REACTION OF ELECTRON-DEFICIENT 3-ACETYL-1-ARYLPENT-2-ENE-1,4-DIONES AS A BUILDING BLOCK OF HETEROCYCLES†

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†Dedicated to Dr. Kazu Kurosawa, Professor Emeritus of Kumamoto University, on his 80th birthday.

Abstract – The BF$_3$-assisted reaction of 3-acetyl-1-arylpent-2-ene-1,4-diones 1a-c with cyclohexanones and piperidin-4-ones 2a-i gave unique 3a,6a-dihydrospiro[furo[2,3-d][1,3]dioxoles 3 in good to high yields. A similar reaction with the 2,3-dihydroquinolin-4(1H)-ones did not occur, but the reaction with 4-hydroxychromenone 5 mainly produced 3-furfuryl-4-hydroxychromenone 6 along with furochromenone 7. The reaction of the electron-deficient pentenedione 1a as a Michael acceptor with indole, pyrrole, furan, and N-methylaniline produced the corresponding 1,4-adducts. Especially, the indole adduct was easily converted by the Paal-Knorr synthesis into the corresponding furanyl-, pyrrolyl-, and thiophenyl-substituted indoles. The reaction details and the structure determination of the products are described.

INTRODUCTION
The synthesis of novel heterocyclic compounds is always a hot topic in organic chemistry because it sometimes can provide enormous opportunities for the discovery of new pharmaceuticals and materials. The cycloaddition reaction is one of the direct and powerful tools for the construction of complex heterocyclic compounds from structurally simple and readily available electron-deficient alkenes as the starting material in a one-step process, and many examples of both ionic and radical reactions have been
found in the literature.\(^2\) In connection with our previous study, we reported the selective transformation of the endoperoxide intermediate\(^1\) obtained by the photosensitized oxygenation of furan I\(^4\) into 3-acetyl-1-phenylpent-2-ene-1,4-dione (Ia) and oxirane II depending on the reaction conditions (Scheme 1).\(^3\) The electron-deficient pentenedione Ia is very attractive as a building block in many reactions.\(^5\) For example, the BF\(_3\)-catalyzed reaction of Ia in the presence of acetylacetone (Hacac) in dry tetrahydrofuran (THF) at rt gave the polyfunctionalized furans III and IV.\(^6\) When the reaction in the absence of Hacac was carried out in wet THF at reflux temperature, bis(furyl)methane V was preferentially produced.\(^7\) A typical Diels-Alder reaction of Ia with cyclopentadiene gave a mixture of the endo/exo VI and bicyclic compound VII.\(^7\) In order to determine the potential of the pentenedione Ia as a building block of heterocyclic compounds, we examined the BF\(_3\)-assisted reaction using cyclic ketones such as cyclohexanones and piperidin-4-ones 2a-i. Surprisingly, the reaction did not produce the furyl-substituted products, but the 3a,6a-dihydrospirofuro[2,3-d][1,3]dioxoles 3. We now report the results of the unique cyclization reaction and also describe the BF\(_3\)-assisted reaction with 4-hydroxychromenone 5. In addition, we describe the Michael addition of Ia with pyrrole, furan, and indole as an electron donor, and also the application using the Paal-Knorr strategy.

**Scheme 1. Some Reactions Using the Pentenedione Ia**
RESULTS AND DISCUSSION

Reaction with Cyclohexanones and Piperidin-4-ones

The pentenedione 1a was easily prepared by the Knoevenagel condensation of phenylglyoxal with Hacac and was not stable in air.\(^{7b}\) When the reaction of 1a with cyclohexanone (3 equiv.) in the presence of BF\(_3\)·Et\(_2\)O (1 equiv.) was carried out in dry THF at room temperature, the spirodioxole 3aa was obtained in 36% yield together with tetrahydrobenzofuran 4aa (14% yield) (Scheme 2 and Table 1, Entry 1). A prolonged reaction time led to a slight increase in 3aa (48% yield) (Entry 2). The use of 4 equivalents of BF\(_3\)·Et\(_2\)O caused the decomposition of 3aa (Entry 4). The best yield of 3aa (58% yield) was realized by the use of 1a (5 equiv.) and BF\(_3\)·Et\(_2\)O (5 equiv.) at 0 °C for 24 h (Entry 3). A similar reaction with 4-tert-butylcyclohexanone (2b) was conducted at room temperature to afford the corresponding spirodioxole 3ab as a 47:53 diastereomixture and tetrahydrobenzofuran 4ab (Entry 5). Interestingly, the reaction at lower than 0 °C led to an increase in the spirodioxole 3ab even though a longer reaction time was required (Entries 6 and 7). The reaction of the 4-chlorophenyl-substituted pent-2-ene-1,4-dione 1b with 2b gave a similar result, but with a much better yield of the corresponding product (Entries 8 and 9). On the other hand, the use of 3-acetyl-1-(4-methoxyphenyl)pent-2-ene-1,4-dione (1c) led to an intractable mixture, and tetrahydrobenzofuran 4cb rather than the spirodioxole 3cb was produced in 47% yield for the reaction at room temperature (Entry 11). The structures of the products 3 and 4 were characterized by spectroscopic methods and elemental analysis. Fortunately, a single crystal of one of the diastereomers 3bb was successfully grown from hexane and subjected to an X-ray crystallographic measurement. We then obtained the exact structure of the spirodioxole 3bb (see experimental section).\(^8\)

![Scheme 2. Reaction of Pentenediones 1a-c with Cyclohexanones 2a,b](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>1/Ar</th>
<th>2/R</th>
<th>1:2:BF(_3)^b</th>
<th>Temp/°C</th>
<th>Time/h</th>
<th>Product Yield/%c</th>
<th>Rec./%d</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a: Ph</td>
<td>2a: H</td>
<td>1:3:1</td>
<td>rt</td>
<td>35</td>
<td>3aa (36)</td>
<td>4aa (14)</td>
</tr>
<tr>
<td>2</td>
<td>1a</td>
<td>2a</td>
<td>1:3:1</td>
<td>rt</td>
<td>45</td>
<td>3aa (48)</td>
<td>4aa (9)</td>
</tr>
</tbody>
</table>
The reaction of 1 (0.5 mmol) with 2a was carried out in dry THF (0.5 mL).

In order to apply the reaction to azacyclic ketones, such as the piperidin-4-ones, we next examined the reaction of pentenedione 1a with 1-methylpiperidin-4-one (2c) (Scheme 3 and Table 2). Although the reaction was carried out in dry THF at room temperature according to the conditions described above, the reaction did not proceed at all (Entry 1). The reaction at reflux temperature afforded the corresponding azaspirodioxole 3ac in a poor yield (Entry 2). When the reaction was carried out in dichloromethane (DCM) at room temperature, the yield of 3ac increased (Entry 3). The reaction was then optimized and a synthetically acceptable yield of 3ac was achieved at 0 °C under neat conditions (Entry 6). Since the viscosity of 2c at -20 °C was much higher than that at 0 °C, a small amount of DCM (0.05 mL) was added to the mixture and the reaction was then conducted at -20 °C to give almost the same result (Entry 7).

Scheme 3. Reaction of Pentenedione 1a with Piperidin-4-ones 2c-i
Table 2. Reaction of Pentenedione 1a with Piperidin-4-ones 2c-i in the Presence of BF₃

<table>
<thead>
<tr>
<th>Entry</th>
<th>2/R</th>
<th>1:2:BF₃</th>
<th>Solvent/mL</th>
<th>Temp/°C</th>
<th>Time/h</th>
<th>Product Yield/%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2c: Me</td>
<td>1:1:1</td>
<td>THF/5</td>
<td>rt</td>
<td>24</td>
<td>no reaction</td>
</tr>
<tr>
<td>2</td>
<td>2e</td>
<td>1:1:3</td>
<td>THF/5</td>
<td>reflux</td>
<td>6</td>
<td>3ac (14)</td>
</tr>
<tr>
<td>3</td>
<td>2e</td>
<td>1:1:1</td>
<td>DCM/5</td>
<td>rt</td>
<td>12</td>
<td>3ac (25)</td>
</tr>
<tr>
<td>4</td>
<td>2e</td>
<td>1:1:5</td>
<td>DCM/5</td>
<td>rt</td>
<td>6</td>
<td>3ac (61)</td>
</tr>
<tr>
<td>5</td>
<td>2e</td>
<td>1:1:5</td>
<td>neat</td>
<td>rt</td>
<td>2.5</td>
<td>3ac (74)</td>
</tr>
<tr>
<td>6</td>
<td>2e</td>
<td>1:1:5</td>
<td>neat</td>
<td>0</td>
<td>2.5</td>
<td>3ac (93)</td>
</tr>
<tr>
<td>7</td>
<td>2e</td>
<td>1:1:5</td>
<td>DCM/0.05</td>
<td>-20</td>
<td>2.5</td>
<td>3ac (94)</td>
</tr>
<tr>
<td>8</td>
<td>2d: Et</td>
<td>1:1:5</td>
<td>neat</td>
<td>0</td>
<td>2.5</td>
<td>3ad (71)</td>
</tr>
<tr>
<td>9</td>
<td>2d</td>
<td>1:1:5</td>
<td>DCM/0.05</td>
<td>-40</td>
<td>3</td>
<td>3ad (88)</td>
</tr>
<tr>
<td>10</td>
<td>2e: Pr</td>
<td>1:1:5</td>
<td>neat</td>
<td>0</td>
<td>2.5</td>
<td>3ae (68)</td>
</tr>
<tr>
<td>11</td>
<td>2e</td>
<td>1:1:5</td>
<td>DCM/0.05</td>
<td>-20</td>
<td>2.5</td>
<td>3ae (77)</td>
</tr>
<tr>
<td>12</td>
<td>2f: Bn</td>
<td>1:1:5</td>
<td>neat</td>
<td>0</td>
<td>2.5</td>
<td>3af (68)</td>
</tr>
<tr>
<td>13</td>
<td>2f</td>
<td>1:1:5</td>
<td>DCM/0.05</td>
<td>-40</td>
<td>4</td>
<td>3af (89)</td>
</tr>
<tr>
<td>14</td>
<td>2g: Ac</td>
<td>1:1:5</td>
<td>neat</td>
<td>0</td>
<td>2.5</td>
<td>3ag (79)</td>
</tr>
<tr>
<td>15</td>
<td>2g</td>
<td>1:1:5</td>
<td>DCM/0.05</td>
<td>-20</td>
<td>2.5</td>
<td>3ag (quant)</td>
</tr>
<tr>
<td>16</td>
<td>2h: Bz</td>
<td>1:1:5</td>
<td>neat</td>
<td>0</td>
<td>2.5</td>
<td>3ah (85)</td>
</tr>
<tr>
<td>17</td>
<td>2h</td>
<td>1:1:5</td>
<td>DCM/0.05</td>
<td>-20</td>
<td>3</td>
<td>3ah (94)</td>
</tr>
<tr>
<td>18</td>
<td>2i: Cbz</td>
<td>1:1:5</td>
<td>neat</td>
<td>0</td>
<td>3</td>
<td>3ai (94)</td>
</tr>
</tbody>
</table>

The reaction of 1a (0.5 mmol) with 2 was carried out in dry solvent or under neat conditions.

<table>
<thead>
<tr>
<th>Solvent/mL</th>
<th>Temp/°C</th>
<th>Time/h</th>
<th>Product Yield/%</th>
</tr>
</thead>
</table>

Molar ratio.

Isolated yield based on 1a used.

A small amount of homocyclization products I and V was isolated.

Having succeeded in the cycloaddition of the pentenedione 1a with the azacyclohexanone 2c, we turned our attention to the reaction with other piperidin-4-ones (Table 2, Entries 8-18). As a result, both the N-alkyl- 2d-f and N-acyl-substituted piperidin-4-ones 2g-i were tolerated during the cycloaddition reaction under neat or low temperature conditions, producing the corresponding azaspirodioxoles 3ad-3ai in high yields. A similar reaction with the 1-methyl- and 1-tosyl-2,3-dihydroquinolin-4(1H)-ones did not occur, but the homocyclization product V of 1a was only produced.

The NMR spectrum of N-acylspirodioxole 3ag in CDCl₃ at room temperature deserves comments. In the ¹H NMR spectrum, two signals appeared at δ 2.13 (s) and 2.11 (s) assigned to the N-acetyl group and most of the signals in the ¹³C NMR spectrum each showed two peaks. When the NMR spectrum was measured in DMSO-d₆ at 80 °C, the N-acetyl group in the ¹H NMR spectrum and the signals that appeared for each of the two peaks in the ¹³C NMR spectrum collapsed into one peak due to existence of the conformational isomer in CDCl₃. Although a similar phenomenon was not observed in other azaspirodioxoles, the methylene peaks of the N-acylspirodioxoles 3ah and 3ai in the ¹³C NMR spectrum
appeared as a weak signal on the NMR time scale, probably depending on the flipping velocity of the azacyclohexane ring.

**Reaction with 4-Hydroxy-2H-chromen-2-one**

With the unique spirodioxole formation in hand, the reaction using 4-hydroxy-2H-chromen-2-one (5) was next investigated. When the reaction was carried out at the molar ratio of 1a:5:BF₃ = 1:3:1 in DCM (1.0 mL) at rt, unfortunately, the corresponding dioxole was not isolated, but furfurylchromenone 6 and furochromenone 7 were obtained together with bis(furyl)methane V as the homocyclization product of 1a (Scheme 4 and Table 3, Entry 1).²⁸ In order to prevent the production of V, the pentenedione 1a was dropwise added to the mixture of 5 and BF₃ at reflux temperature. As a result, the yield of 6 was improved (Entry 2), but bis(furyl)methane V was still produced. We then scrutinized the solvent and reaction temperature, and eventually, the use of chlorobenzene at 130 °C led to the maximum yield of 6 and suppressed the production of V (Entry 6).

![Scheme 4. Reaction of Pentenedione 1a with 4-Hydroxy-2H-chromene-2-one (5)](image)

**Table 3. Reaction of Pentenedione 1a with 4-Hydroxychromenone (5) in the Presence of BF₃**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent/mL</th>
<th>Temperature/°C</th>
<th>Time/min</th>
<th>Product Yield/%⁶</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>DCM/1</td>
<td>rt</td>
<td>70</td>
<td>6 24 7 16</td>
</tr>
<tr>
<td>2⁵</td>
<td>DCM/1</td>
<td>40</td>
<td>50</td>
<td>6 41 7 12</td>
</tr>
<tr>
<td>3</td>
<td>DCE/1</td>
<td>80</td>
<td>20</td>
<td>6 51 7 3</td>
</tr>
<tr>
<td>4</td>
<td>C₆H₅Cl/1</td>
<td>100</td>
<td>10</td>
<td>6 57 7 14</td>
</tr>
<tr>
<td>5</td>
<td>C₆H₅Cl/1</td>
<td>130</td>
<td>5</td>
<td>6 69 7 7</td>
</tr>
<tr>
<td>6</td>
<td>C₆H₅Cl/0.5</td>
<td>130</td>
<td>3</td>
<td>6 77 7 5</td>
</tr>
</tbody>
</table>

⁴ The reaction of 1a (0.3 mmol) with 5 (0.9 mmol) was carried out in the presence of BF₃•OEt₂ (0.3 mmol).

⁵ Isolated yield based on 1a used.

⁶ Bis(3-acetyl-5-phenyl-2-furyl)methane (V) as a homocyclization product of 1a.

⁵ Pentenedione 1a (0.3 mmol) in solvent (0.3 mL) was dropwise added to the mixture of 5 (0.9 mmol) and BF₃•OEt₂ (0.3 mmol) in solvent.
**Proposed Mechanism for the Formation of the Products**

The BF₃-assisted cyclization of pentenediones 1 with cyclic ketones 2 could be similarly understood by the previously reported literature as depicted in Scheme 5.² The production of two diastereomers in the reaction using 4-tert-butylocyclohexanone (2b) would be caused by exclusive occupation of the tert-butyl group at the equatorial position. That is, the carbonyl group of the cyclohexanone equatorial fixed tert-butyl group might be attacked by the pentenedione 1 from the equatorial or axial direction, affording the corresponding diastereomeric dioxoles. In the case of 1c (Ar = 4-MeOC₆H₄) (Table 1, Entries 10 and 11), the production of the spirodioxole 3cb was suppressed because the electron-donating methoxy group might change the electrostatic potential of 1c.

\[
\text{Scheme 5. Proposed Mechanism for the Formation of Dioxoles 3}
\]

\[
\text{Scheme 6. Proposed Mechanism for the Formation of Tetrahydrobenzofurans 4}
\]
On the other hand, the production of the by-products 4 would be explained by an aldol-type condensation briefly shown in Scheme 6. This reaction could not be retarded under all of the conditions. However, the corresponding by-product, such as tetrahydrobenzofuran 4, was not produced during the reaction using the azacyclohexanones 2c-i. The furfurylchromonene 6 would be formed by the reaction of methylenedihydrofuranol A prepared by the enolization of 1a followed by in situ cyclization (Scheme 7). It was considered that the by-product furochromonene 7 would be obtained by a similar reaction sequence as shown in Scheme 6.

**Scheme 7. Plausible Mechanism for the Formation of Furfurylchromonene 6**

**Michael Addition Using Indole, Pyrrole, Furan, and N-Methylaniline**

In order to further study the reactivity of the electron-deficient pentenedione 1a as a Michael acceptor, we next investigated the reaction with indole as an electron-donor (Scheme 8). The reaction was examined in various solvents and the Michael adduct 8 was obtained in all the solvents (see Experimental section). The best yield of 8 (97% yield) was realized in acetonitrile at reflux temperature for 9.5 h. A similar reaction with pyrrole gave the 1,4-adduct 9 in 84% yield.

**Scheme 8. Michael Addition of 1a with Indole, Pyrrole, Furan, and N-Methylaniline**
In addition, the use of a one-half equivalent of pyrrole provided the 2,5-disubstituted adduct in 79% yield (see Experimental section). On the other hand, the reaction with furan did not proceed in acetonitrile, but the corresponding adduct 10 (76% yield) was obtained in acetic acid at room temperature. N-Methylaniline also afforded the 1,4-adduct 11 (75% yield) in boiling acetic acid.

**Conversion into Heterocycle-substituted Indole Derivatives via Paal-Knorr Strategy**

With the 1,4-dicarbonyl-functionalized indole 8 in hand, we finally embarked on the synthesis of the five-membered heterocycle-substituted indoles using the Paal-Knorr strategy (Scheme 9). Since it was reported that the treatment of 1a with indole in the presence of methanesulfonic acid gave the 3-furyl-substituted indole, we initially examined the BF₃-catalyzed reaction of 1a with indole in DCM at reflux temperature. Pleasingly, the reaction finished in only 30 min and the reported product 12 (88% yield) was obtained during the formation of 8. The Michael adduct 8 underwent the typical Paal-Knorr reaction with ammonium acetate to produce the desired pyrrole-substituted indole 13a in quantitative yield without purification. Use of benzylamine and ethanolamine also gave the desired products 13b and 13c in high yields. Similarly, the treatment of 8 with Lawesson's reagent in toluene at 50 °C afforded the thienyl-substituted indole 14 (49% yield) together with 12 (23% yield).

**Scheme 9. Synthesis of Heterocycle-substituted Indole Derivatives**

**CONCLUSION**

We have accomplished the unique synthesis of spirodioxoles and azaspirodioxoles 3 by the cycloaddition of pentenediones 1 with cyclohexanones and piperidin-4-ones 2. The reaction with chromenone 5 did not
give the spirodioxole, but furfurylchromenone 6 along with furochromenone 7. There is no precedent for the synthesis of bicyclo-spirodioxoles 3 except for a similar protecting diol of sugars¹³ and kendomycin analogues which have a cytotoxic property.¹⁴ We also demonstrated the usefulness of pentenedione 1a as a convenient building block in the Michael addition followed by the Paal-Knorr heterocycle synthesis using indole.

EXPERIMENTAL

Measurements. Melting points were taken using a Yanagimoto micromelting point apparatus and are uncorrected. The NMR spectra were recorded using a JNM ECX 500 or AL300 FT-NMR spectrometer at 500 MHz for the ¹H and at 125 MHz for ¹³C, with tetramethylsilane as the internal standard. The chemical shifts are reported as δ values (ppm) and the coupling constants in Hz. The following abbreviations are used for the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; and brs, broad singlet for the ¹H NMR spectrum. The IR spectra were measured in CHCl₃ or KBr using a Shimadzu 8400 FT IR spectrometer and expressed in cm⁻¹. The high-resolution mass spectra and the elemental analyses were performed at the Instrumental Analysis Center, Kumamoto University, Kumamoto, Japan. The X-ray analysis was performed by a Rigaku RAXIS RAPID imaging plate area detector with graphite monochromated Mo-Kα radiation.

Materials. The 3-acetyl-1-aryl-2-pentene-1,4-diones 1a-c and piperidin-4-ones 2e, 2h, 2i were prepared according to the literature method.¹⁴ Cyclohexanone (2a), 4-tert-butylocyclohexanone (2b), 1-methylpiperidin-4-one (2c), 1-ethylpiperidin-4-one (2d), 1-benzylpiperidin-4-one (2f), 4-hydroxy-2H-chromen-4-one (5), indole, pyrrole, furan, and N-methylaniline were purchased from Tokyo Kasei Co., Ltd., and 1-acetylpiperidin-4-one (2g) and the boron trifluoride diethyl ether complex were from Wako Pure Chemical Ind., Ltd., and used as received. Flash column chromatography was performed on silica gel 60N (40-50 mm), which was purchased from Kanto Chemical Co., Inc., and preparative thin layer chromatography (TLC) on Wakogel B-5F from Wako Pure Chemical Ind., Ltd. The solvents were commercially available first grade and used as received.

Reaction of 1 with Cyclohexanones 2a and 2b in the Presence of BF₃·OEt₂. A solution of pentenedione 1a (216.8 mg, 1.0 mmol) and cyclohexanone (2a) (490.6 mg, 2.5 mmol) in dry THF (1.0 mL) was cooled at 0°C under argon, and BF₃·Et₂O (254 µL, 2.0 mmol) was slowly added using a syringe. After the reaction was completed, water (10 mL), brine (10 mL), and a saturated aqueous solution of NaHCO₃ (30 mL) were then added, and the aqueous mixture was extracted with CHCl₃ (3×20 mL). The combined extracts were washed with water (20 mL), dried over anhydrous sodium sulfate, and then concentrated to dryness. The residue was purified by column chromatography on silica gel eluting with
EtOAc/hexane (1:5 v/v), giving the desired spirodioxole 3aa (183 mg, 58%) and tetrahydrobenzofuran 4aa (25.6 mg, 9%) (Table 1, Entry 3).

6'-Acetyl-5'-methyl-3a'-phenyl-3a',6a'-dihydrospiro[cyclohexane-1,2'-furo[2,3-d][1,3]dioxole] (3aa): Reaction time, 24 h; yield 58%; pale yellow oil; \( R_f = 0.44 \) (EtOAc-hexane 1:4 v/v); IR (CHCl\(_3\)) \( \nu = 2939 \) (PhH), 1672 (C=O); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta = 7.46-7.38 \) (5H, m, arom. H), 5.31 (1H, s, H-6a'), 2.40 (3H, s, Me), 2.29 (3H, s, Ac), 1.86-1.45 (8H, m, 4×CH\(_2\)), 1.44 (2H, quin, \( J = 4.5 \) Hz, CH\(_2\)); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta = 194.7 \) (C=O), 171.1 (C-5'), 137.6 (arom. C), 129.2 (arom. CH), 128.5 (2C) (arom. CH), 125.0 (2C) (arom. CH), 114.9 (C-3a'), 114.8 (C-6'), 114.2 (C-2'), 88.7 (C-6a'), 37.2 (2×CH\(_2\)), 29.4 (O=CMe), 24.8, (2×CH\(_2\)), 23.9 (CH\(_2\)), 15.3 (Me); FAB HRMS (acetone/NBA): calcd for C\(_{33}\)H\(_{49}\)O\(_4\)Na 337.1416 (M+Na); Found 337.1395.

6'-Acetyl-4-(tert-butyl)-5'-methyl-3a'-phenyl-3a',6a'-dihydrospiro[cyclohexane-1,2'-furo[2,3-d][1,3]-dioxole] (3ab): Reaction time, 24 h; yield 22%; colorless needles (from hexane); mp 84-87 °C; \( R_f = 0.60 \) (EtOAc-hexane 1:4 v/v); IR (KBr) \( \nu = 2957 \) (PhH), 1672 (C=O); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta = 7.46-7.39 \) (5H, m, arom. H), 5.32 (1H, s, H-6a'), 2.41 (3H, s, Me), 2.30 (3H, s, Ac), 1.96-1.83 (4H, m, 2×CH\(_2\)), 1.73-1.64 (2H, m, CH\(_2\)), 1.40 (1H, dq, \( J = 10.0, 3.0 \) Hz, H-CH), 1.30-1.25 (1H, m, H-CH), 1.06 (1H, tt, \( J = 12.5, 3.0 \) Hz, H-4), 0.87 (3H×3, s, 3×Me); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta = 194.9 \) (C=O), 171.2 (C-5'), 137.6 (arom. C), 129.3 (arom. CH), 128.6 (2C) (arom. CH), 125.1 (2C) (arom. CH), 115.0 (C-3a'), 114.7 (C-6'), 113.9 (C-2'), 88.9 (C-6a'), 46.7 (C-4), 37.2 (CH\(_2\)), 36.9 (CH\(_2\)), 32.3 (C(Me)\(_3\)), 29.5 (O=CMe), 27.6 (3×Me), 24.8 (CH\(_2\)), 24.7 (CH\(_2\)), 15.3 (Me); FAB HRMS (acetone/NBA): calcd for C\(_{33}\)H\(_{30}\)O\(_4\)Na 393.2042 (M+Na); Found 393.2014.

6'-Acetyl-4-(tert-butyl)-5'-methyl-3a'-phenyl-3a',6a'-dihydrospiro[cyclohexane-1,2'-furo[2,3-d][1,3]-dioxole] (3ab'): Reaction time, 24 h; yield 33%; colorless oil; \( R_f = 0.54 \) (EtOAc-hexane 1:4 v/v); IR (CHCl\(_3\)) \( \nu = 2955 \) (PhH), 1672 (C=O); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta = 7.46-7.39 \) (5H, m, arom. H), 5.29 (1H, s, H-6a'), 2.41 (3H, s, Me), 2.29 (3H, s, Ac), 1.97-1.95, 1.90-1.83, 1.78-1.72 (5H, m, CH\(_2\)), 1.58 (1H, dt, \( J = 13.0, 4.0 \) Hz, H-CH), 1.49 (1H, dq, \( J = 13.0, 4.0 \) Hz, H-CH), 1.40 (1H, dq, \( J = 13.0, 4.0 \) Hz, H-CH), 1.40 (1H, dq, \( J = 13.0, 4.0 \) Hz, H-CH),
1.06 (1H, tt, J = 13.0, 4.0 Hz, H-4), 0.87 (3H×3, s, 3×Me); 13C NMR (125 MHz, CDCl3) δ 194.7 (C=O), 171.2 (C-5'), 137.7 (arom. C), 129.3 (arom. CH), 128.6 (2C) (arom. CH), 125.1 (2C) (arom. CH), 115.1 (C-3a'), 115.0 (C-6'), 114.5 (C-2'), 88.6 (C-6a'), 47.0 (C-4), 37.5 (CH2), 37.4 (CH2), 32.3 (C(Me)3), 29.4 (O=CMe), 27.6 (3×Me), 24.9 (CH2), 24.8 (CH2), 15.3 (Me); FAB HRMS (acetone/NBA): calcd for C23H30O4Na 393.2042 (M+Na); Found 393.2029.

ORTEP Drawing of 3bb

6'-Acetyl-4-(tert-butyl)-3a'-(4-chlorophenyl)-5'-methyl-3a',6a'-dihydrospiro[cyclohexane-1,2'-furo[2,3-d][1,3]dioxole] (3bb): Reaction time, 74 h; yield 29%; colorless prisms (from hexane); mp 140-143 °C; Rf = 0.67 (EtOAc-hexane 1:4 v/v); IR (KBr) ν 2953 (PhH), 1682 (C=O); 1H NMR (500 MHz, CDCl3) δ 7.37 (4H, s, arom. H), 5.28 (1H, s, H-6a'), 2.39 (3H, s, Me), 2.30 (3H, s, Ac), 1.92-1.86 (4H, m, 2×CH2), 1.73-1.63 (2H, m, CH2), 1.40 (1H, dq, J = 12.3, 3.5 Hz, H-CH), 1.25 (1H, dq, J = 12.3, 3.5 Hz, H-CH), 1.06 (1H, tt, J = 11.5, 3.0 Hz, H-4), 0.87 (3H×3, s, 3×Me); 13C NMR (125 MHz, CDCl3) δ 194.7 (C=O), 171.0 (C-5'), 136.2, 135.3 (Cl-C, arom. C), 128.8 (2C) (arom. CH), 126.6 (2C) (arom. CH), 115.2 (C-3a'), 114.1 (C-6'), 113.9 (C-2'), 88.9 (C-6a'), 46.6 (C-4), 37.2 (CH2), 36.8 (CH2), 32.2 (C(Me)3), 29.5 (O=CMe), 27.5 (3×Me), 24.8 (CH2), 24.6 (CH2), 15.3 (Me); Anal Calcd for C23H29ClO4: C, 67.89; H, 7.09. Found C, 68.22; H, 7.22. X-Ray crystallographic data: empirical formula C23H29ClO4; formula weight 404.18; colorless prisms; orthorhombic; space group Pbca; cell lengths a = 11.4756(7), b = 19.2308(12), c = 19.830(1) Å; cell volume 4376.2(4) Å³; formula units per cell Z = 8; total data collected 5352; R = 0.0557; Rw = 0.1068; GOF = 3.006.

ORTEP Drawing of 3bb'
furo[2,3-d][1,3]dioxole (3bb’): Reaction time, 74 h; yield 41%; colorless oil; \( R_f = 0.56 \) (EtOAc-hexane 1:4 v/v); IR (CHCl\(_3\)) \( \nu \) 1672 (C=O); \( \text{\textsuperscript{1}H NMR (500 MHz, CDCl\(_3\))} \) \( \delta \) 7.39-7.35 (4H, m, arom. H), 5.26 (1H, s, H-6a’), 2.40 (3H, s, Me), 2.27 (3H, s, Ac), 1.95-1.72 (5H, m, H-CH, 2×CH\(_2\)), 1.58 (1H, dt, \( J = 13.0, 3.0 \) Hz, H-CH), 1.47 (1H, dq, \( J = 13.0, 3.0 \) Hz, H-CH), 1.38 (1H, dq, \( J = 13.0, 3.0 \) Hz, H-CH), 1.06 (1H, tt, \( J = 13.0, 3.0 \) Hz, H-4), 0.87 (3H×3, s, 3×Me); \( \text{\textsuperscript{13}C NMR (125 MHz, CDCl\(_3\))} \) \( \delta \) 194.5 (C=O), 170.9 (C-5’), 136.3, 135.2 (Cl-C, arom. C), 128.7 (2C) (arom. CH), 126.6 (2C) (arom. CH), 115.1 (C-3a’), 114.4 (C-2’, C-6’), 88.5 (C-6a’), 46.9 (C-4), 37.4 (CH\(_2\)), 37.3 (CH\(_2\)), 32.3 (C(Me\(_3\))), 29.4 (O=CMe), 27.6 (3×Me), 24.9 (CH\(_2\)), 24.8 (CH\(_2\)), 15.3 (Me); FAB HRMS (acetone/NBA): calcd for C\(_{23}\)H\(_{29}\)ClO\(_4\)Na 427.1652 (M+Na); Found 427.1650.

6’-Acetyl-4-(tert-butyl)-3a’-(4-methoxyphenyl)-5’-methyl-3a’,6a’-dihydrospiro[cyclohexane-1,2’-furo[2,3-d][1,3]dioxole] (3cb): Reaction time, 185 h; yield 3%; colorless oil; \( R_f = 0.45 \) (EtOAc-hexane 1:4 v/v); IR (CHCl\(_3\)) \( \nu \) 2961 (PhH), 1709, 1670 (C=C–C=O); \( \text{\textsuperscript{1}H NMR (500 MHz, CDCl\(_3\))} \) \( \delta \) 7.38-7.36 (2H, m, arom. H), 6.92-6.90 (2H, m, arom. H), 5.28 (1H, s, H-6a’), 3.82 (3H, s, OMe), 2.39 (3H, s, Me), 2.30 (3H, s, Ac), 1.93-1.81 (4H, m, 2×CH\(_2\)), 1.72-1.63 (2H, m, CH\(_2\)), 1.40 (1H, dq, \( J = 12.0, 3.0 \) Hz, H-CH), 1.27-1.24 (1H, m, H-CH), 1.06 (1H, tt, \( J = 12.0, 3.0 \) Hz, H-4), 0.87 (3H×3, s, 3×Me); \( \text{\textsuperscript{13}C NMR (125 MHz, CDCl\(_3\))} \) \( \delta \) 194.9 (C=O), 171.2 (C-5’), 160.3 (MeO-C), 129.8 (arom. C), 126.5 (2C) (arom. CH), 114.8 (C-3a’), 114.7 (C-6’), 113.9 (C-2’), 113.9 (2C) (arom. CH), 88.8 (C-6a’), 55.3 (OMe), 46.7 (C-4), 37.3 (CH\(_2\)), 36.9 (CH\(_2\)), 32.3 (C(Me\(_3\))), 29.5 (O=CMe), 27.6 (3×Me), 24.8 (CH\(_2\)), 24.7 (CH\(_2\)), 15.3 (Me); FAB HRMS (acetone/NBA): calcd for C\(_{24}\)H\(_{32}\)O\(_5\)Na 423.2174 (M+Na); Found 423.2169.

6’-Acetyl-4-(tert-butyl)-3a’-(4-methoxyphenyl)-5’-methyl-3a’,6a’-dihydrospiro[cyclohexane-1,2’-furo[2,3-d][1,3]dioxole] (3cb’): Reaction time, 185 h; yield 5%; colorless oil; \( R_f = 0.42 \) (EtOAc-hexane 1:4 v/v); IR (CHCl\(_3\)) \( \nu \) 2959 (PhH), 1710, 1670 (C=C–C=O); \( \text{\textsuperscript{1}H NMR (500 MHz, CDCl\(_3\))} \) \( \delta \) 7.38-7.36 (2H, m, arom. H), 6.94-6.91 (2H, m, arom. H), 5.26 (1H, s, H-6a’), 3.82 (3H, s, OMe), 2.39 (3H, s, Me), 2.30 (3H, s, Ac), 1.95-1.82 (5H, m, H-CH, 2×CH\(_2\)), 1.72-1.63 (1H, m, H-CH), 1.48 (1H, dq, \( J = 12.0, 3.5 \) Hz, H-CH), 1.40 (1H, dq, \( J = 12.0, 3.5 \) Hz, H-CH), 1.06 (1H, tt, \( J = 12.0, 3.5 \) Hz, H-4), 0.87 (3H×3, s, 3×Me); \( \text{\textsuperscript{13}C NMR (125 MHz, CDCl\(_3\))} \) \( \delta \) 194.8 (C=O), 171.0 (C-5’), 160.3 (MeO-C), 129.9 (arom. C), 126.5 (2C) (arom. CH), 115.2 (C-3a’), 114.7 (C-6’), 114.5 (C-2’), 113.9 (2C) (arom. CH), 88.5 (C-6a’),
55.4 (OMe), 47.0 (C-4), 37.5 (2×CH₂), 32.3 (C(Me)₃), 29.4 (O=CMe), 27.7 (3×Me), 24.9 (2×CH₂), 15.4 (Me); FAB HRMS (acetone/NBA): calcd for C₂₆H₃₂O₅Na 423.2174 (M+Na); Found 423.2140.

(Z)-4-Hydroxy-3-(3-phenyl-4,5,6,7-tetrahydrobenzofuran-2-yl)pent-3-en-2-one (4aa): Reaction time, 24 h; yield 9%; colorless cubes (from methanol); mp 92-97 °C; IR (KBr) ν 2941 (PhH), 1605 (C=C–C=O); ¹H NMR (500 MHz, CDCl₃) δ 16.81 (1H, s, OH), 7.35-7.32 (2H, m, arom. H), 7.25-7.21 (3H, m, arom. H), 2.65 (2H, t, J = 5.5 Hz, CH₂), 2.51 (2H, t, J = 5.5 Hz, CH₂), 1.91 (6H, s, 2×Me), 1.91-1.89 (2H, m, CH₂), 1.79-1.76 (2H, m, CH₂); ¹³C NMR (125 MHz, CDCl₃) δ 193.7 (C=O), 151.0 (C-7a), 143.1 (C-2), 133.5 (arom. C), 128.6 (2C) (arom. CH), 127.8 (arom. CH), 126.6 (2C) (arom. CH), 124.8 (C-3), 117.1 (C-3a), 105.6 (C-3’), 23.9 (2×Me), 23.3 (CH₂), 23.2 (CH₂), 22.8 (CH₂), 22.1 (CH₂); Anal Calcd for C₁₉H₂₀O₃: C, 77.00; H, 6.80. Found C, 76.85; H, 6.89.

(Z)-3-(5-(tert-Butyl)-3-phenyl-4,5,6,7-tetrahydrobenzofuran-2-yl)-4-hydroxypent-3-en-2-one (4ab): Reaction time, 24 h; yield 16%; colorless oil; Rₜ = 0.78 (EtOAc-hexane 1:4 v/v); IR (CHCl₃) ν 2963 (PhH), 1605 (C=C–C=O); ¹H NMR (500 MHz, CDCl₃) δ 16.80 (1H, s, OH), 7.37-7.21 (5H, m, arom. H), 2.74 (1H, dd, J = 16.5, 4.5 Hz, H-CH), 2.61(1H, m, H-CH), 2.49 (1H, m, H-CH), 2.31 (1H, t, J = 13.5, Hz, H-5), 2.11 (1H, m, H-CH), 2.05 (3H, s, Me), 1.76 (3H, s, Me), 1.55-1.43 (2H, m, CH₂), 0.96 (9H, s, 3×Me); ¹³C NMR (125 MHz, CDCl₃) δ 194.5, 192.9 (C=O), 151.0 (C-7a), 143.4 (C-2), 133.5 (arom. C), 128.6 (2C) (arom. CH), 127.9 (arom. CH), 126.6 (2C) (arom. CH), 125.1 (C-3), 117.3 (C-3a), 105.6 (C-3’), 45.3 (C-5), 32.5 (C(Me)₃), 27.5 (3×Me), 24.3 (CH₂), 24.2 (CH₂), 24.0 (CH₂), 23.3 (2×Me); FAB HRMS (acetone/NBA): calcd for C₂₃H₂₈O₃ 352.2038 (M); Found 352.2052.

(Z)-3-(5-(tert-Butyl)-3-(4-chlorophenyl)-4,5,6,7-tetrahydrobenzofuran-2-yl)-4-hydroxypent-3-en-2-one (4bb): Reaction time, 74 h; yield 19%; colorless prisms (from CH₂Cl₂); mp 113-116 °C; Rₜ = 0.70 (EtOAc-hexane 1:4 v/v); IR (CHCl₃) ν 2963 (PhH), 1607 (C=C–C=O); ¹H NMR (500 MHz, CDCl₃) δ 16.82 (1H, s, OH), 7.33-7.32 (2H, m, arom. H), 7.17-7.15 (2H, m, arom. H), 2.73 (1H, dd, J = 16.0, 4.5 Hz, H-CH), 2.60 (1H, t, J = 15.0 Hz, H-CH), 2.45 (1H, d, J = 13.5 Hz, H-CH), 2.28 (1H, t, J = 12.5, Hz, H-5), 2.11 (1H, m, H-CH), 2.05 (3H, s, Me), 1.76 (3H, s, Me), 1.52-1.46 (2H, m, CH₂), 0.96 (9H, s,
$\text{C NMR (125 MHz, CDCl}_3\text{)}\delta$: 194.5, 192.8 (C=O), 151.3 (C-7a), 143.6 (C-2), 132.5, 132.0 (Cl-C, arom. C), 129.1 (2C) (arom. CH), 128.9 (2C) (arom. CH), 124.0 (C-3), 117.1 (C-3a), 105.3 (C-3'), 45.3 (C-5), 32.6 (C(Me)), 27.5 (3×Me), 24.2 (CH$_2$), 24.0 (CH$_2$), 23.5 (CH$_2$), 23.2 (2×Me); FAB HRMS (acetone/NBA): calcd for C$_{23}$H$_{27}$ClO$_3$ 386.1649 (M); Found 386.1646.

**Reaction of 1a with Piperidin-4-ones 2c-i in the Presence of BF$_3$·Et$_2$O.** A solution of pentenedione 1a (106.7 mg, 0.5 mmol) and 1-methylpiperidin-4-one (2c) (57.6 mg, 0.5 mmol) was cooled at 0 °C under argon, and BF$_3$·Et$_2$O (315 mL, 2.5 mmol) was slowly added using a syringe. After the reaction was completed, a saturated aqueous solution of NaHCO$_3$ (30 mL) was then added and the aqueous mixture was extracted with CHCl$_3$ (3×20 mL). The combined extracts were dried over anhydrous sodium sulfate, then concentrated to dryness. The residue was purified by column chromatography on silica gel eluting with CHCl$_3$/MeOH (95:5 v/v), giving the desired azaspirodioxole 3ac (149.6 mg, 93%) (Table 2, Entry 6).

**6-Acetyl-1',5-dimethyl-3a-phenyl-3a,6a-dihydrospiro[furo[2,3-d][1,3]dioxole-2,4'-piperidine] (3ac):** Reaction time, 2.5 h; yield 93%; yellow oil; $R_t = 0.22$ (CHCl$_3$/MeOH 95:5 v/v); IR (CHCl$_3$) ν 1674 (C=C–C=O); $^1$H NMR (500 MHz, CDCl$_3$) δ 7.45-7.39 (5H, m, arom. H), 5.34 (1H, s, H-6a), 2.64-2.47 (4H, m, 2×NCH$_2$), 2.40 (3H, s, Me), 2.31 (3H, s, NMe), 2.29 (3H, s, Ac), 2.03-1.86 (4H, m, 2×CH$_2$); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 194.4 (C=O), 171.0 (C-5), 137.1 (arom. C), 129.2, 128.5 (2C) (arom. CH),
124.9 (arom. CH), 114.6 (C-3a), 113.9 (C-6), 112.3 (C-2), 88.7 (C-6a), 45.6 (NMe), 36.7, 36.5 (2×CH2), 29.3 (Ac), 15.1 (Me); FAB HRMS (acetone/NBA): calcd for C19H24O4N 330.1705 (M+H); Found 330.1712.

6-Acetyl-1'-ethyl-5-methyl-3a-phenyl-3a,6a-dihydrospiro[furo[2,3-d][1,3]dioxole-2,4'-piperidine](3ad): Reaction time, 3.0 h; yield 88%; yellow oil; Rf = 0.27 (CHCl3-MeOH 95:5 v/v); IR (CHCl3) ν 1674 (C=C–C=O); 1H NMR (500 MHz, CDCl3) δ 7.46-7.39 (5H, m, arom. H), 5.34 (1H, s, H-6a), 2.68-2.59 (4H, m, 2×NCH2), 2.46 (2H, q, J = 7.3 Hz, NCH2CH3), 2.40 (3H, s, Me), 2.30 (3H, s, Ac), 2.03-1.87 (4H, m, 2×CH2), 1.10 (3H, t, J = 7.3 Hz, NCH2CH3); 13C NMR (125 MHz, CDCl3) δ 194.4 (C=O), 170.9 (C-5), 137.2 (arom. C), 129.2, 128.4 (2C) (arom. CH), 124.9 (arom. CH), 114.6 (C-3a), 113.9 (C-6), 112.8 (C-2), 88.6 (C-6a), 51.6, 50.6 (2×NCH2, NCH2CH3), 36.7, 36.5 (2×CH2), 29.3 (Ac), 15.1 (Me), 12.2 (NCH2CH3); FAB HRMS (acetone/NBA): calcd for C20H26O4N 344.1862 (M+H); Found 344.1867.

6-Acetyl-5-methyl-3a-phenyl-1'-propyl-3a,6a-dihydrospiro[furo[2,3-d][1,3]dioxole-2,4'-piperidine](3ae): Reaction time, 3.0 h; yield 77%; yellow oil; Rf = 0.38 (CHCl3-MeOH 95:5 v/v); IR (CHCl3) ν 1674 (C=C–C=O); 1H NMR (500 MHz, CDCl3) δ 7.45-7.39 (5H, m, arom. H), 5.33 (1H, s, H-6a), 2.67-2.49 (4H, m, H-2', H-6'), 2.40 (3H, s, Me), 2.34 (2H, t, J = 7.6 Hz, NCH2Et), 2.29 (3H, s, Ac), 2.02-1.86 (4H, m, H-3', H-5'), 1.54-1.49 (2H, sex, J = 7.6 Hz, NCH2CH2CH3), 0.90 (3H, t, J = 7.6 Hz, NC2H4CH3); 13C NMR (125 MHz, CDCl3) δ 194.6 (C=O), 171.1 (C-5), 137.4 (arom. C), 129.3, 128.6 (2C) (arom. CH), 125.0 (arom. CH), 114.7 (C-3a), 114.0 (C-6), 113.0 (C-2), 88.8 (C-6a), 60.1 (NCH2CH2), 51.2 (C-2', C-6'), 36.9, 36.7 (C-3', C-5'), 29.5 (Ac), 20.4 (NCH2CH2), 15.3 (Me), 11.9 (NC2H4CH3); FAB HRMS (acetone/NBA): calcd for C21H28O4N 358.2018 (M+H); Found 358.2027.

6-Acetyl-1'-benzyl-5-methyl-3a-phenyl-3a,6a-dihydrospiro[furo[2,3-d][1,3]dioxole-2,4'-piperidine](3af): Reaction time, 4.0 h; yield 89%; orange oil; Rf = 0.34 (CHCl3-MeOH 95:5 v/v); IR (CHCl3) ν 1674 (C=C–C=O); 1H NMR (500 MHz, CDCl3) δ 7.45-7.37 (5H, m, arom. H), 7.31-7.28 (4H, m, arom. H), 7.25-7.22 (1H, m, arom. H), 5.32 (1H, s, H-6a), 3.50 (2H, s, NBn), 2.64-2.50 (4H, m, 2×NCH2), 2.37 (3H, s, Me), 2.28 (3H, s, Ac), 1.99-1.83 (4H, m, 2×CH2); 13C NMR (125 MHz, CDCl3) δ 194.5 (C=O), 171.0
(C-5), 138.4, 137.4 (arom. C), 129.3, 128.6 (2C) (arom. CH), 125.0 (arom. CH), 114.7 (C-3a), 114.0 (C-6), 113.0 (C-2), 88.7 (C-6a), 62.4 (NCH$_2$Ph), 51.0 (2×NCH$_2$), 36.8, 36.6 (2×CH$_2$), 29.4 (Ac), 15.2 (Me); FAB HRMS (acetone/NBA): calcd for C$_{25}$H$_{28}$O$_4$N 406.2018 (M+H); Found 406.2032.

1',6-Diacetyl-5-methyl-3a-phenyl-3a,6a-dihydrospiro[furo[2,3-d][1,3]dioxole-2,4'-piperidine] (3ag):
Reaction time, 2.5 h; yield quant; yellow microcrystals (from Et$_2$O/hexane); mp 126 °C; $R_f = 0.28$ (CHCl$_3$-MeOH 95:5 v/v); IR (KBr) ν 1676 (C=O), 1636 (NC=O), $^1$H NMR (500 MHz, CDCl$_3$) δ 7.44-7.41 (5H, m, arom. H), 5.38 (1H, s, H-6a), 3.83-3.80 (1H, m, NCH$_a$), 3.71 (1H, t, $J = 5.9$ Hz, NCH$_b$), 3.65 (1H, t, $J = 5.9$ Hz, NCH$_b'$), 2.41 (3H, s, Me), 2.29 (3H, s, Ac), 2.13, 2.11 (3H, s, NAc, 1:1.3), 1.98-1.77 (4H, m, 2×CH$_2$); $^1$H NMR (500 MHz, DMSO-d$_6$ at 80 °C) δ 7.49-7.43 (5H, m, arom. H), 5.51 (1H, s, H-6a), 3.72-3.43 (4H, m, 2×NCH$_2$), 2.34 (3H, s, Me), 2.23 (3H, s, Ac), 2.01 (3H, s, NAc), 1.97-1.63 (4H, m, 2×CH$_2$); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 194.3, 194.1 (C=O), 171.1 (C-5), 168.8, 168.7 (NC=O), 136.9, 136.8 (arom. C), 129.54, 129.52 (arom. CH), 128.68, 128.66 (2C (arom. CH), 124.9 (2C (arom. CH), 114.9, 114.8 (C-3a), 114.1, 114.0 (C-6), 112.23, 112.20 (C-2), 88.99, 88.95 (C-6a), 44.2, 44.1 (NCH$_2$), 39.4, 39.3 (NC’H$_2$), 37.5, 37.2 (CH$_2$), 36.7, 36.4 (C’H$_2$), 29.41, 29.39 (Ac), 21.3 (NAc), 15.28, 15.25 (Me); $^{13}$C NMR (125 MHz, DMSO-d$_6$ at 80 °C) δ 194.5 (C=O), 171.1 (C-5), 169.4 (NC=O), 138.3 (arom. C), 130.6 (arom. CH), 129.8 (2C (arom. CH), 126.3 (2C (arom. CH), 115.6 (C-3a), 115.3 (C-6), 113.2 (C-2), 89.4 (C-6a), 30.4 (Ac), 22.2 (NAc), 16.0 (Me); FAB HRMS (acetone/NBA): calcd for C$_{20}$H$_{24}$O$_5$N 358.1654 (M+H); Found 358.1665.

6-Acetyl-1'-benzoyl-5-methyl-3a-phenyl-3a,6a-dihydrospiro[furo[2,3-d][1,3]dioxole-2,4'-piperidine] (3ah):
Reaction time, 3.0 h; yield 94%; yellow microcrystals (from Et$_2$O/hexane); mp 64-65 °C; $R_f = 0.37$ (CHCl$_3$-MeOH 95:5 v/v); IR (KBr) ν 1684 (C=C-C=O), 1653 (NC=O), 1558 (arom); $^1$H NMR (500 MHz, CDCl$_3$) δ 7.56-7.35 (10H, m, arom. H), 5.59 (1H, s, H-6a), 4.18-3.77 (2H, m, NCH$_2$), 3.71-3.37 (2H, m, NCH$_2'$), 2.42, 2.36 (3H, s, Me, 1:1.3), 2.28 (3H, s, Ac), 2.14-2.00 (2H, m, CH$_2$), 1.99-1.69 (2H, m, C’H$_2$); $^1$H NMR (500 MHz, DMSO-d$_6$ at 80 °C) δ 7.48-7.43 (10H, m, arom. H), 5.53 (1H, s, H-6a), 3.79-3.42 (4H, m, 2×NCH$_2$), 2.34 (3H, s, Me), 2.25 (3H, s, Ac), 1.97-1.63 (4H, m, 2×CH$_2$); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 194.0 (C=O), 170.9 (C-5), 170.2 (NC=O), 136.7, 135.5 (arom. C), 129.6 (arom. CH), 129.4 (arom. CH), 128.5 (2C (arom. CH), 128.3 (2C (arom. CH), 126.6 (2C (arom. CH), 124.8 (2C (arom.
1494 (C-3a), 113.9 (C-6), 112.1 (C-2), 88.9 (C-6a), 45.3 (NCH$_2$), 39.9 (NC'H$_2$), 37.5 (CH$_2$), 36.3
(C'H$_2$), 29.3 (Ac), 15.1 (Me); \(^{13}\text{C} \text{NMR}\ (125 \text{ MHz, DMSO-}d_6 \text{ at } 80 ^\circ \text{C}) \delta 193.6 \text{ (C=O), 170.3 \text{ (C-5), 169.6 \text{ (NC=O), 137.4 \text{ (arom. C), 136.5 \text{ (arom. C), 129.7 \text{ (arom. CH), 129.0 \text{ (arom. CH), 128.7 \text{ (4C) (arom. CH), 127.1 \text{ (2C) (arom. CH), 125.4 \text{ (2C) (arom. CH), 114.7 \text{ (C-3a), 114.4 \text{ (C-6), 112.3 \text{ (C-2), 88.6 \text{ (C-6a), 37.1 \text{ (CH)}_2, 36.7 \text{ (C'H)}_2, 29.5 \text{ (Ac), 15.1 (Me); FAB HRMS (acetone/NBA): calcd for C}_{25}\text{H}_{26}\text{O}_{5}\text{N}_{4} 420.1811 (M+H); Found 420.1822.}}}}}$

**Benzyl 6-Acetyl-5-methyl-3a-phenyl-3a,6a-dihydropipero- [furo[2,3-d][1,3]-dioxole-2,4'-piperidine]-1'-carboxylate (3ai):** Reaction time, 3.0 h; yield 94%; pale yellow oil; $R_f = 0.36$ (EtOAc-hexane 3:7 v/v); IR (CHCl$_3$) $\nu$ 1682 (C=C–C=O); \(^1\text{H} \text{NMR}\ (500 \text{ MHz, CDCl}_3) \delta 7.44-7.32 \text{ (10H, m, arom, H), 5.36 (1H, s, H-6a), 5.14 (2H, s, OCH}_2\text{Ph), 3.72 (2H, t, } J = 5.8 \text{ Hz, NCH}_2, 3.63-3.59 \text{ (2H, m, NC'H)_2), 2.40 (3H, s, Me), 2.28 (3H, s, Ac), 1.93 (2H, m, CH$_2$), 1.82 (2H, m, C'H$_2$); \(^{13}\text{C} \text{NMR}\ (125 \text{ MHz, CDCl}_3) \delta 194.3 \text{ (C=O), 171.1 \text{ (C-5), 155.0 \text{ (NC=O), 136.9 \text{ (arom. C), 136.6 \text{ (arom. C), 129.5 \text{ (arom. CH), 128.6 \text{ (arom. CH), 128.4 \text{ (arom. CH), 128.0 \text{ (arom. CH), 127.8 \text{ (arom. CH), 124.9 \text{ (arom. CH), 114.8, 114.0, 112.4 \text{ (C-3a, C-2, C-6), 88.9 \text{ (C-6a), 67.2 (CH}_2\text{Ph), 41.9 \text{ (NCH}_2, 41.8 \text{ (NC'H)}_2, 36.9 \text{ (CH)}_2, 36.6 \text{ (C'H)}_2, 29.4 \text{ (Ac), 15.2 \text{ (Me); FAB HRMS (acetone/NBA): calcd for C}_{26}\text{H}_{28}\text{O}_6\text{N} 450.1917 (M+H); Found 450.1911.}}}}}$

**Reaction of 1a with 4-Hydroxy-2H-chromen-2-one (5) in the Presence of BF$_3$•Et$_2$O.** To a 10 mL two-necked flask, 4-hydroxy-2H-chromen-2-one (5) (145.6 mg, 0.9 mmol), BF$_3$•Et$_2$O (38 $\mu$L, 0.3 mmol) and dry chlorobenzene (0.5 mL) were added under argon and the mixture was heated at 130 °C. After boiling, a solution of pentenedione 1a (79.0 mg, 0.3 mmol) in dry chlorobenzene (0.3 mL) was dropwise added over 10 min. The reaction mixture was continued to heat at 130 °C until the reaction was completed. Water (30 mL) was added to the mixture and the aqueous solution was extracted with CHCl$_3$ (3×20 mL). The combined extracts were dried over anhydrous sodium sulfate, then concentrated to dryness. The residue was purified by column chromatography on silica gel eluting with DCM, giving furfurylchromone 6 (101.5 mg, 77%) and furochromone 7 (17.3 mg, 13%) (Table 3, Entry 6).
3-((3-Acetyl-5-phenylfuran-2-yl)methyl)-4-hydroxy-2H-chromen-2-one (6): Reaction time, 3.0 min; yield 77%; colorless needles (from CHCl$_3$/hexane); mp 241-242 °C; $R_f$ = 0.29 (EtOAc-hexane 3:7 v/v); IR (KBr) $\nu$ 3482-2720 (OH), 1701 (OC=O), 1653 (C=C–C=O); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 10.9 (1H, s, OH), 7.87 (1H, dd, $J = 7.9, 1.8$ Hz, H-5), 7.69 (2H, dd, $J = 7.5, 2.0$ Hz, arom, H), 7.48 (1H, td, $J = 7.9, 1.8$ Hz, H-7), 7.36 (2H, t, $J = 7.5$ Hz, arom, H), 7.30-7.22 (3H, m, H-6, H-8, arom, H), 6.79 (1H, s, H-4'), 4.29 (2H, s, CH$_2$), 2.62 (3H, s, Me); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 200.5 (C=O), 163.6 (OC=O), 162.4 (C-4), 158.3 (C-2'), 153.6 (C-5'), 152.6 (C-8a), 132.0 (arom. CH), 128.9 (arom. C), 128.8 (arom. CH), 128.5 (arom. CH), 124.1 (arom. CH), 123.8 (arom. CH), 123.7 (arom. CH), 122.8 (C-3'), 116.3 (arom. CH), 116.2 (C-4a), 103.7 (C-4'), 99.2 (C-3), 28.9 (Me), 22.9 (CH$_2$); Anal. Calcd for C$_{21}$H$_{19}$O$_3$N: C, 73.33; H, 4.48. Found: C, 73.00; H, 4.53.

(Z)-2-(2-Hydroxy-4-oxopent-2-en-3-yl)-3-phenyl-4H-furo[3,2-c]chromen-4-one (7): Reaction time, 3.0 min; yield 13%; colorless microcrystals (from Et$_2$O/hexane); mp 174 °C; $R_f$ = 0.62 (EtOAc-hexane 3:7 v/v); IR (KBr) $\nu$ 3500-3200 (OH), 1744 (OC=O), 1632 (C=C–C=O); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 16.99 (1H, s, OH), 7.92 (1H, d, $J = 6.5$ Hz, H-9), 7.57 (1H, t, $J = 7.3$ Hz, H-7), 7.49-7.36 (7H, m, H-6, H-8, arom, H), 1.96 (6H, s, 2×Me); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 193.9 (C=O), 157.8 (C-10), 157.4 (OC=O), 152.7 (C-5a), 149.0 (C-2), 131.1 (C-7), 129.4 (arom. C), 129.2 (2C) (arom. CH), 128.5 (2C) (arom. CH), 128.3 (arom. CH), 124.8 (C-3), 124.5 (C-8), 120.9 (C-9), 117.3 (C-6), 112.6 (C-9a), 109.4 (C-3a), 103.6 (C-3'), 24.0 (Me); Anal. Calcd for FAB HRMS (acetone/NBA): calcd for C$_{22}$H$_{19}$O$_5$ 361.1076 (M+H); Found 361.1061.

Michael Addition of Pentenedione 1a with Indole. A solution of 1a (214.9 mg, 1.0 mmol) and indole (118.3 mg, 1.0 mmol) in MeCN (1.0 mL) was heated under reflux for 9.5 h. The solvent was then removed under reduced pressure and the residue was purified by column chromatography on silica gel eluting with EtOAc/hexane (3:7 v/v), giving the desired Michael adduct 8 (136.8 mg, 97%). The reaction was also carried out in MeCN (3.0 mL) for 19 h to give 8 (98%); DCM for 24 h, 8 (93%); MeOH for 14 h, 8 (80%) along with 12 (16%); THF for 48 h, 8 (40%); DMF for 3 h, 8 (83%) and 12 (8%); DCE for 36 h, 8 (98%); and toluene for 23 h, 8 (97%) (Scheme 8).
3-Acetyl-2-(1H-indol-3-yl)-1-phenylpentane-1,4-dione (8): Reaction time, 9.5 h; yield 97%; colorless microcrystals (from benzene); mp 157 °C; \( R_f = 0.20 \) (EtOAc-hexane 2:8 \( v/v \)); IR (KBr) \( \nu = 3500-3200 \) (NH), 1717, 1705, 1676 (C=O); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta = 8.34 \) (1H, br s, NH), 7.95 (2H, \( dd, J = 8.0, 1.3 \) Hz, arom. H), 7.74-7.72 (1H, m, H-4), 7.39 (1H, \( t, J = 8.0 \) Hz, arom. H), 7.30-7.25 (3H, m, H-7, arom. H), 7.18-7.13 (2H, m, H-5, H-6), 7.03 (1H, \( d, J = 3.0 \) Hz, H-2), 5.68 (1H, \( d, J = 10.5 \) Hz, H-2'), 5.05 (1H, \( d, J = 10.5 \) Hz, H-3'), 2.30 (3H, s, Ac), 1.88 (3H, s, Ac); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta = 203.7, 202.0 \) (MeC=O), 197.7 (PhC=O), 136.3 (arom. C), 135.7 (C-7a), 133.0 (arom. CH), 128.7 (2C) (arom. CH), 128.4 (2C) (arom. CH), 125.7 (C-3a), 123.9 (C-2), 122.6 (C-5), 120.4 (C-6), 119.0 (C-4), 111.5 (C-7), 109.3 (C-3), 70.2 (C-3'), 45.3 (C-2'), 31.4, 30.2 (2×Me); Anal. Calcd for C\(_{21}\)H\(_{19}\)O\(_3\)N: C, 75.66; H, 5.74; N, 4.20. Found: C, 75.72; H, 5.79; N, 4.10.

Michael Addition of Pentenedione 1a with Pyrrole. A solution of 1a (108.3 mg, 0.5 mmol) and pyrrole (102.0 mg, 1.5 mmol) in MeCN (0.5 mL) was heated under reflux for 3.5 h. The solvent was then removed in vacuo and the residue was purified by column chromatography on silica gel eluting with EtOAc/hexane (2:8-4:6 \( v/v \)), giving the desired monoalkylpyrrole 9 (122.7 mg, 87%) (Scheme 8).

3-Acetyl-1-phenyl-2-(1H-pyrrol-2-yl)pentane-1,4-dione (9): Reaction time, 3.5 h; yield 84%; colorless microcrystals (from Et\(_2\)O); mp 115-116 °C; \( R_f = 0.43 \) (EtOAc-hexane 3:7 \( v/v \)); IR (KBr) \( \nu = 3500-3160 \) (NH), 1724, 1701, 1663 (C=O); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta = 8.38 \) (1H, br s, NH), 7.96 (2H, \( dd, J = 7.4, 1.2 \) Hz, arom. H), 7.51 (1H, \( tt, J = 7.4, 1.2 \) Hz, arom. H), 7.40 (2H, \( t, J = 7.4 \) Hz, arom. H), 6.69 (1H, \( dt, J = 5.0, 2.1 \) Hz, H-5), 6.06 (1H, \( dd, J = 5.0, 2.1 \) Hz, H-3), 6.00 (1H, \( td, J = 5.0, 1.5 \) Hz, H-4), 5.47 (1H, \( d, J = 11 \) Hz, H-2'), 4.86 (1H, \( d, J = 11 \) Hz, H-3'), 2.24 (3H, s, Ac), 2.02 (3H, s, Ac); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta = 204.1, 201.4 \) (MeC=O), 197.3 (PhC=O), 135.7 (arom. C), 133.4 (arom. CH), 128.8 (arom. CH), 70.2 (C-3'), 45.3 (C-2'), 31.4, 30.2 (2×Me).
128.6 (arom. CH), 123.7 (C-2), 119.1 (C-5), 109.3 (C-4), 108.8 (C-3), 70.1 (C-3'), 46.6 (C-2'), 31.6, 30.1 (2×Me); FAB HRMS (acetone/NBA): calcd for C_{17}H_{17}O_{3}N 283.1208 (M+); Found 283.1205.

To a 10-mL round-bottomed flask, 1a (230.6 mg, 1.0 mmol), pyrrole (35.7 mg, 0.5 mmol), and MeCN (0.5 mL) were added, and the mixture was heated under reflux for 1 h. After work-up as previously described, bis(alkyl)pyrrole was obtained (208.7 mg; 79% yield).

2,2'-(1H-Pyrrole-2,5-diyl)bis(3-acetyl-1-phenylpentane-1,4-dione): Pink microcrystals (from Et_{2}O); mp 240 °C; R_{f} = 0.20 (EtOAc-hexane 3:7 v/v); IR (KBr) ν 3400–3200 (NH), 1734, 1684, 1653 (C=O), 1558 (arom); ^{1}H NMR (500 MHz, CDCl_{3}) δ 8.56 (1H, br s, NH), 7.89 (4H, dd, J = 8.5, 1.0 Hz, arom, H), 7.46-7.43 (2H, m, arom. H), 7.30 (4H, t, J = 8.0 Hz, arom. H), 5.80 (2H, d, J = 2.5 Hz, H-3, H-4), 4.75 (2H, d, J = 10.8 Hz, 2×H-2'), 2.23 (6H, s, 2×Ac), 1.83 (6H, s, 2×Ac); ^{13}C NMR (125 MHz, CDCl_{3}) δ 204.0, 201.2 (MeC=O), 196.4 (PhC=O), 135.5 (arom. C), 133.1 (arom. CH), 128.8 (arom. CH), 128.4 (arom. CH), 125.8 (C-2, C-5), 109.6 (C-3, C-4), 69.5 (C-3'), 47.1 (C-2'), 32.0, 30.3 (2×Me); FAB HRMS (acetone/NBA): calcd for C_{30}H_{29}O_{6}N 499.1995 (M+); Found 499.2004.

Michael Addition of Pentenedione 1a with Furan. A solution of 1a (108.0 mg, 0.5 mmol) and furan (362 μL, 5.0 mmol) in AcOH (0.5 mL) was stirred at room temperature for 4.0 h. The solvent was then removed under reduced pressure and the residue was purified by column chromatography on silica gel eluting with EtOAc/hexane (1:3 v/v), giving the desired alkylfuran 10 (107.4 mg, 76%) (Scheme 8).

3-Acetyl-2-(furan-2-yl)-1-phenylpentane-1,4-dione (10): Reaction time, 4.0 h; yield 76%; colorless prisms (from Et_{2}O); mp 95-96 °C; R_{f} = 0.47 (EtOAc-hexane 3:7 v/v); IR (KBr) ν 1734, 1701, 1653 (C=O), 1558 (arom); ^{1}H NMR (500 MHz, CDCl_{3}) δ 7.98 (2H, d, J = 7.5 Hz, arom. H), 7.51 (1H, t, J = 7.5 Hz, arom. H), 7.40 (2H, t, J = 7.8 Hz, arom. H), 7.30 (1H, d, J = 1.7 Hz, H-5), 6.25 (1H, dd, J =3.2, 1.7 Hz, H-4), 6.20 (1H, d, J = 3.2 Hz, H-3), 5.56 (1H, d, J = 11.3 Hz, H-2'), 4.92 (1H, d, J = 11.3 Hz, H-3'), 2.29 (3H, s, Ac), 2.09 (3H, s, Ac); ^{13}C NMR (125 MHz, CDCl_{3}) δ 202.5, 201.0 (MeC=O), 194.7 (PhC=O), 148.3 (C-2), 142.9 (C-5), 135.3 (arom. C), 133.4 (arom. CH), 128.8 (arom. CH), 128.5 (arom. CH), 111.1 (C-4), 109.3 (C-3), 68.6 (C-3'), 47.0 (C-2'), 30.3, 30.0 (2×Me); FAB HRMS (acetone/NBA): calcd for C_{17}H_{17}O_{4} 285.1127 (M+H); Found 285.1137.
Michael Addition of Pentenedione 1a with N-Methylaniline. A solution of 1a (107.5 mg, 0.5 mmol) and N-methylaniline (165 μL, 1.5 mmol) in AcOH (0.5 mL) was heated under reflux for 6.0 min. The solvent was then removed under reduced pressure and the residue was purified by thin layer chromatography on silica gel eluting with CHCl₃/MeOH (98:2 v/v), giving the desired adduct 11 (120.3 mg, 75%) (Scheme 8).

3-Acetyl-2-(4-(methylamino)phenyl)-1-phenylpentane-1,4-dione (11): Reaction time, 6.0 min; yield 75%; pale yellow amorphous; \( R_f = 0.38 \) (CHCl₃-MeOH 98:2 v/v); IR (CH₃Cl) ν 3474-3360 (NH), 1730, 1697, 1676 (C=O); \(^1\)H NMR (500 MHz, CDCl₃) \( \delta \) 7.93 (2H, dd, \( J = 7.8, 1.0 \) Hz, arom. H), 7.43 (1H, tt, \( J = 7.8, 1.0 \) Hz, arom. H), 7.34 (2H, t, \( J = 7.8 \) Hz, arom. H), 7.05 (2H, dd, \( J = 6.6, 1.9 \) Hz, H-3), 6.49 (2H, dd, \( J = 6.6, 1.9 \) Hz, H-2), 5.24 (1H, d, \( J = 11.5 \) Hz, H-2'), 4.81 (1H, d, \( J = 11.5 \) Hz, H-3'), 3.72 (1H, br s, NH), 2.75 (3H, s, NMe), 2.26 (3H, s, Ac), 1.95 (3H, s, Ac); \(^1^3\)C NMR (125 MHz, CDCl₃) \( \delta \) 203.7, 201.7 (2×MeC=O), 197.9 (PhC=O), 148.8 (C-1), 135.8 (arom. C), 132.8 (arom. CH), 129.5 (arom. CH), 128.8 (arom. CH), 128.3 (arom. C), 122.4 (C-4), 112.9 (C-2), 71.1 (C-3'), 53.0 (C-2'), 31.7 (NMe), 30.3, 30.1 (2×Me); FAB HRMS (acetone/NBA): calcd for C₂₀H₂₁O₃N 323.1521 (M+); Found 323.1529.

Synthesis of Furanyl-substituted Indole 12. To a 10-mL two-necked flask, pentenedione 1a (108.3 mg, 0.5 mmol), indole (70.1 mg, 0.6 mmol), BF₃·Et₂O (32 μg, 0.25 mmol) and DCM (1.5 mL) were added and the mixture was heated under reflux for 30 min. After the reaction was completed, water (10 mL), brine (10 mL), and a saturated aqueous solution of NaHCO₃ (30 mL) were then added, and the aqueous mixture was extracted with CHCl₃ (3×20 mL). The combined extracts were washed with water (20 mL), dried over anhydrous sodium sulfate, then concentrated to dryness. The residue was separated by column chromatography on silica gel eluting with EtOAc/hexane (2:8 v/v), giving the desired furanyl-substituted indole 12 (138.9 mg, 88%) (Scheme 9).

3-(3-Acetyl-2-methyl-5-phenylfuran-4-yl)-1H-indole (12): Yellow cubes (from DCM); mp 141 °C; \( R_f = 0.47 \) (EtOAc-hexane 3:7 v/v); IR (KBr) ν 3400–3200 (NH), 1653 (C=O), 1558 (arom); \(^1\)H NMR (500 MHz, CDCl₃) \( \delta \) 8.63 (1H, br s, NH), 7.43-7.38 (4H, m, arom, H), 7.23 (1H, t, \( J = 7.0 \) Hz, arom. H), 7.05 (2H, dd, \( J = 6.6, 1.9 \) Hz, H-2), 5.24 (1H, d, \( J = 11.5 \) Hz, H-2'), 4.81 (1H, d, \( J = 11.5 \) Hz, H-3'), 3.72 (1H, br s, NH), 2.75 (3H, s, NMe), 2.26 (3H, s, Ac), 1.95 (3H, s, Ac); \(^1^3\)C NMR (125 MHz, CDCl₃) \( \delta \) 203.7, 201.7 (2×MeC=O), 197.9 (PhC=O), 148.8 (C-1), 135.8 (arom. C), 132.8 (arom. CH), 129.5 (arom. CH), 128.8 (arom. CH), 128.3 (arom. C), 122.4 (C-4), 112.9 (C-2), 71.1 (C-3'), 53.0 (C-2'), 31.7 (NMe), 30.3, 30.1 (2×Me); FAB HRMS (acetone/NBA): calcd for C₂₀H₂₁O₃N 323.1521 (M+); Found 323.1529.
7.14-7.08 (5H, m, arom. H), 2.69 (3H, s, Me), 1.85 (3H, s, Ac); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 196.9 (C=O), 157.6 (C-5’), 148.5 (C-2’), 136.1 (C-7a), 130.5 (arom, C), 128.2 (arom, CH), 127.7 (C-3a), 127.2 (arom, CH), 125.3 (C-4’), 125.1 (arom. CH), 123.7 (arom. CH), 122.6 (arom. CH), 120.4 (arom. CH), 119.7 (arom, CH), 113.2 (C-3’), 111.4 (arom, CH), 108.3 (C-3), 29.9 (Ac), 14.7 (Me).

**Paal-Knorr Reaction of Alkylindole 8 to Pyrrolylindole 13.** To a 10-mL round-bottomed flask, alkylindole 8 (128.9 mg, 0.4 mmol), ammonium acetate (66.2 mg, 0.8 mmol) and AcOH (0.3 mL) were added and the mixture was heated at 110 °C for 45 min. After the reaction was completed, water (10 mL) was added to the reaction mixture. The resulting aqueous mixture was then extracted with CHCl$_3$ (3×20 mL) and the combined extracts were washed with a saturated aqueous solution of NaHCO$_3$ (20 mL), water (20 mL), dried over anhydrous sodium sulfate, then concentrated to dryness, giving the desired pyrrole-substituted indole 13a (125.0 mg, quant) without purification (Scheme 9).

3-(3-Acetyl-2-methyl-5-phenyl-1H-pyrrol-4-yl)-1H-indole (13a): Reaction time, 45 min; yield quant; yellow microcrystals (from DCM); mp 96 °C; $R_f$ = 0.33 (EtOAc-hexane 3:7 v/v); IR (KBr) ν 3500-2500 (NH), 1636 (C=O); $^1$H NMR (500 MHz, CDCl$_3$) δ 9.13 (1H, br s, pyrrole-NH), 8.45 (1H, br s, indole-NH), 7.41 (1H, d, $J$ = 7.8 Hz, H-4), 7.36 (1H, d, $J$ = 7.8 Hz, H-7), 7.18 (1H, t, $J$ = 7.8 Hz, H-6), 7.15-7.13 (2H, m, arom. H), 7.07-7.03 (4H, m, arom. H), 6.94 (1H, d, $J$ = 2.5 Hz, H-2), 2.60 (3H, s, Me), 1.84 (3H, s, Ac); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 198.0 (C=O), 136.1 (C-7a), 135.9 (C-2’), 132.4 (arom. C), 128.9 (C-3a), 128.6 (C-5’), 128.3 (2C) (arom. CH), 126.3 (3C) (arom. CH), 123.7 (C-2), 123.6 (C-3’), 122.1 (C-5), 119.97, 119.94 (C-4, C-6), 114.0 (C-4’), 111.2 (C-7), 111.1 (C-3), 29.7 (O=CMe), 14.6 (Me); FAB HRMS (acetone/NBA): calcd for C$_{21}$H$_{18}$ON$_2$ 314.1419 (M+); Found 314.1427.

The alkylindole 8 (99.8 mg, 0.3 mmol) and benzylamine (66 mL, 0.6 mmol) were heated in AcOH (0.3 mL) at 110 °C for 20 min. After the previously described work-up, the residue was purified by column chromatography on silica gel eluting with EtOAc/hexane (4:6 v/v), giving the desired pyrrole 13b (107.4 mg, 89%) (Scheme 9).
3-(3-Acetyl-1-benzyl-2-methyl-5-phenyl-1H-pyrrol-4-yl)-1H-indole (13b): Reaction time, 20 min; yield 89%; colorless microcrystals (from DCM/hexane); mp 264 °C; $R_f = 0.37$ (EtOAc-hexane 3:7 v/v); IR (KBr) ν 3500-3100 (NH), 1636 (C=O); $^1$H NMR (500 MHz, CDCl$_3$) δ 8.02 (1H, br s, NH), 7.26 (1H, t, $J = 7.3$ Hz, arom. H), 7.17 (1H, td, $J = 7.4, 1.3$ Hz, arom. H), 7.13-7.03 (6H, m, H-5, H-6, arom. H), 6.95 (2H, d, $J = 6.5$ Hz, arom. H), 6.87 (1H, d, $J = 2.5$ Hz, H-2), 5.08 (2H, s, CH$_2$), 2.52 (3H, s, Me), 1.92 (3H, s, Ac); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 197.9 (C=O), 137.7 (arom. C), 135.7 (C-7a), 135.5 (C-2'), 133.1 (C-5'), 132.0 (arom. C), 130.8 (2C) (arom. CH), 129.2 (C-3a), 128.8 (2C) (arom. CH), 127.8 (2C) (arom. CH), 127.4 (arom. CH), 127.3 (arom. CH), 125.7 (2C) (arom. CH), 123.5 (C-2), 122.9 (C-3'), 121.9 (C-5), 119.9, 119.8 (C-4, C-6), 115.0 (C-4'), 111.5 (C-3), 110.9 (C-7), 47.8 (CH$_2$), 30.0 (O=CM$$e$), 12.3 (Me); FAB HRMS (acetone/NBA): calcd for C$_{28}$H$_{24}$ON$_2$ 404.1889 (M+); Found 404.1904.

The alkylindole 8 (101.5 mg, 0.3 mmol) and ethanolamine (36.6 μL, 0.6 mmol) were heated in AcOH (0.3 mL) at 110 °C for 1 h. After work-up according to a similar already mentioned procedure, the residue was purified by column chromatography on silica gel eluting with EtOAc/hexane (3:7 v/v), giving the desired pyrrole 13c (80.9 mg, 74%) (Scheme 9).

3-(3-Acetyl-1-(2-hydroxyethyl)-2-methyl-5-phenyl-1H-pyrrol-4-yl)-1H-indole (13c): Reaction time, 1.0 h; yield 74%; colorless microcrystals (from DCM/hexane); mp 200-201 °C; $R_f = 0.12$ (EtOAc-hexane 3:7 v/v); IR (KBr) ν 3600-2500 (NH, OH), 1616 (C=O); $^1$H NMR (500 MHz, DMSO-$d_6$) δ 10.9 (1H, br s,
NH), 7.27 (1H, d, J = 7.8 Hz, H-4), 7.24-7.20 (5H, m, arom. H), 7.16 (1H, d, J = 7.8 Hz, H-7), 7.04 (1H, d, J = 2.5 Hz, H-2), 7.50 (1H, td, J = 7.8, 1.0 Hz, H-6), 6.89 (1H, td, J = 7.8, 1.5 Hz, H-5), 4.90 (1H, t, J = 5.5 Hz, OH), 3.87 (2H, t, J = 7.4 Hz, CH2OH), 3.39 (2H, td, J = 7.4, 4.6 Hz, NCH2), 2.57 (3H, s, Me), 1.66 (3H, s, Ac); 13C NMR (125 MHz, DMSO-d6) δ 195.6 (C=O), 135.6 (C-7a), 134.5 (C-2’), 132.2 (arom. C), 131.9 (C-5’), 131.2 (2C) (arom. CH), 128.6 (C-3a), 127.8 (2C) (arom. CH), 127.5 (arom. CH), 124.7 (C-2), 121.8 (C-3’), 120.8 (C-5), 118.8, 118.7 (C-4, C-6), 114.8 (C-4’), 111.4 (C-7), 109.6 (C-3), 60.0 (CH2OH), 45.8 (NCH2), 29.5 (O=CMe), 12.0 (Me); FAB HRMS (acetone/NBA): calcd for C23H22O2N3 358.1681 (M+); Found 358.1689.

**Paal-Knorr Reaction of 8 to Thierylindole 14.** A mixture of 8 (66.3 mg, 0.2 mmol) and Lawesson’s reagent (123.1 mg, 0.3 mmol) was heated in toluene (3.0 mL) at 50 °C for 30 min under argon. After the reaction was completed, water (10 mL) was added. The resulting aqueous mixture was extracted with CHCl3 (3×20 mL) and the combined extracts were dried over anhydrous sodium sulfate, then concentrated to dryness. The obtained residue was separated by column chromatography on silica gel eluting with EtOAc/hexane (2:8 v/v), giving the desired thienylindole 14 (32.5 mg, 45%) together with furylindole 12 (14.2 mg, 23%) (Scheme 9).

3-(3-Acetyl-2-methyl-5-phenylthiophen-4-yl)-1H-indole (14): Reaction time, 30 min; yield 45%; yellow microcrystals (from DCM); mp 159 °C; Rf = 0.12 (EtOAc-hexane 3:7 v/v); IR (KBr) ν 3500-3120 (NH), 1655 (C=O); 1H NMR (500 MHz, CDCl3) δ 8.29 (1H, br s, NH), 7.35 (1H, d, J = 8.0 Hz, H-4), 7.30 (1H, d, J = 8.0 Hz, H-7), 7.19-7.11 (6H, m, H-6, arom. H), 7.02 (1H, t, J = 7.0 Hz, H-5), 6.95 (1H, d, J = 2.5 Hz, H-2), 2.62 (3H, s, Me), 1.82 (3H, s, Ac); 13C NMR (125 MHz, CDCl3) δ 200.2 (C=O), 142.5 (C-2’), 141.3 (C-3’), 136.9 (C-4’), 135.8 (C-7a), 134.1 (arom. C), 129.4 (C-5’), 128.6 (2C) (arom. CH), 128.2 (2C) (arom. CH), 127.4 (C-3a), 127.1 (arom. CH), 123.7 (C-2), 122.5 (C-6), 120.3 (C-5), 119.9 (C-4), 111.8 (C-3), 111.1 (C-7), 30.4 (O=CMe), 15.1 (Me); FAB HRMS (acetone/NBA): calcd for C21H17ONS 331.1031 (M+); Found 331.1031.

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REFERENCES AND NOTES


8. X-Ray coordinates were deposited with the Cambridge Crystallographic Data Centre (https://www.ccdc.cam.ac.uk), deposition number: CCDC 1546190.


11. It took 8 h until the reaction in the presence of methanesulfonic acid was finished in boiling MeCN, giving 12 (96% yield).\(^{10c}\)

