Chapter 4: Highly Diastereoselective ABB’ Three-component Synthesis of Spirooxindoles Bearing Five Consecutive Asymmetric Carbons

Graphical Abstract

One-pot, 3 CR, High atom economy
Waste-free (side product: 2H2O), Four new bonds (3 C–C, 1 C–O),
Five consecutive asymmetric carbons (One spiro and one tetrasubstituted stereocentres)
Two new rings (one carbo- and one heterocycle), Highly diastereoselective

Newly created bonds

up to 78% yield
15 examples
4.1. Introduction

4.1.1. Biological Relevance of Spirooxindoles

Spirooxindole is a very significant structural motif found in numerous natural products with promising pharmacological activities exemplified by coerulescine 4.1a, horsfiline 4.1b, spirotryprostatin A 4.2, citrinadin B 4.3 and welwitindolinone A 4.4. In addition to naturally existing bioactive spirooxindoles, a large number of synthetic analogs are also known to display a wide range of biological activities.\(^1\,^2\) The representative examples including the antimalarial agent NITD 609 4.5,\(^3\) CR TH2 receptor antagonist 4.6\(^4\) and progesterone receptor agonist 4.7\(^5\) are displayed in Figure 4.1. These spirooxindoles are also known to exhibit additional remarkable activities including antimicrobial,\(^6\) antitumoral,\(^7\,^8\) anti-HIV,\(^9\) antiviral,\(^10\) antituberculosis,\(^11\) anti-inflammatory\(^12\) and anesthetic\(^13\) activities. Other potential pharmacological function of spirooxindoles includes the selective inhibition of MDM2-p53 interaction associated with antitumor activity.\(^14\)

![Figure 4.1](image-url)
4.1.2. Multicomponent Synthesis of Spirooxindoles: Recent Advances

Owing to the prominence of the spirooxindoles, prodigious effort has been devoted to the development of synthetic procedures for these compounds and their enantioselective versions. In this section, we summarize the recent examples for the construction of spirooxindoles starting from isatin/oxindole derivatives comprising a multicomponent approach.

Yan, Lin and co-workers demonstrated a three-component synthesis of diastereomeric spirooxindoles 4.11 and 4.12 involving a base catalyzed reaction between isatins 4.8, heterocyclic ketene aminals 4.9 and ethyl trifluoroacetate 4.10 (Scheme 4.1). Initial base catalyzed reaction of isatin 4.8 and ethyl trifluoroacetate 4.10 generated the condensation product, which subsequently reacted with heterocyclic ketene aminals 4.9 to deliver the products via a sequential aza-ene addition-tautomerization-intramolecular cyclization steps. Although excellent diastereoselectivity (up to >99:1) was obtained when R³ = H, 1:1 mixtures of compounds 4.11 and 4.12 were obtained when R³ is substituted by methyl group.

![Scheme 4.1. Three-component synthesis of spirooxindoles 4.11 and 4.12](image)

Synthesis of dispirocyclopentanebisoxindoles was achieved involving an ABB’ three-component reaction 3-phenacylideneoxindoles and amines or alcohols (Scheme 4.2). Treatment of two equivalent 3-phenacylideneoxindoles 4.13 with one
equivalent of amines 4.14 in the presence of piperidine furnished dispirocyclopentanebisoxindoles 4.15 in good yields. On the other hand, compounds 4.13 reacted with alcohols 4.16 to produce excellent yields of compounds 4.17. Dispirocyclopentanebisoxindoles 4.18 were isolated in high yields when compounds 4.13 reacted with aryl thiols.

Scheme 4.2. ABB’ three-component synthesis of dispirocyclopentanebisoxindoles

Trifluoroacetic acid catalyzed three-component reaction of isatins 4.19, amino ester 4.20 and dialkyl acetylenedicarboxylates 4.21 afforded spirooxindole 4.22 bearing a 2,5-dihydropyrrole scaffold in good to excellent yields (Scheme 4.3).19 The reaction involved 1,3-dipolar cycloaddition of azomethine ylide, which was in situ generated from isatin and amino ester, with electron deficient alkynes.
An isocyanide based multicomponent reaction was developed for the synthesis of spirooxindoles containing [5,5] fused heterocycle. The three-component reaction of isatin 4.23 with isocyanide 4.24 and substituted allenoates 4.25 delivered spirooxindoles 4.26 in good yields under catalyst-free conditions. In this reaction two new heterocycle rings and five new bonds were generated in a single operation (Scheme 4.4).

A large number of enantioselective approaches have been developed for the synthesis of chiral spirooxindoles. For instance, an organocatalyzed Michael-aldol-hemiacetalization cascade was developed to access chiral spirooxindole 4.29 (Scheme 4.5). The chiral amine I catalyzed ABB’ three-component reaction of compounds 4.27 and aldehydes 4.28 furnished spirooxindoles 4.29 fused with tetrahydropyran in high yields with excellent diastereo- and enantioselectivities.
Chen and co-workers established a three-component domino reaction of \((E)\)-4-(1-methyl-2-oxoindolin-3-ylidene)-3-oxobutanoates 4.30 and two molecules of \(\alpha,\beta\)-unsaturated aldehydes 4.31/4.32 in the presence of chiral amine catalyst I to access spirooxindoles 4.33 with excellent diastereo- and enantioselectivities (Scheme 4.6). The reactions proceeded via Michael-Michael-Michael-aldol cascade to deliver the products in high yields involving quadruple iminium-enamine-iminium-enamine catalysis.

Chroman-fused spirooxindole derivatives 4.37 with potential anticancer activity were synthesized involving a chiral amine catalyzed three-component reaction between 2-nitrovinyl phenols 4.34, \(\alpha,\beta\)-unsaturated aldehydes 4.35 and
electron-deficient olefinic oxindole 4.36 (Scheme 4.7). The mechanism of this reaction involves oxa-Michael-Michael-Michael-aldol cascade.

Scheme 4.7. Synthesis of chroman-fused spirooxindole derivatives

A recyclable fluorous bifunctional Cinchona alkaloid/thiourea-catalyzed synthesis of spirooxindoles was achieved involving a four-component reaction. As depicted in Scheme 4.8, electron-deficient olefinic oxindole 4.38 reacted with diethyl malonate 4.39, ammonium acetate or primary amines 4.40 and aldehydes 4.41 furnished 2-piperidone-fused spirooxindoles 4.42 in good yields with high enantioselectivity. On the other hand, under similar conditions, 1,3-dicarbonyl compounds 4.43 delivered tetrahydropyridine-fused spirooxindoles 4.44.
4.2. Results and Discussion

4.2.1. Design of Experiment

Although a large number of methodologies have been developed for the synthesis of spirooxindoles starting from a variety of isatin/oxindole-derived compounds, exploration of the reactivity of \((E)-2-(2\text{-oxoindolin-3-ylidene})\)acetaldehydes 4.45 to access such compounds is rather limited.\(^{25}\) The presence of \(\alpha,\beta\)-unsaturated aldehyde moiety together with the highly reactive oxindole fragment allows the possibility of discovering novel cascade processes for the construction of complex spirooxindoles. Consequently, we envisaged a new ABB’ three-component cascade process for the construction of spirooxindoles 4.47 fused with tetrahydro-\(4H\)-cyclopenta[\(b\)]furan framework by combining isatin-derived aldehydes 4.45 with two equivalents of 1,3-dicarbonyl compounds 4.46 (Scheme 4.9).
Scheme 4.9. Proposed ABB’ three-component cascade process for the construction of spirooxindoles

Initial Knoevenagel condensation can be achieved under basic conditions to generate the diene intermediate A. Subsequent regioselective Michael addition, directed by the R³ and R⁴ substituents, can also be effected. Successive oxa-Michael and intramolecular aldol reaction would deliver the expected spirooxindoles 4.47 containing five consecutive asymmetric carbons including a spiro and tetrasubstituted carbons. Though the proposed route is viable to achieve, due to the presence of several asymmetric carbons, controlling the diastereoselectivity would be challenging.

4.2.2. Synthesis of (E)-2-(2-Oxindolin-3-ylidene)acetaldehydes 4.45

We commenced our investigation by preparing suitable precursors to execute the proposed cascade process. As illustrated in Scheme 4.10, N-protection of isatins 4.48 were achieved under standard experimental conditions.²⁶ Isatins 4.48 were treated with benzyl bromide or methyl iodide or allyl bromide in the presence of potassium carbonate in DMF to obtain the corresponding N-benzyl, N-methyl and N-allyl derivatives 4.49 in good yields.
Next, $N$-protected isatin derivatives 4.49 were transformed into the corresponding $(E)$-2-(2-oxoindolin-3-ylidene)acetaldehydes 4.45 in good yields involving a one-pot two step reaction sequence (Scheme 4.11).$^{25b}$ Compounds 4.49 were treated with five equivalents of acetaldehydes in the presence of catalytic amount of DBU in THF at $-25^\circ$C for 15 h to afford the intermediate aldol products A. Subsequent dehydration of compounds A was achieved in one-pot by treating the crude reaction mixture with AcOH/water and few drops of conc. H$_2$SO$_4$ under reflux for a period of 30 minutes to obtain aldehydes 4.45 in good yields.
4.2.3. Optimization of Reaction Conditions

Initially, the ABB' three-component reaction of (E)-2-(1-benzyl-2-oxoindolin-3-ylidene)acetaldehyde 4.45a and two equivalents of ethyl acetoacetate 4.46a was employed as a model reaction to optimize the reaction conditions (Table 4.1). Encouragingly, the proposed cascade reaction proceeded in the presence of 10 mol% of piperidine in ethanol to afford the product 4.47a in 38% yield as a single diastereomer at 25 °C in 90 minutes (entry 1). As illustrated in entries 2-4, gradual increase in the reaction temperature improved the product yield. At 80 °C, a maximum yield of 73% was observed within 45 minutes.
Table 4.1. Optimization of reaction conditions for the ABB’ three-component synthesis of spirooxindoles

![Diagram of reaction](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (10 mol%)</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>Time (min)</th>
<th>Yield of 4.47a (%)</th>
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<tr>
<td>1</td>
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<td>EtOH</td>
<td>25</td>
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<td>48&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reaction conditions: Unless otherwise noted, all reactions were carried out with 4.45a (0.5 mmol, 1.0 equiv), 4.46a (1.0 mmol, 2 equiv) and base (10 mol%) in 3 mL of solvent at 80 °C. <sup>b</sup> Isolated yield. <sup>c</sup> Optimized reaction condition. <sup>d</sup> No product formation was observed and compound 4.45a was decomposed. <sup>e</sup> Mixture of diastereomers was observed in the crude ¹H NMR spectrum.

Further increase of reaction time did not improve the yields as the aldehyde 4.45a disappeared in the reaction mixture. With an aim to achieve better yield, we carried out the optimization in various common organic solvents including MeCN, DCE, DCM, THF, Toluene and Et₂O in the presence of piperidine at elevated temperature (entries 5-10). Although all the tested solvents furnished the product...
4.47a in a range of 24-65%, only MeCN, DCE and THF delivered moderate yields. The green reaction medium, water failed to yield the product and decomposition of the starting material was observed (entry 11).

Subsequently, we screened organic bases pyrrolidine and morpholine in ethanol, MeCN and THF. As shown in entries 12-18, pyrrolidine furnished the product in 62-67% yield and morpholine delivered relatively lower yield (47-55%). Both the tested bases failed to give the product in water medium (entries 15 and 19). Finally, we tested pyridine and triethylamine bases in order to improve the yield. But, pyridine completely failed to provide the product and triethylamine delivered the desired products in 40% yield (entries 20 and 21). Surprisingly, a mixture of diastereomers was obtained in the presence of 10 mol% of L-proline and 48% of the major diastereomer was separated and characterized (entry 22). Thus we fixed the entry 4 (10 mol % of piperidine, ethanol, 80 °C) as the optimized reaction conditions for further experiments.

4.2.4. ABB' Three-Component Synthesis of Spirooxindoles: Scope and Limitations

With the optimal reaction conditions established, we next investigated the scope and limitations of the ABB' three-component synthesis of spirooxindoles 4.47 and the results are summarized in Scheme 4.12. A set of (E)-2-(1-benzyl-2-oxoindolin-3-ylidene)acetaldehydes 4.45a-f were treated with a variety of 1,3-dicarbonyl compounds 4.46 in the presence of catalytic amount of piperidine in ethanol to synthesize the corresponding spirooxindoles 4.47.
All reactions were carried out with \( 4.45 \) (0.5 mmol, 1.0 equiv), \( 4.46 \) (1.0 mmol, 2.0 equiv) and base (10 mol\%) in 3 mL of solvent at 80 °C.

**Scheme 4.12.** Scope and limitations of the synthesis of spirooxindoles 4.47

In the aldehyde component, compounds with \( N \)-benzyl (4.47a-d, f-j, n, o), \( N \)-methyl (4.47k-m) and \( N \)-allyl (4.47e) derivatives were successfully employed to access the spirooxindoles in good yields. In addition, aldehydes 4.45 bearing both electron-withdrawing groups including chloro (4.47i, j), bromo (4.47f-h) substituents and releasing group di-Me (4.47n, o) were also successfully utilized.
The scope of the methodology was successfully extended to \( \beta \)-ketoesters such as methyl (4.47b, g, j, l, o), ethyl (4.47a, e, f, i, k, n) and \( t \)-butyl (4.47c, h, m) acetoacetates. Ethyl 3-oxo-3-phenylpropanoate (\( R^3 = \text{Ph} \)) was also successfully employed to obtain the corresponding product in 69% yield (4.47d). As summarized in Scheme 4.12, in all the cases a range of 60-78% yield was obtained. However, 1,3-diketones including acetylacetone failed to give the corresponding product under optimized conditions.

4.2.5. Stereochemistry of the Spirooxindoles 4.47

The stereochemistry of the synthesized spirooxindoles 4.47 was established from single crystal X-ray data of a representative compound 4.47a (Figure 4.2). The two hydrogens of dihydrofuran ring were cis to each other and the methyl and ester functionalities of the cyclopentane ring were also cis to each other.

![Figure 4.2. ORTEP diagram of compound 4.47a](image)
4.2.6. Proposed Mechanism for the ABB' Three-component Synthesis of Spirooxindoles

The proposed mechanism for the diastereoselective three-component reaction is depicted in Scheme 4.13. Initial base-catalyzed Knoevenagel condensation between aldehyde 4.45 with the first equivalent of 1,3-dicarbonyl compound 4.46 furnishes intermediate A, which subsequently undergoes regioselective Michael addition with second equivalent of compound 4.46 to deliver species C. Intramolecular oxa-Michael addition of intermediate C involving 5-exo-trig cyclization in the Re face of the enone moiety generates species D by fixing the cis stereochemistry of the dihydrofuran ring.

**Scheme 4.13. Proposed mechanism for the three-component synthesis of spirooxindoles**

Final intramolecular aldol-type reaction (5-exo-trig cyclization) again in the Re face affords the target compound 4.47 diastereoselectively. The Re face attack is
presumably stabilized by the hydroxyl group with the adjacent COR\textsuperscript{4} group \textit{via} hydrogen bonding in the transition state to deliver the product with \textit{cis} relationship between the hydroxyl and COR\textsuperscript{4} groups.

4.3. Conclusions

In conclusion, we have developed a novel synthesis of spirooxindoles fused with tetrahydro-4\textit{H}-cyclopenta\textit{b}furan framework starting from isatin-derived aldehydes and two equivalents of 1,3-dicarbonyl compounds involving a base-catalyzed ABB' three-component domino process. This new reaction is highly diastereoselective affording a single diastereomer of spirooxindoles with five consecutive asymmetric carbons including a spiro and tetrasubstituted carbon centers. In addition, this waste-free (-2H\textsubscript{2}O) reaction shows high atom- and step economy by creating four new bonds including three C–C and one C–O bonds and two rings (one carbo- and one heterocycle) in a single operation. The mechanism of this three-component domino process involved sequential Knoevenagel condensation-Michael addition-\textit{oxa}-Michael addition-Intramolecular aldol reactions.

4.4. Experimental Section

4.4.1. General Information

For general information please refer Section 2.4.1 in Chapter 2.

4.4.2. Synthesis of \textit{N}-Protected Isatins 4.49\textsuperscript{26}
To a stirred solution of isatin 4.48 (30 mmol) in DMF (90 mL), was added K$_2$CO$_3$ (90 mmol). After 10 minutes stirring at room temperature, benzyl bromide or methyl iodide or allyl bromide (39 mmol) was added dropwise and stirring was continued for 10 h. After completion of the reaction, water was added and the precipitated product 4.49 was filtered as red solid washed with water and dried.

1-Benzylindoline-2,3-dione 4.49a:

![4.49a]

Appearance: Red solid; Yield: 91% (6.48 g); mp: 134-136 °C.

(Lit. 135 °C)$^{27}$

1-Benzyl-5-bromoindoline-2,3-dione 4.49b:

![4.49b]

Appearance: Red solid; Yield: 87% (8.25 g); mp: 145-147 °C.

(Lit. 147-148 °C)$^{28}$

1-Benzyl-5-chloroindoline-2,3-dione 4.49c:

![4.49c]

Appearance: Red solid; Yield: 89% (7.25 g); mp: 133-134 °C.

(Lit. 134 °C)$^{29}$

1-Benzyl-4,6-dimethylindoline-2,3-dione 4.49d:

![4.49d]

Appearance: Red solid; Yield: 79% (6.28 g); mp: 172-174 °C.

1-Methylindoline-2,3-dione 4.49e:

![4.49e]

Appearance: Red solid; Yield: 83% (4.01 g); mp: 135-137 °C.

(Lit. 136 °C)$^{27}$
1-Allylindoline-2,3-dione 4.49f:

Appearance: Red solid; Yield: 90% (5.05 g); mp: 89-90 °C. (Lit. 89-90 °C)\(^{30}\)

4.4.3. Synthesis of (E)-2-(2-Oxindolin-3-ylidene)acetaldehydes 4.45\(^{25b}\)

\[
\begin{array}{c}
\text{R}^1 \\
\text{N} \\
\text{O} \\
\text{O} \\
\text{R}^2 \\
\text{N} \\
\text{O} \\
\text{O} \\
\text{R}^1
\end{array}
\text{4.49} \quad \xrightarrow{\text{CH}_2\text{CHO (5 equiv)}} \quad \text{DBU (10 mol\%)} \quad \text{THF, -25 °C} \quad 15 \text{ h}
\]

\[
\begin{array}{c}
\text{R}^2 \\
\text{N} \\
\text{O} \\
\text{O} \\
\text{R}^1 \\
\text{HO} \quad \text{CHO}
\end{array}
\quad \xrightarrow{\text{AcOH/H}_2\text{O (3:1)}} \quad \text{H}_2\text{SO}_4 \quad \text{Reflux, 30 min}
\]

\[
\begin{array}{c}
\text{R}^2 \\
\text{N} \\
\text{O} \\
\text{O} \\
\text{R}^1
\end{array}
\text{4.45a-f}
\]

*N-Protected isatin 4.49* (10 mmol) was dissolved in THF (20 mL) and DBU (10 mol%) was added under nitrogen atmosphere. To this solution, acetaldehyde (50 mmol) was added and the reaction mixture was kept at -25 °C to 15 h. After completion of the reaction, temperature was raised to room temperature and 3:1 mixture of AcOH/H\(_2\)O (10 mL) and few drops of conc. H\(_2\)SO\(_4\) were added and the mixture was refluxed for 30 minutes. The reaction mixture was diluted with water and extracted with dichloromethane, washed with water followed by brine. The organic layer was dried over anhydrous Na\(_2\)SO\(_4\) and concentrated under reduced pressure. The crude product was purified by silica column chromatography using petroleum ether–ethyl acetate mixture as eluent (90:10 v/v).
**(E)-2-(1-Benzyl-2-oxoindolin-3-ylidene)acetaldehyde 4.45a:**

Appearance: Red solid; Yield: 71% (1.87 g); mp: 134-135 °C. (Lit. 135-137 °C)\(^{25c}\)

\[^1^H\] NMR (300 MHz, CDCl\(_3\)): \(\delta\) 4.86 (s, 2H), 6.67-6.69 (m, 2H), 6.97 (t, \(J = 7.8\) Hz, 1H), 7.19-7.40 (m, 6H), 7.20 (d, \(J = 7.5\) Hz, 1H), 11.07 (d, \(J = 7.5\) Hz, 1H).

**(E)-2-(1-Benzyl-5-bromo-2-oxoindolin-3-ylidene)acetaldehyde 4.45b:**

Appearance: Red solid; Yield: 83% (2.84 g); mp: 169-170 °C. (Lit. 169-171 °C)\(^{25c}\)

**(E)-2-(1-Benzyl-5-chloro-2-oxoindolin-3-ylidene)acetaldehyde 4.45c:**

Appearance: Red solid; Yield: 65% (1.93 g); mp: 136-138 °C. (Lit. 137-139 °C)\(^{25c}\)

**(E)-2-(1-Benzyl-4,6-dimethyl-2-oxoindolin-3-ylidene)acetaldehyde 4.45d:**

Appearance: Red solid; Yield: 59% (1.75 g); mp: 135-137 °C.

**(E)-2-(1-Methyl-2-oxoindolin-3-ylidene)acetaldehyde 4.45e:**

Appearance: Red solid; Yield: 67% (1.25 g); mp: 130-131 °C. (Lit. 131-133 °C)\(^{25c}\)
(Z)-2-(1-Allyl-2-oxoindolin-3-ylidene)acetaldehyde 4.45f:

Appearance: Red solid; Yield: 57% (1.21 g); mp: 91-92 °C. (Lit. 92-94 °C)\textsuperscript{25c}

4.4.4. General Procedure for the Synthesis of Spirooxindoles 4.47

To a stirred solution of α,β-unsaturated aldehyde 4.45 (0.5 mmol) in EtOH (3 mL) was added 1,3-dicarbonyl compound 4.46 (1.0 mmol) followed by piperidine (10 mol%). The resulting mixture was allowed to stir at 80 °C for 45 min. After completion of the reaction, as indicated by TLC, the reaction mixture was diluted with dichloromethane and washed with water followed by brine. The organic layer was dried over anhydrous Na\textsubscript{2}SO\textsubscript{4} and concentrated under reduced pressure. The crude product was purified by silica column chromatography using petroleum ether–ethyl acetate mixture as eluent (93:7 v/v).

4.4.5. Characterization Data of Compounds 4.47

(±) Diethyl 1'-benzyl-5-hydroxy-2,5-dimethyl-2'-oxo-3a,4,5,6a-tetrahydrospiro[cyclopenta[b]furan-6,3'-indoline]-3,4-dicarboxylate 4.47a:

Appearance: Off-white solid; Yield: 73% (184 mg); mp: 138-140 °C.

IR (neat): 3438.8, 3060.9, 2981.1, 2930.2, 2903.0, 1702.0,
1H NMR (300 MHz, CDCl₃): δ 1.04 (s, 3H), 1.25 (t, J = 7.2 Hz, 3H), 1.32 (t, J = 7.2 Hz, 3H), 2.18 (d, J = 1.2 Hz, 3H), 3.67 (brs, 1H), 4.06 (d, J = 8.7 Hz, 1H), 4.14-4.32 (m, 5H), 4.76 (d, J = 15.9 Hz, 1H), 5.01 (d, J = 15.9 Hz, 1H), 5.47 (d, J = 10.8 Hz, 1H), 6.73 (d, J = 7.8 Hz, 1H), 7.06 (td, J = 7.8, 0.9 Hz, 1H), 7.21-7.30 (m, 6H), 7.65 (d, J = 7.2 Hz, 1H).

13C NMR (75 MHz, CDCl₃): δ 14.1, 14.3, 14.4, 21.4, 43.6, 49.2, 58.6, 50.5, 61.2, 68.4, 84.3, 92.3, 105.6, 108.7, 122.8, 126.6, 127.1, 127.1, 127.6, 128.7, 128.9, 135.7, 143.4, 165.4, 168.5, 173.5, 174.5.

Anal Calcd for C₂₉H₃₁NO₇: C, 68.90; H, 6.18; N, 2.77. Found: C, 68.58; H, 6.05; N, 2.98.

(±) Dimethyl 1'-benzyl-5-hydroxy-2,5-dimethyl-2'-oxo-3a,4,5,6a-tetrahydrospiro[cyclopenta[b]furan-6,3'-indoline]-3,4-dicarboxylate 4.47b:

Appearance: Off-white solid; Yield: 70% (163 mg); mp: 174-176 °C.

IR (neat): 3436.9, 2976.6, 2949.8, 2851.2, 1688.1, 1646.1, 1610.2, 1488.2, 1435.5, 1358.8, 1250.9, 1176.0, 1093.3 cm⁻¹.

1H NMR (300 MHz, CDCl₃): δ 1.02 (s, 3H), 2.12 (d, J = 1.2 Hz, 3H), 3.68 (s, 3H), 3.76 (brs, 1H), 3.83 (s, 3H), 4.07 (d, J = 9.0 Hz, 1H), 4.25 (dd J =10.5, 9.0 Hz, 1H), 4.76 (d, J = 15.9 Hz, 1H), 5.01 (d, J = 15.9 Hz, 1H), 5.48 (d, J = 10.5 Hz, 1H), 6.73 (d, J = 7.8 Hz, 1H), 7.07 (td, J = 7.5, 0.9 Hz, 1H), 7.20-7.33 (m, 6H), 7.66 (d, J = 7.2 Hz, 1H).

13C NMR (75 MHz, CDCl₃): δ 14.0, 21.4, 43.7, 40.8, 50.8, 52.2, 58.4, 68.3, 84.2, 92.4, 105.2, 108.7, 122.9, 126.7, 127.0, 127.2, 128.6, 128.1, 128.9, 135.7, 143.4, 165.7, 168.9, 173.5, 175.3.
Anal Calcd for C_{27}H_{27}NO_{7}: C, 67.91; H, 5.70; N, 2.93. Found: C, 67.81; H, 5.80; N, 3.18.

(+)-**Di-tert-buty**l 1'-benzyl-5-hydroxy-2,5-dimethyl-2'-oxo-3a,4,5,6a-tetrahydrospiro[cyclopenta[b]furan-6,3'-indoline]-3,4-dicarboxylate 4.47c:

Appearance: Off-white solid; Yield: 68% (191 mg); mp: 91-93 °C.

**IR** (neat): 3427.8, 2975.7, 2929.4, 1680.6, 1646.6, 1609.6, 1485.9, 1378.7, 1363.2, 1252.6, 1146.3, 1090.0 cm\(^{-1}\).

**\(^1\)H NMR** (300 MHz, CDCl\(_3\)): \(\delta\) 1.02 (s, 3H), 1.50 (s, 9H), 1.53 (s, 9H), 2.04 (d, \(J = 1.2\) Hz, 3H), 3.88 (d, \(J = 9.0\) Hz, 1H), 4.18 (dd, \(J = 10.5, 9.0\) Hz, 1H), 4.35 (s, 1H), 4.77 (d, \(J = 15.9\) Hz, 1H), 5.00 (d, \(J = 15.9\) Hz, 1H), 5.38 (d, \(J = 10.5\) Hz, 1H), 6.71 (d, \(J = 7.8\) Hz, 1H), 7.06 (td, \(J = 7.5, 0.9\) Hz, 1H), 7.21 (td, \(J = 7.8, 1.2\) Hz, 1H), 7.24-7.33 (m, 5H), 7.68 (d, \(J = 7.5\) Hz, 1H).

**\(^{13}\)C NMR** (75 MHz, CDCl\(_3\)): \(\delta\) 14.4, 21.3, 28.1, 28.4, 43.6, 50.5, 59.0, 68.4, 79.8, 81.9, 84.3, 92.0, 107.9, 108.5, 122.8, 126.9, 127.1, 127.5, 127.5, 128.6, 128.7, 135.8, 143.4, 164.6, 165.2, 173.8, 174.6.

Anal Calcd for C\(_{33}\)H\(_{39}\)NO\(_{7}\): C, 70.57; H, 7.00; N, 2.49. Found: C, 70.45; H, 7.01; N, 2.59.

(+)-**Diethyl** 1'-benzyl-5-hydroxy-2'-oxo-2,5-diphenyl-3a,4,5,6a-tetrahydrospiro[cyclopenta[b]furan-6,3'-indoline]-3,4-dicarboxylate 4.47d:

Appearance: Off-white solid; Yield: 69% (217 mg); mp: 216-218 °C.

**IR** (neat): 3422.1, 3058.6, 2978.7, 2929.3, 1702.7, 1680.7, 1608.4, 1490.2, 1445.0, 1346.8, 1248.2, 1178.8, 1093.8 cm\(^{-1}\).
$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 1.12 (t, $J = 7.2$ Hz, 3H), 1.18 (t, $J = 6.9$ Hz, 3H), 4.02-4.12 (m, 2H), 4.16-4.27 (m, 2H), 4.39 (d, $J = 15.9$ Hz, 1H), 4.58 (dd, $J = 10.8, 9.0$ Hz, 1H), 4.68 (d, $J = 15.9$ Hz, 1H), 4.72 (s, 1H), 5.14 (d, $J = 8.7$ Hz, 1H), 5.78 (d, $J = 10.8$ Hz, 1H), 6.35-6.37 (m, 1H), 6.48 (d, $J = 7.2$ Hz, 2H), 6.98 (t, $J = 7.2$ Hz, 2H), 7.06-7.16 (m, 5H), 7.20 (tt, $J = 7.2, 1.2$ Hz, 1H), 7.27-7.42 (m, 5H), 7.65 (dd, $J = 8.4, 1.8$ Hz, 2H), 7.93-7.94 (m, 1H).

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 13.9, 14.2, 43.2, 51.3, 56.2, 59.8, 61.2, 69.9, 86.6, 92.1, 106.3, 108.6, 122.5, 126.5, 126.7, 126.8, 126.9, 127.0, 127.5, 127.6, 128.1, 128.5, 128.8, 129.4, 130.1, 130.1, 133.2, 137.9, 143.2, 164.6, 166.6, 172.5, 175.1.

Anal Calcd for C$_{39}$H$_{35}$NO$_7$: C, 74.39; H, 5.60; N, 2.22. Found: C, 74.05; H, 5.63; N, 2.33.

(±) Diethyl 1'-allyl-5-hydroxy-2,5-dimethyl-2'-oxo-3a,4,5,6a-tetrahydrospiro[cyclopenta[b]furan-6,3'-indoline]-3,4-dicarboxylate 4.47e:

Appearance: Off-white solid; Yield: 69% (157 mg); mp: 187-189 °C.

IR (neat): 3417.1, 3109.5, 2974.0, 2928.3, 1732.3, 1679.8, 1642.5, 1609.4, 1467.3, 1371.6, 1331.0, 1245.1, 1151.5, 1088.3 cm$^{-1}$.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 0.94 (s, 3H), 1.18 (t, $J = 7.2$ Hz, 3H), 1.25 (t, $J = 7.2$ Hz, 3H), 2.04 (d, $J = 1.2$ Hz, 3H), 3.56 (s, 1H), 3.94 (d, $J = 8.7$ Hz, 1H), 4.02-4.34 (m, 7H), 5.09-5.15 (m, 2H), 5.37 (d, $J = 10.8$ Hz, 1H), 5.67-5.79 (s, 1H), 6.74 (d, $J = 7.8$ Hz, 1H), 7.03 (td, $J = 7.5, 0.9$ Hz, 1H), 7.23 (td, $J = 7.8, 1.2$ Hz, 1H), 7.58 (dd, $J = 7.5, 0.9$ Hz, 1H).
1^3C NMR (75 MHz, CDCl₃): δ 14.1, 14.3, 14.4, 21.3, 42.0, 49.3, 58.3, 59.5, 61.1, 68.4, 84.2, 92.1, 105.5, 108.5, 117.1, 122.7, 126.5, 127.0, 128.8, 130.9, 143.5, 165.4, 168.5, 173.1, 174.4.

Anal Calcd for C₂₅H₂₉NO₇: C, 65.92; H, 6.42; N, 3.08. Found: C, 65.68; H, 6.24; N, 3.17.

(±) Diethyl 1'-benzyl-5'-bromo-5-hydroxy-2,5-dimethyl-2'-oxo-3a,4,5,6a-tetrahydrospiro[cyclopenta[b]furan-6,3'-indoline]-3,4-dicarboxylate 4.47f:

Appearance: Off-white solid; Yield: 77% (225 mg); 115-117 °C.

IR (neat): 3458.0, 2975.6, 2928.9, 1733.3, 1703.6, 1678.0, 1634.9, 1606.8, 1479.7, 1375.22, 1325.5, 1246.3, 1146.3, 1089.0 cm⁻¹.

1^H NMR (300 MHz, CDCl₃): δ 0.97 (s, 3H), 1.16 (t, J = 7.2 Hz, 3H), 1.26 (t, J = 7.2 Hz, 3H), 2.04 (d, J = 1.2 Hz, 3H), 3.96 (d, J = 8.5 Hz, 1H), 4.02-4.35 (m, 6H), 4.65 (d, J = 15.9 Hz, 1H), 4.94 (d, J = 15.9 Hz, 1H), 5.36 (d, J = 10.5 Hz, 1H), 6.51 (d, J = 8.4 Hz, 1H), 7.16-7.29 (m, 6H), 7.75 (d, J = 1.8 Hz, 1H).

1^3C NMR (75 MHz, CDCl₃): δ 14.1, 14.3, 14.4, 21.3, 43.7, 49.6, 58.6, 59.6, 61.3, 68.5, 84.3, 92.3, 105.6, 110.1, 115.6, 127.1, 127.5, 128.8, 129.2, 130.0, 131.6, 135.2, 142.4, 165.3, 168.4, 173.0, 174.5.

Anal Calcd for C₂₉H₃₉BrNO₇: C, 59.60; H, 5.17; N, 2.40 Found: C, 59.43; H, 5.28; N, 2.67.
(±) Dimethyl 1'-benzyl-5'-bromo-5-hydroxy-2,5-dimethyl-2'-oxo-3a,4,5,6a-tetrahydrospiro[cyclopenta[b]furan-6,3'-indoline]-3,4-dicarboxylate 4.47g:

Appearance: Off-white solid; Yield: 75% (209 mg); mp: 213-215 °C.

IR (neat): 3444.6, 2949.8, 2931.4, 2851.8, 1699.9, 1682.4, 1644.2, 1606.0, 1481.6, 1438.0, 1339.3, 1181.4, 1091.1 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ 1.02 (s, 3H), 2.12 (d, J = 1.2 Hz, 3H), 3.68 (s, 3H), 3.84 (s, 3H), 3.91 (s, 1H), 4.04 (d, J = 8.7 Hz, 1H), 4.22 (dd, J = 10.5, 8.7 Hz, 1H), 4.72 (d, J = 15.9 Hz, 1H), 5.01 (d, J = 15.9 Hz, 1H), 5.44 (d, J = 10.5 Hz, 1H), 6.58 (d, J = 8.4 Hz, 1H), 7.23-7.36 (m, 5H), 7.34 (dd, J = 8.4, 2.1 Hz, 1H), 7.83 (d, J = 2.1 Hz, 1H).

¹³C NMR (75 MHz, CDCl₃): δ 14.0, 21.3, 43.7, 50.0, 50.8, 52.3, 58.4, 68.3, 84.3, 92.4, 105.3, 110.1, 115.6, 127.0, 127.8, 128.8, 129.1, 130.0, 131.7, 135.2, 142.4, 165.6, 168.8, 172.9, 175.3.

Anal Calcd for C₂₇H₂₆BrNO₇: C, 58.28; H, 4.71; N, 2.52. Found: C, 58.06; H, 4.89; N, 2.92.

(±) Di-tert-butyl 1'-benzyl-5'-bromo-5-hydroxy-2,5-dimethyl-2'-oxo-3a,4,5,6a-tetrahydrospiro[cyclopenta[b]furan-6,3'-indoline]-3,4-dicarboxylate 4.47h:

Appearance: Off-white solid; liquid; Yield: 71% (227 mg); mp: 95-97 °C.

IR (neat): 3410.9, 2963.4, 2929.3, 1705.5, 1685.1, 1640.1, 1605.1, 1480.2, 1452.6, 1364.3, 1337.4, 1252.1, 1145.6, 1091.0 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ 0.95 (s, 3H), 1.43 (s, 9H), 1.46 (s, 9H), 1.97 (d, J = 1.2 Hz, 3H), 3.78 (d, J = 9.0 Hz, 1H), 4.09 (dd, J = 10.5, 9.0
Hz, 1H), 4.37 (s, 1H), 4.67 (d, J = 15.6 Hz, 1H), 4.92 (d, J = 15.6 Hz, 1H), 5.27 (d, J = 10.5 Hz, 1H), 6.50 (d, J = 8.1 Hz, 1H), 7.17-7.27 (m, 6H), 7.76 (d, J = 2.1 Hz, 1H).

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 1.04 (s, 3H), 1.26 (t, J = 7.2 Hz, 3H), 1.33 (t, J = 7.2 Hz, 3H), 2.12 (d, J = 1.5 Hz, 3H), 3.81 (s, 1H), 4.04 (d, J = 8.7 Hz, 1H), 4.09-4.38 (m, 5H), 4.73 (d, J = 15.9 Hz, 1H), 5.01 (d, J = 15.9 Hz, 1H), 5.43 (d, J = 10.5 Hz, 1H), 6.62 (d, J = 8.1 Hz, 1H), 7.20 (dd, J = 8.1, 2.4 Hz, 1H), 7.27-7.33 (m, 5H), 7.68 (d, J = 2.1 Hz, 1H).

$^1$C NMR (75 MHz, CDCl$_3$): $\delta$ 14.1, 14.3, 14.4, 21.3, 43.7, 49.6, 58.6, 59.6, 61.30, 68.5, 84.3, 92.3, 105.6, 109.6, 127.1, 127.3, 127.7, 128.2, 128.7, 128.8, 128.9, 135.2, 141.9, 165.3, 168.4, 173.1, 174.5.

Anal Calcd for C$_{33}$H$_{38}$BrNO$_7$: C, 61.88; H, 5.98; N, 2.19. Found: C, 61.62; H, 5.79; N, 3.54.

(±) Diethyl 1'-benzyl-5'-chloro-5-hydroxy-2,5-dimethyl-2'-oxo-3a,4,5,6a-tetrahydrospiro[cyclopenta[b]furan-6,3'-indoline]-3,4-dicarboxylate 4.47i:

Appearance: Off-white solid; Yield: 76% (205 mg); mp: 186-188 °C.

IR (neat): 3523.2, 3068.2, 2980.1, 2932.2, 1706.0, 1681.4, 1639.6, 1605.9, 1480.3, 1428.3, 1338.4, 1375.8, 1149.5, 1087.8 cm$^{-1}$.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 1.04 (s, 3H), 1.26 (t, J = 7.2 Hz, 3H), 1.33 (t, J = 7.2 Hz, 3H), 2.12 (d, J = 1.5 Hz, 3H), 3.81 (s, 1H), 4.04 (d, J = 8.7 Hz, 1H), 4.09-4.38 (m, 5H), 4.73 (d, J = 15.9 Hz, 1H), 5.01 (d, J = 15.9 Hz, 1H), 5.43 (d, J = 10.5 Hz, 1H), 6.62 (d, J = 8.1 Hz, 1H), 7.20 (dd, J = 8.1, 2.4 Hz, 1H), 7.27-7.33 (m, 5H), 7.68 (d, J = 2.1 Hz, 1H).

$^1$C NMR (75 MHz, CDCl$_3$): $\delta$ 14.1, 14.3, 14.4, 21.3, 43.7, 49.6, 58.6, 59.6, 61.30, 68.5, 84.3, 92.3, 105.6, 109.6, 127.1, 127.3, 127.7, 128.2, 128.7, 128.8, 128.9, 135.2, 141.9, 165.3, 168.4, 173.1, 174.5.

Anal Calcd for C$_{29}$H$_{30}$ClNO$_7$: C, 64.50; H, 5.60; N, 2.59; Found: C, 64.22; H, 5.56; N, 2.80.
(±) Dimethyl 1'-benzyl-5'-chloro-5-hydroxy-2,5-dimethyl-2'-oxo-3a,4,5,6a-tetrahydrospro[cyclopenta[b]furan-6,3'-indoline]-3,4-dicarboxylate 4.47j:

Appearance: Off-white solid; Yield: 75% (192 mg); mp: 203-205 °C.
IR (neat): 3484.1, 2942.8, 2851.8, 1737.2, 1703.2, 1682.0, 1634.6, 1609.1, 1482.4, 1431.0, 1330.2, 1248.5, 1149.4, 1091.0 cm\(^{-1}\).

\(^1\)H NMR (300 MHz, CDCl\(_3\)): δ 1.02 (s, 3H), 2.12 (d, J = 1.2 Hz, 3H), 3.68 (s, 3H), 3.84 (s, 3H), 3.91 (s, 1H), 4.05 (d, J = 8.7 Hz, 1H), 4.23 (dd, J = 10.5, 8.7 Hz, 1H), 4.72 (d, J = 15.9 Hz, 1H), 5.01 (d, J = 15.9 Hz, 1H), 5.44 (d, J = 10.5 Hz, 1H), 6.62 (d, J = 8.1 Hz, 1H), 7.20 (dd, J = 8.4, 2.1 Hz, 1H), 7.26-7.34 (m, 5H), 7.68 (d, J = 2.1 Hz, 1H).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)): δ* 14.0, 21.3, 43.7, 50.0, 50.8, 52.3, 58.4, 68.4, 84.2, 92.4, 105.3, 109.6, 127.1, 127.3, 127.8, 128.2, 128.8, 135.2, 141.9, 155.6, 168.8, 173.0, 175.3. * One sp\(^2\) carbon is merged with others.
Anal Calcd for C\(_{27}\)H\(_{26}\)ClNO\(_7\): C, 63.34; H, 5.12; N, 2.74. Found: C, 63.19; H, 5.12; N, 2.87.

(±) Diethyl 5-hydroxy-1',2,5-trimethyl-2'-oxo-3a,4,5,6a-tetrahydrospro[cyclopenta[b]furan-6,3'-indoline]-3,4-dicarboxylate 4.47k:

Appearance: Off-white solid; Yield: 78% (167 mg); mp: 141-143 °C.
IR (neat): 3469.3, 3056.7, 2920.6, 2851.7, 1736.8, 1555.8, 1544.1, 1494.5, 1473.0, 1434.8, 1364.1, 1280.9, 1222.6, 1067.2 cm\(^{-1}\).
\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 0.97 (s, 3H), 1.26 (t, \(J = 6.9\) Hz, 3H), 1.31 (t, \(J = 6.9\) Hz, 3H), 2.13 (s, 3H), 3.18 (s, 3H), 3.64 (s, 1H), 3.99 (d, \(J = 8.7\) Hz, 1H), 4.13-4.34 (m, 5H), 5.44 (d, \(J = 10.2\) Hz, 1H), 6.84 (d, \(J = 7.5\) Hz, 1H), 7.11 (t, \(J = 7.2\) Hz, 1H), 7.34 (t, \(J = 7.5\) Hz, 1H), 7.62 (d, \(J = 6.6\) Hz, 1H).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 14.1, 14.2, 14.4, 21.1, 26.1, 49.4, 58.4, 59.5, 61.1, 68.4, 84.2, 91.9, 105.4, 107.8, 122.8, 126.4, 126.9, 128.9, 144.4, 165.4, 168.6, 173.3, 74.5.

Anal Calcd for C\(_{23}\)H\(_{27}\)NO\(_7\): C, 64.32; H, 6.34; N, 3.26. Found: C, 64.02; H, 6.24; N, 3.18.

(±) Dimethyl 5-hydroxy-1’,2,5-trimethyl-2’-oxo-3a,4,5,6a-tetrahydrospiro[cyclopenta[b]furan-6,3’-indoline]-3,4-dicarboxylate 4.471: Appearance: Off-white solid; Yield: 76% (152 mg); mp: 134-136 °C.

IR (neat): 3314.3, 2984.5, 2946.3, 1747.4, 1684.3, 1642.3, 1607.7, 1434.4, 1375.6, 1349.1, 1323.6, 1251.0, 1089.0 cm\(^{-1}\).

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 0.96 (s, 3H), 2.13 (d, \(J = 1.2\) Hz, 3H), 3.18 (s, 3H), 3.68 (s, 3H), 3.74 (s, 1H), 3.82 (s, 3H), 4.00 (d, \(J = 8.7\) Hz, 1H), 4.22 (dd, \(J = 10.8, 8.7\) Hz, 1H), 5.45 (d, \(J = 10.8\) Hz, 1H), 6.84 (d, \(J = 7.8\) Hz, 1H), 7.11 (td, \(J = 7.5, 0.9\) Hz, 1H), 7.34 (td, \(J = 7.5, 1.2\) Hz, 1H), 7.62 (dd, \(J = 7.5, 0.9\) Hz, 1H).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 14.0, 21.1, 26.2, 49.8, 50.7, 52.2, 58.2, 68.2, 84.2, 92.0, 105.1, 107.8, 122.8, 126.4, 126.9, 128.9, 144.3, 165.74, 169.0, 173.2, 175.2.

Anal Calcd for C\(_{21}\)H\(_{23}\)NO\(_7\): C, 62.84; H, 5.78; N, 3.49. Found: C, 62.55; H, 5.74; N, 3.82.
(±) Di-tert-butyl 5-hydroxy-1',2,5-trimethyl-2'-oxo-3a,4,5,6a-tetrahydrospiro[cyclopenta[b]furan-6,3'-indoline]-3,4-dicarboxylate 4.47m:

Appearance: Off-white solid; Yield: 60% (146 mg); mp: 163-165 °C.

IR (neat): 3486.7, 2971.9, 2929.3, 1703.0, 1673.2, 1611.0, 1470.4, 1364.8, 1346.4, 1258.4, 1141.4, 1091.5 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ 0.88 (s, 3H), 1.43 (s, 9H), 1.46 (s, 9H), 1.99 (d, J = 1.2 Hz, 3H), 3.11 (s, 3H), 3.74 (d, J = 9.0 Hz, 1H), 4.09 (dd, J = 10.8, 9.0 Hz, 1H), 4.24 (s, 1H), 5.28 (d, J = 10.8 Hz, 1H), 6.76 (d, J = 7.8 Hz, 1H), 7.03 (td, J = 7.5, 0.9 Hz, 1H), 7.25 (td, J = 7.8, 1.2 Hz, 1H), 7.57 (d, J = 7.5 Hz, 1H).

¹³C NMR (75 MHz, CDCl₃): δ 14.4, 21.0, 26.1, 28.1, 28.4, 50.5, 58.8, 68.3, 79.7, 81.8, 84.3, 91.6, 107.6, 107.8, 122.7, 126.6, 127.3, 128.7, 144.3, 164.7, 165.3, 173.5, 174.6.

Anal Calcd for C₂₇H₃₅NO₇: C, 66.79; H, 7.27; N, 2.88. Found: C, 66.58; H, 7.13; N, 2.98.

(±) Diethyl 1'-benzyl-5-hydroxy-4',6'-dimethyl-2,5-dimethyl-2'-oxo-3a,4,5,6a-tetrahydrospiro[cyclopenta[b]furan-6,3'-indoline]-3,4-dicarboxylate 4.47n:

Appearance: Off-white solid; Yield: 69% (195 mg). mp: 137-139 °C.

IR (neat): 3412.7, 2982.6, 2917.0, 1698.0, 1647.0, 1618.0, 1453.1, 1378.1, 1348.0, 1217.4, 1161.8, 1091.7 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ 0.96 (s, 3H), 1.18 (t, J = 7.2 Hz, 3H), 1.23 (t, J = 7.2 Hz, 3H), 2.06 (d, J = 1.2 Hz, 3H), 2.18 (s, 3H), 2.46 (s, 3H), 3.47 (s, 1H), 3.96 (d, J = 9.0 Hz, 1H), 4.01-4.16 (m, 3H), 4.20-4.32 (m, 2H), 4.72 (d, J = 15.9 Hz, 1H), 4.84 (d,
$J = 15.6$ Hz, 1H), 5.78 (d, $J = 10.8$ Hz, 1H), 6.36 (s, 1H), 6.63 (s, 1H), 7.15-7.25 (m, 5H).

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 14.1, 14.2, 14.4, 21.1, 21.5, 21.9, 43.6, 49.3, 57.8, 59.5, 61.1, 70.4, 86.3, 87.4, 105.3, 107.4, 120.6, 127.1, 127.4, 127.5, 128.7, 135.9, 137.6, 138.6, 144.3, 165.5, 168.7, 174.0, 174.6.

Anal Calcd for C$_{31}$H$_{35}$NO$_9$: C, 65.83; H, 6.24; N, 2.48; Found: C, 65.61; H, 6.55; N, 2.38.

(±) Dimethyl 1'-benzyl-5-hydroxy-4',6'-dimethyl-2,5-dimethyl-2'-oxo-3a,4,5,6a-tetrahydrosphiro[cyclopenta[b]furan-6,3'-indoline]-3,4-dicarboxylate 4.47o:

Appearance: Off-white solid; Yield: 65% (175 mg); mp: 208-201 °C

IR (neat): 3416.8, 2977.6, 2923.1, 1694.2, 1642.5, 1609.5, 1479.6, 1437.3, 1376.0, 1181.6, 1089.1 cm$^{-1}$.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 0.95 (s, 3H), 2.07 (d, $J = 1.2$ Hz, 3H), 2.18 (s, 3H), 2.46 (s, 3H), 3.56 (s, 1H), 3.60 (s, 3H), 3.74 (s, 3H), 3.97 (d, $J = 9.0$ Hz, 1H), 4.21 (dd, $J = 10.8, 9.0$ Hz, 1H), 4.71 (d, $J = 15.9$ Hz, 1H), 4.83 (d, $J = 15.9$ Hz, 1H), 5.80 (d, $J = 10.8$ Hz, 1H), 6.36 (s, 1H), 6.63 (s, 1H), 7.15-7.30 (m, 5H).

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 14.1, 21.1, 21.5, 21.8, 43.6, 49.6, 50.7, 52.2, 57.5, 70.2, 86.3, 87.5, 105.0, 107.4, 120.5, 127.2, 127.3, 127.5, 128.7, 135.8, 137.6, 138.6, 144.3, 165.9, 169.2, 174.0, 175.3.

Anal Calcd for C$_{29}$H$_{31}$NO$_9$: C, 64.80; H, 5.81; N, 2.61. Found: C, 64.41; H, 5.87; N, 2.91.
4.5. References


