu (0.017 g, 0.15 mmol) in THF (2.0 mL) at 30 °C for 40 h followed by flash column chromatography afforded tert-butyl -2',5-dioxo-2-phenyl-3-(p-tolyl)spiro[cyclopentane-1,3'-indoline]-1'-carboxylate 3n as a white solid (0.147 g, 63% yield).

\( R_f \) (Pet. ether / EtOAc = 80/20): 0.59; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.68 (d, \( J = 7.5 \) Hz, 1H), 7.37-7.30 (m, 3H), 7.24-7.22 (m, 2H), 7.11-7.09 (m, 5H), 7.04-7.02 (m, 2H), 4.87-4.79 (m, 1H), 4.01 (d, \( J = 12.4 \) Hz, 1H), 3.45-3.38 (m, 1H), 2.84-2.70 (m, 1H), 2.29 (s, 3H), 1.54 (s, 9H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 209.45, 170.83, 148.40, 140.96, 137.44, 136.76, 134.32, 129.60, 129.37, 128.35, 128.32, 127.74, 127.37, 126.80, 125.03, 123.19, 115.26, 84.46, 70.97, 60.68, 47.75, 40.64, 28.06, 21.10. HRMS calculated [M+Na]\(^+\) for C\(_{30}\)H\(_{29}\)O\(_4\)NNa: 490.1989, found: 490.1975. FTIR (cm\(^{-1}\)) 3024, 1781, 1725, 1665, 1608, 1479, 1424, 1355, 1301, 1261, 1216, 1153, 1096, 1030, 839, 759, 669.
**tert-Butyl -2',5-dioxo-2-phenyl-3-(4-(trifluoromethyl)phenyl)spiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3o)**

Following the general procedure, treatment of \((E)-3-(4-(trifluoromethyl)phenyl)acrylaldehyde\) 2o (0.150 g, 0.75 mmol) and tert-butyl \((E)-3-benzylidene-2-oxoindoline-1-carboxylate\) 1a (0.160 g, 0.5 mmol) with imidazolium salt 4 (0.027 g, 0.075 mmol) and KOt-Bu (0.017 g, 0.15 mmol) in THF (2.0 mL) at 30 °C for 40 h followed by flash column chromatography afforded tert-butyl -2',5-dioxo-2-phenyl-3-(4-(trifluoromethyl)phenyl)spiro[cyclopentane-1,3'-indoline]-1'-carboxylate 3o as a white solid (0.143 g, 55% yield).

\[ R_f \text{ (Pet. ether /EtOAc = 80/20): 0.51; } ^1\text{H NMR (400 MHz, CDCl}_3\text{)} \delta 7.63-7.40 (m, 6H), 7.35-7.31 (m, 2H), 7.11-7.08 (m, 2H), 7.04-7.00 (m, 2H), 5.01-4.90 (m, 1H), 3.98 (d, J = 12.3 Hz, 1H), 3.50-3.36 (m, 1H), 2.85-2.77 (m, 1H), 1.52 (s, 9H). \]

\[ ^{13}\text{C NMR (100 MHz, CDCl}_3\text{)} \delta 207.96, 172.99, 153.20, 148.65, 142.14, 141.98, 135.03, 129.15, 128.37, 128.04, 127.59, 125.22, 124.14 (d, J_{C-F} = 35.71Hz), 115.72, 110.46, 106.74, 84.93, 70.41, 56.03, 44.53, 36.94, 28.18. \]

HRMS calculated \([M+Na]^+\) for C\(_{30}\)H\(_{26}\)O\(_4\)F\(_3\)Na: 544.1706, found: 544.1707.

FTIR (cm\(^{-1}\)) 3022, 2971, 2403, 1782, 1736, 1665, 1611, 1482, 1426, 1322, 1216, 1138, 1025, 928, 766, 671.

**tert-Butyl -3-(2-methoxyphenyl)-2',5-dioxo-2-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3p)**

Following the general procedure, treatment of \((E)-3-(2-methoxyphenyl)acrylaldehyde\) 2p (0.122 g, 0.75 mmol) and tert-butyl \((E)-3-benzylidene-2-oxoindoline-1-carboxylate\) 1a (0.160 g, 0.5 mmol) with imidazolium salt 4 (0.027 g, 0.075 mmol) and KOt-Bu (0.017 g, 0.15 mmol) in THF (2.0 mL) at 30 °C for 40 h followed by flash column chromatography afforded tert-butyl -3-(2-methoxyphenyl)-2',5-dioxo-2-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate 3p as a white solid (0.150 g, 62% yield).

\[ R_f \text{ (Pet. ether /EtOAc = 80/20): 0.56; } ^1\text{H NMR (400 MHz, CDCl}_3\text{)} \delta 7.68 (d, J = 8.3 Hz, 1H), 7.37-7.28 (m, 3H), 7.20-7.17 (m, 2H), 7.09-7.02 (m, 5H), 6.90-6.82 (m, 2H), 5.02-4.94 (m, 1H), 4.36 (d, J = 12.1 Hz, 1H), 3.92 (s, 3H), 3.49-3.41 (m, 1H), 2.93-2.85 (m, 1H), 1.53 (s, 9H). \]

\[ ^{13}\text{C NMR (100 MHz, CDCl}_3\text{)} \delta 210.14, 170.77, 157.84, 148.47, 141.01, 135.02, 129.24, 128.83, \]
128.64, 128.31, 128.21, 127.55, 127.22, 124.98, 123.35, 120.81, 115.21, 111.02, 84.34, 70.79, 57.87, 55.38, 45.41, 37.31, 28.06. \text{HRMS calculated [M+Na]$^+$ for C$_{30}$H$_{29}$O$_5$NNa: 506.1938, found: 506.1923.} \text{FTIR (cm$^{-1}$) 3022, 2403, 1780, 1739, 1666, 1605, 1482, 1355, 1216, 1153, 1096, 1034, 921, 766, 670.}

\textit{tert-Butyl -3-(furan-2-yl)-2',5-dioxo-2-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3q)}

Following the general procedure, treatment of (\textit{E})-3-(furan-2-yl)acrylaldehyde \textbf{2q} (0.092 g, 0.75 mmol) and \textit{tert}-butyl (\textit{E})-3-benzylidene-2-oxoindoline-1-carboxylate \textbf{1a} (0.160 g, 0.5 mmol) with imidazolium salt \textbf{4} (0.027 g, 0.075 mmol) and KOt-Bu (0.017 g, 0.15 mmol) in THF (2.0 mL) at 30 °C for 40 h followed by flash column chromatography afforded \textit{tert}-butyl -3-(furan-2-yl)-2',5-dioxo-2-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate \textbf{3q} as a white solid (0.113 g, 51% yield). Compound having unknown impurity.

$R_f$ (Pet. ether /EtOAc = 80/20): 0.54; $^1$H NMR (400 MHz, CDCl$_3$) \(\delta\) 7.69 (d, \(J = 8.3\) Hz, 1H), 7.34-7.31 (m, 2H), 7.19-7.16 (m, 2H), 7.08-7.05 (m, 4H), 6.30-6.19 (m, 2H), 6.08-6.04 (m, 1H), 4.59 (d, \(J = 12.6\) Hz, 1H), 4.40-4.32 (m, 1H), 3.75-3.57 (m, 1H), 3.23-3.17 (m, 1H), 3.07-3.00 (m, 1H), 1.62 (s, 9H). $^{13}$C NMR (100 MHz, CDCl$_3$) \(\delta\) 207.96, 172.99, 153.20, 141.98, 140.39, 135.03, 129.15, 128.37, 128.04, 127.99, 125.22, 124.31, 123.96, 115.72, 110.46, 106.74, 84.93, 70.41, 56.03, 44.53, 36.94, 28.18. \text{HRMS calculated [M+Na]$^+$ for C$_{27}$H$_{25}$O$_5$NNa: 466.1625, found: 466.1624.} \text{FTIR (cm$^{-1}$) 3024, 2403, 1780, 1651, 1617, 1483, 1308, 1264, 1216, 1155, 1022, 926, 842, 764, 669.}

\textit{tert-Butyl -3-ethyl-2',5-dioxo-2-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3r)}

Following the general procedure, treatment of (\textit{E})-pent-2-enal \textbf{2r} (0.063 g, 73 \(\mu\)L, 0.75 mmol) and \textit{tert}-butyl (\textit{E})-3-benzylidene-2-oxoindoline-1-carboxylate \textbf{1a} (0.160 g, 0.5 mmol) with imidazolium salt \textbf{4} (0.027 g, 0.075 mmol) and KOt-Bu (0.017 g, 0.15 mmol) in THF (2.0 mL) at 30 °C for 40 h followed by flash column chromatography afforded \textit{tert}-butyl -3-
ethyl-2',5-dioxo-2-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate 3r as a white solid (0.085 g, 42% yield).

$R_f$ (Pet. ether /EtOAc = 80/20): 0.56; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.62 (d, $J = 8.0$ Hz, 1H), 7.28-7.15 (m, 6H), 7.04-7.02 (m, 2H), 3.51-3.46 (m, 1H), 3.39 (d, $J = 12.1$ Hz, 1H), 3.19-3.12 (m, 1H), 2.34-2.27 (m, 1H), 1.50 (s, 9H), 1.29-1.21(m, 2H), 0.97 (t, $J = 7.4$ Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 210.39, 170.82, 148.47, 140.89, 135.15, 131.27, 129.48, 129.16, 128.46, 128.40, 127.79, 124.90, 123.08, 115.14, 84.36, 71.06, 60.77, 44.76, 37.61, 28.07, 26.76, 12.52. HRMS calculated [M+Na]$^+$ for C$_{25}$H$_{27}$O$_4$NNa: 428.1832, found: 428.1821. FTIR (cm$^{-1}$) 3023, 2975, 2403, 1779, 1739, 1660, 1609, 1522, 1481, 1427, 1355, 1216, 1154, 1035, 928, 768, 671.

Characterization of Chiral cyclopentanone-fused spirooxindole (Chiral-3a)

tert-Butyl -2',5-dioxo-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (Chiral-3a)

Following the general procedure, treatment of trans cinnamaldehyde 2a (0.049 g, 47 μL, 0.375 mmol) and tert-butyl (E)-3-benzylidene-2-oxoindoline-1-carboxylate 1a (0.080 g, 0.25 mmol) with chiral triazolium salt 12 (0.008 g, 0.025 mmol) and KOr-Bu (0.006 g, 0.05 mmol) in THF (1.0 mL) at 50 °C for 36 h followed by flash column chromatography afforded tert-butyl -2',5-dioxo-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (Chiral-3a) as a white solid (0.024 g, 22% yield; the absolute stereochemistry of Chiral-3a was not determined).

$R_f$ (Pet. ether /EtOAc = 60/40): 0.61; 97% ee, $[\alpha]_D^{25} = -5.76$ (c 0.1, CHCl$_3$). HPLC (Kromasil-5-Amycoat, 15:85 IPA / n-Hexane, 0.7 mL/min.) Major: 7.56 min, Minor: 8.89 min.
**tert-Butyl -3-(2-methoxyphenyl)-2',5-dioxo-2-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (Chiral-3p)**

Following the general procedure, treatment of \((E)-3-(2\text{-methoxyphenyl})\text{acrylaldehyde 2p}\) (0.030 g, 0.187 mmol) and \(\text{tert-butyl (E)-3-benzylidene-2-oxoindoline-1-carboxylate 1a}\) (0.040 g, 0.125 mmol) with chiral triazolium salt \(8\) (0.004 g, 0.0125 mmol) and \(\text{KOT-Bu (0.003 g, 0.025 mmol)}\) in THF (0.5 mL) at 50 °C for 36 h followed by flash column chromatography afforded \(\text{tert-Butyl -3-(2-methoxyphenyl)-2',5-dioxo-2-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (Chiral-3p)}\) as a white solid (0.015 g, 24% yield; the absolute stereochemistry of \(\text{Chiral-3p}\) was not determined).

\(Rf\) (Pet. ether /EtOAc = 60/40): 0.56; 54% ee, \([\alpha]_D^{25} = -4.52\) (c 0.1, CHCl3). **HPLC** (Chiralpak AD, 10:90 IPA / n-Hexane, 1.0 mL/min.) Major: 9.46 min, Minor: 10.67 min.

**tert-Butyl -5-(hydroxyimino)-2'-oxo-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (9a)**

To a flame-dried screw-capped test tube equipped with a magnetic stir bar was charged with hydroxylamine hydrochloride (0.052 g, 0.75 mmol, 5.0 equiv.) and sodium acetate (0.049 g, 0.60 mmol, 4.0 equiv.). The resultant mixture was dissolved in ethanol (2.0 mL) followed by addition of \(\text{tert-butyl -2',5-dioxo-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate 3a}\) (0.068 g, 0.15 mmol) and the resulting reaction mixture was stirred at rt for 48 h. Water (2 mL) was added to quench the reaction. The organic layer was extracted with ethyl acetate, dried over Na2SO4 and concentrated under reduced pressure.5 The crude reaction mixture was purified by flash column chromatography through silica gel (petroleum ether: ethyl acetate 60:40) to afford \(\text{tert-Butyl -5-(hydroxyimino)-2'-oxo-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate 9a}\) inseparable mixture of diastereomers as a white solid (0.045 g, 64% yield).

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2,3-Diphenylspiro[cyclopentane-1,3'-indoline]-2',5-dione (10a)

To a stirred solution of *tert*-butyl -2',5-dioxo-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate 3a (0.068 g, 0.15 mmol) in 2.0 mL of dry CH$_2$Cl$_2$ was added trifluoroacetic acid (0.068 g, 0.60 mmol, 45 µL) under argon atmosphere. After stirring for 2 h at 0 °C to rt, the mixture was concentrated under reduced pressure. The crude reaction mixture was purified by flash column chromatography through silica gel (petroleum ether: ethyl acetate 40:60) to afford 2,3-diphenylspiro[cyclopentane-1,3'-indoline]-2',5-dione 10a as a white solid (0.043 g, 81% yield).

$R_f$ (Pet. ether /EtOAc = 40/60): 0.47  $^1$H NMR (400 MHz, DMSO-d$_6$) δ 10.05 (s, 1H, NH), 7.55 (d, $J = 7.2$ Hz, 1H), 7.20 (t, $J = 7.5$ Hz, 1H), 7.10 (d, $J = 7.2$ Hz, 2H), 7.07-7.03 (m, 3H), 6.95 (d, $J = 7.1$ Hz, 1H), 6.87-6.95 (m, 3H), 6.66 (d, $J = 7.6$ Hz, 1H), 6.59 (d, $J = 7.1$ Hz, 2H), 4.11 (d, $J = 3.8$ Hz, 1H).
Hz, 1H), 3.95 (d, J = 8.9 Hz, 1H), 3.68 (dd, J1 = 4.2 Hz, J2 = 11.8 Hz, 1H), 2.73 (dd, J1 = 4.2 Hz, J2 = 11.6 Hz, 1H); 13C NMR (100 MHz, DMSO-d6) δ 177.58, 173.36, 143.20, 142.22, 138.39, 128.97, 128.48, 128.18, 127.82, 127.31, 127.21, 127.06, 126.27, 126.09, 124.92, 121.31, 109.44, 51.01, 47.99, 44.04, 39.65; HRMS calculated [M+Na] + for C24H19O2NNa: 376.1308, found: 376.1313; FTIR (cm⁻¹) 3410, 3063, 3025, 2942, 1960, 1890, 1715, 1637, 1592, 1493, 1450, 1375, 1315, 1269, 1166, 1039, 984, 870, 760, 697.

5-Hydroxy-2,3-diphenylspiro[cyclopentane-1,3'-indolin]-2'-one (11a)

To a stirred solution of 2,3-diphenylspiro[cyclopentane-1,3'-indoline]-2',5-dione 10a (0.040 g, 0.11 mmol) in 2.0 mL of dry MeOH was added NaBH4 (0.007 g, 0.17 mmol) under argon atmosphere. After stirring for 1 h at 0 °C to rt, the reaction was quenched with water. The organic layer was extracted with ethyl acetate, dried over Na2SO4 and concentrated under reduced pressure. The crude reaction mixture was purified by flash column chromatography through silica gel (petroleum ether: ethyl acetate 60:40) to afford 5-hydroxy-2,3-diphenylspiro[cyclopentane-1,3'-indolin]-2'-one 11a inseparable mixture of diastereomers as a white solid (0.031 g, 77% yield).

Rf(Pet. ether /EtOAc = 40/60): 0.38 1H NMR (400 MHz, CDCl3) δ 7.99 (s, 1H, NH, proton exchangeable with D2O), 7.89 (d, J = 7.4 Hz, 1H), 7.70-7.65 (m, 1H), 7.62 (d, J = 7.6 Hz, 2H), 7.54-7.48 (m, 4H), 7.47-7.43 (m, 1H), 7.42-7.40 (m, 2H), 7.35-7.31 (m, 2H), 6.95 (d, J = 7.5 Hz, 1H), 4.75-4.70 (m, 1H), 4.65-4.53 (m, 1H), 4.22 (d, J = 11.9 Hz, 1H), 3.54-3.46 (m, 1H), 2.50-2.33 (m, 2H, OH peak is merged, one of the proton is exchangeable with D2O); 13C NMR (100 MHz, CDCl3) δ 179.59, 143.54, 141.23, 136.54, 128.60, 128.52, 128.48, 128.36, 128.10, 127.95, 127.88, 126.99, 126.34, 126.07, 122.42, 109.62, 75.94, 60.74, 46.37, 43.40; Representative Peaks of Minor Isomer: 1H NMR δ 8.58 (s), 3.89 (d, J = 11.6 Hz), 2.89-2.82 (m), 2.70-2.62 (m);
$^{13}$C NMR δ: 143.81, 140.28, 128.80, 128.64, 128.26, 128.04, 127.48, 124.98, 122.67, 110.26, 78.21, 66.61, 46.88, 43.58; HRMS calculated [M+H]$^+$ for C$_{24}$H$_{22}$O$_2$N: 365.1645, found: 356.1643. FTIR (cm$^{-1}$) 3442, 3039, 2975, 2935, 2728, 1950, 1682, 1600, 1485, 1380, 1260, 1162, 1111, 1024, 915, 858, 744, 704, 664.
8. $^1$H and $^{13}$C NMR Spectra cyclopentanone-fused spirooxindoles

terr-Butyl-2',5-dioxo-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3a)
1'-Acetyl-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-2',5-dione (3b)
1'-Benzyl-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-2',5-dione (3c)
tert-Butyl-2-(4-chlorophenyl)-2',5-dioxo-3-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3d)
**3e**

*tert-Butyl-2',5-dioxo-3-phenyl-2-(p-tolyl)spiro[cyclopentane-1,3'-indoline]-1'-carboxylate*
**tert-Butyl-2',5-dioxo-3-phenyl-2-(4-(trifluoromethyl)phenyl)spiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3f)**

![Chemical Structure of 3f](image)
*tert-Butyl-2-(3-bromophenyl)-2',5-dioxo-3-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3g)*
tert-Butyl 2',5-dioxo-2-(perfluorophenyl)-3-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3h)
tert-Butyl-5'-methoxy-2',5-dioxo-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3i)
tert-Butyl -5'-fluoro-2',5-dioxo-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3j)
**tert-Butyl 2',5-dioxo-3-phenyl-2-(pyridin-2-yl)spiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3k)**
*tert*-Butyl -2-(furan-2-yl)-2',5-dioxo-3-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3l)
*tert*-Butyl -3-(4-methoxyphenyl)-2',5-dioxo-2-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3m)
*tert*-Butyl 2',5-dioxo-2-phenyl-3-(p-tolyl)spiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3n)
*tert*-Butyl -2',5-dioxo-2-phenyl-3-(4-(trifluoromethyl)phenyl)spiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3o)
**tert-Butyl 3-(2-methoxyphenyl)-2',5-dioxo-2-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3p)**
tert-Butyl 3-(furan-2-yl)-2',5-dioxo-2-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3q)
tert-Butyl-3-ethyl-2',5-dioxo-2-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (3r)
tert-Butyl -5-(hydroxyimino)-2'-oxo-2,3-diphenylspiro[cyclopentane-1,3'-indoline]-1' -carboxylate (9a)
2,3-Diphenylspiro[cyclopentane-1,3’-indoline]-2’,5-dione (10a)
5-Hydroxy-2,3-diphenylspiro[cyclopentane-1,3'-indolin]-2'-one (11a)

11a
mixture of diastereomers

11a
mixture of diastereomers
9. HPLC Data of *Chiral-3a* and *Chiral-3p*
**tert-Butyl 2',5-dioxo-2-phenylspiro[cyclopentane-1,3'-indoline]-1'-carboxylate (Chiral-3p)**

### Chromatogram Details

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**Method:** C:\Documents and Settings\admin\Desktop\lab.net  
**Acquired:** 9/10/2015 11:53:05 PM  
**Printed:** 9/11/2015 2:53:00 AM

#### VWD: Signal A, 220 nm Results

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**Column:** Chiralpak AD  
**Eluent System:** 90 : 10 (HEXANE:IPA)  
**Flow rate:** 1.0 ml/min  
**Injection vol.:** 10ul  
**Wavelength:** 220 nm  
**Sample Conc.:** 1 mg/ml