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AN UNPRECEDENTED SYNTHESIS OF 8b-HYDROXY-3a-(1*H*-PYRROL-2-YL)/(1*H*-INDOL-3-YL)-3a,8b-DIHYDROINDENO[1,2-*b*]-PYRROL-4(1*H*)-ONE DERIVATIVES FROM PYRROLE/INDOLE WITH NINHYDRIN AND β-ENAMINOCARBONYLS

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Abstract – Heterocyclic systems containing (1*H*-pyrrol-2-yl) or (1*H*-indol-3-yl)-dihydroindenopyrrole moieties were synthesized using heterocyclization of pyrrole or indole with ninhydrin and β-enaminocarbonyls in water under reflux conditions. An efficient, facile, and environmentally friendly protocol was found for the production of new heterocyclic compounds. This reaction was used to gain access to a wide range of pyrrole/indole derivatives. Plate chromatography was utilized to isolate the products whose structures were established from their spectroscopic data.

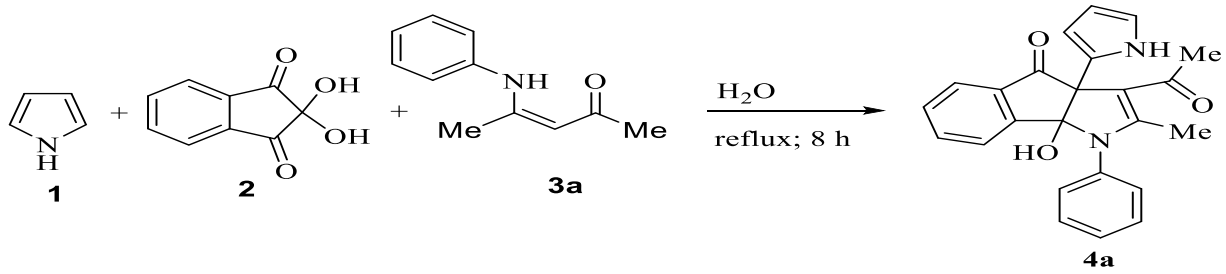
INTRODUCTION

Multicomponent reaction (MCR) is a new instrument to design and develop a rational approach to the preparation of different bioactive heterocyclic compounds.[1] A mixture of various pharmacophores in a pyrrole ring system has allowed forming more active compounds. Pyrrole-containing analogs are potentially a source of biologically active compounds and encompass an important set of beneficial properties.[2] Pyrrole is naturally found in nature, but its derivatives are mostly found in diverse cofactors, naturally-occurring products,[3,4] different biologically active alkaloids[5] and chemosensors in laser production and image recognition.[6] They show significant activities against antiviral,[7] anti-cancer,[8] antimicrobial,[9] antifungal,[10] antitumor,[11] anti-inflammatory[12] activities. In addition, several pyrroles have viably been utilized as intermediates in preparing various natural products, agrochemicals, flavorings, dyes, and functional materials.[13] Ninhydrin has been used in a lot of heterocyclic preparations and is indeed a key building block in organic synthesis. A broad range of reactions include ninhydrin in the synthesis of heterocyclic compounds.[14] Finally, indeno[1,2-*b*]pyrroles show many diverse biological

activities.[15] Recent research on the synthesis of heterocycles incorporating pyrrole or pyrrolidine rings have attracted much attention, especially the syntheses of indenopyrrole derivatives have been of principal significance.[16] Indenopyrroles are prominent for their important biological activities as hypoglycemic agents[17] or as antagonists of N-methyl-D-aspartate receptor.[18] There are various heterocycles of indole derivatives, which contain multiple rings in nature and they usually serve as "privileged structures" for discovering and developing drugs based on their attractive capacity of binding to many cell receptors with high affinity[19] and subsequent potent biological and pharmaceutical profiles.[20] Given the significance of pyrrole and indole derivatives from synthetic and biological perspectives, chemists have used various methods to focus on core skeletons of their derivatives. Also due to biological significances of indenopyrrole derivatives, an environmentally benign protocol is reported here for the production of a new pyrrole or indole/dihydroindenopyrrole pair through a domino process in water as a green solvent under reflux conditions in the absence of any catalyst within 8 h. The synthesis of 8b-hydroxy-3a-(1*H*-pyrrol-2-yl)/(1*H*-indol-3-yl)-3a,8b-dihydroindeno[1,2-*b*]pyrrol-4(1*H*)-one derivatives **4a-g** and **6a-f** from a one-pot three-component reaction of pyrrole or indole with ninhydrin and β-enaminocarbonyls in good yields has been subject to incessant efforts (Schemes 2,3).

RESULTS AND DISCUSSION

The synthesis of 3-acetyl-8b-hydroxy-2-methyl-1-phenyl-3a-(1*H*-pyrrol-2-yl)-3a,8b-dihydroindeno[1,2-*b*]pyrrol-4(1*H*)-one **4a** from the condensation of pyrrole **1**, ninhydrin **2**, and (*Z*)-4-(phenylamino)-pent-3-en-2-one **3a** in the absence of any catalyst was examined under various reaction conditions to detect the optimal conditions (Table 1).



Scheme 1. A typical reaction between pyrrole, ninhydrin and (*Z*)-4-(phenylamino)pent-3-en-2-one

It was studied how to optimize the reaction conditions, including the reaction solvent, the reaction temperature, and the equivalents of starting materials. The reaction of pyrrole, ninhydrin and (*Z*)-4-(phenylamino)pent-3-en-2-one was selected as the model reaction in the absence of any catalyst (Scheme 1). The role of water was studied as a solvent by obtaining monosubstituted pyrrole derivatives.

When the reaction was conducted in acetonitrile as solvent, disubstituted pyrrole derivatives were obtained. In the following of the optimization of reaction solvent, various solvents were investigated (Table 1, entries 1-4), and it was found that water was the suitable solvent for this reaction. Then, the effect of different temperatures was explored on this reaction. When the reaction was conducted for 8 h at room temperature, no product was obtained, which was not satisfactory, but under reflux conditions for the same duration, the product was formed in 30% yield (Table 1, entries 4 and 8). Finally, it was observed that the amount of starting materials is also influential on the reaction (Table 1, entries 8–11). The yield was increased to 82% in the presence of a larger amount of ninhydrin **2**, and (*Z*)-4-(phenylamino)pent-3-en-2-one **3a** (for example, 1.3 mmol) in water at reflux temperature (Table 1, entry 11). On the other hand, extending the reaction time in the same conditions had not influence on improving the yield (Table 1, entry 12). This series of experiments indicates that the best yield was attained by the reaction of pyrrole **1** (1 mmol) with ninhydrin **2** (1.3 mmol) and (*Z*)-4-(phenylamino)-pent-3-en-2-one **3a** (1.3 mmol), in water under reflux conditions for 8 h. In these optimized conditions, the yield of **4a** reached 82%. Under the optimized reaction conditions, two series of pyrrole or indole/dihydroindenopyrrole pair **4a–g** and **6a–f** were produced by the reaction of pyrrole **1** or indole **5** with ninhydrin **2** and β-enaminocarbonyls **3** to give the corresponding products. Since enaminoketones can be produced in situ by condensing acetylacetone and amines, it was perceived to be necessary to investigate the reaction in the presence of 1,3-dicarbonyl compounds and amines instead of enaminone derivatives. We saw that pyrrole or indole reacted with ninhydrin, pentane-2,4-dione, and aniline under the same conditions in this style after 8 h, but the corresponding (1*H*-pyrrol-2-yl) or (1*H*-indol-3-yl)-dihydroindenopyrrole derivatives were obtained in low yields and it was extremely difficult to remove impurities because of the production of byproducts. So, the reaction was investigated with enaminone derivatives in lieu of 1,3-dicarbonyl compounds and amines. The outcome is listed in Tables 2 and 3. The reaction is compatible with different enaminocarbonyls. All the reactions were monitored to produce good yields (73–84% for **4a-g** and 74–80% for **6a-f**) versus other procedures (Schemes 2, 3). All the products shown in Tables 2 and 3 are stable and the structure assignments of new products have been established based on spectral data and elemental analysis. The IR spectrum of 3-acetyl-8b-hydroxy-2-methyl-1-phenyl-3a-(1*H*-pyrrol-2-yl)-3a,8b-dihydroindeno[1,2-*b*]pyrrol-4(1*H*)-one **4a** showed absorption bands at 3440 cm^{-1} for NH and 1648 cm^{-1} for C=O groups. For example, the ^{1}H NMR spectrum of the compound **4a** is composed of two singlets at δ = 1.98 and 2.38 ppm for the methyl groups in the product. A singlet integrated for one hydrogen was seen at δ = 5.94 ppm for the hydroxyl proton, the aromatic protons resonated in the region δ = 7.00-7.68 ppm and NH proton resonated at 8.97 ppm. The ^{13}C NMR spectrum of compound **4a** exhibited 22 distinct signals consistent with the proposed structure.

Table 1. Optimization of the reaction conditions

Entry	Solvent	Temp.[a]	mmol of 1:2:3a	Yield (%)[b]
1	EtOH	rt	1:1:1	N.R.
2	DMF	rt	1:1:1	N.R.
3	DCM	rt	1:1:1	N.R.
4	H_2O	rt	1:1:1	N.R.
5	EtOH	reflux	1:1:1	trace
6	DMF	reflux	1:1:1	trace
7	DCM	reflux	1:1:1	trace
8	H_2O	reflux	1:1:1	30
9	H_2O	reflux	1.3:1:1.3	45
10	H_2O	reflux	1.3:1.3:1	53
11	H_2O	reflux	1:1.3:1.3	82
12	H_2O	reflux	1:1.3:1.3	82

[a]Reaction conditions: solvent was 15 mL, reaction time was 8 h.

[b]Isolated yields.

[c]Reaction time was 14 h.

Table 2. The reaction between pyrrole, ninhydrin and β-enaminocarbonyls

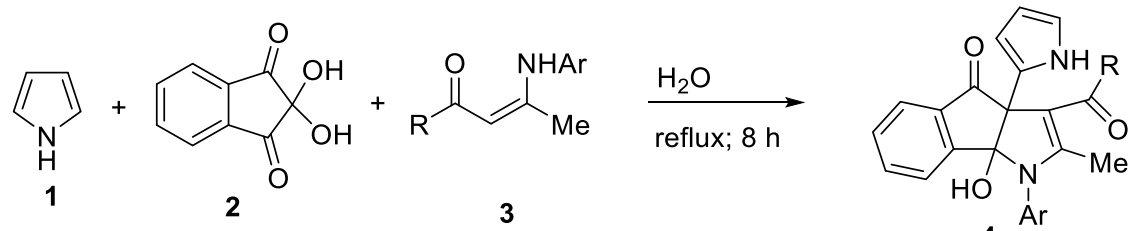
Entry	Product	Ar	R	Yield[a] (%)
1	**4a**	-C_6H_5	Me	82
2	**4b**	- $CH_2C_6H_5$	OMe	83
3	**4c**	- $CH_2C_6H_5$	OEt	80
4	**4d**	4-ClC_6H_4	Me	76
5	**4e**	4-$MeOC_6H_4CH_2$	Me	78
6	**4f**	-C_6H_5	OEt	73
7	**4g**	4-MeC_6H_4	Me	84

[a] Isolated yield. Conditions: H_2O, 100 °C, 8 h.

Table 3. The reaction between indole, ninhydrin and β-enaminocarbonyls

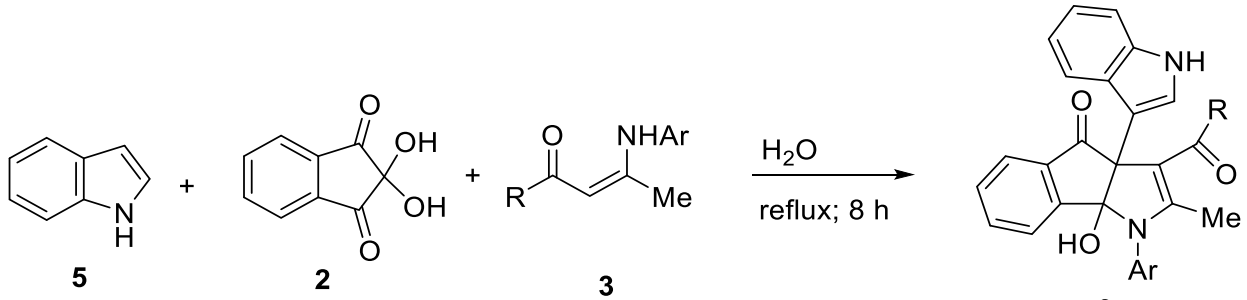
Entry	Product	Ar	R	Yield[a] (%)
1	**6a**	-C_6H_5	Me	80
2	**6b**	4-ClC_6H_4	Me	74
3	**6c**	4-MeC_6H_4	Me	80
4	**6d**	4-IC_6H_4	Me	75
5	**6e**	-C_6H_5	OMe	78
6	**6f**	- $CH_2C_6H_5$	Me	80

[a] Isolated yield. Conditions: H_2O, 100 °C, 8 h.



Ar = C_6H_5, $CH_2C_6H_5$, 4-ClC_6H_4, 4-$MeOC_6H_4CH_2$, 4-MeC_6H_4
R = Me, OMe, OEt

Scheme 2. Reaction between pyrrole, ninhydrin and β-enaminocarbonyls

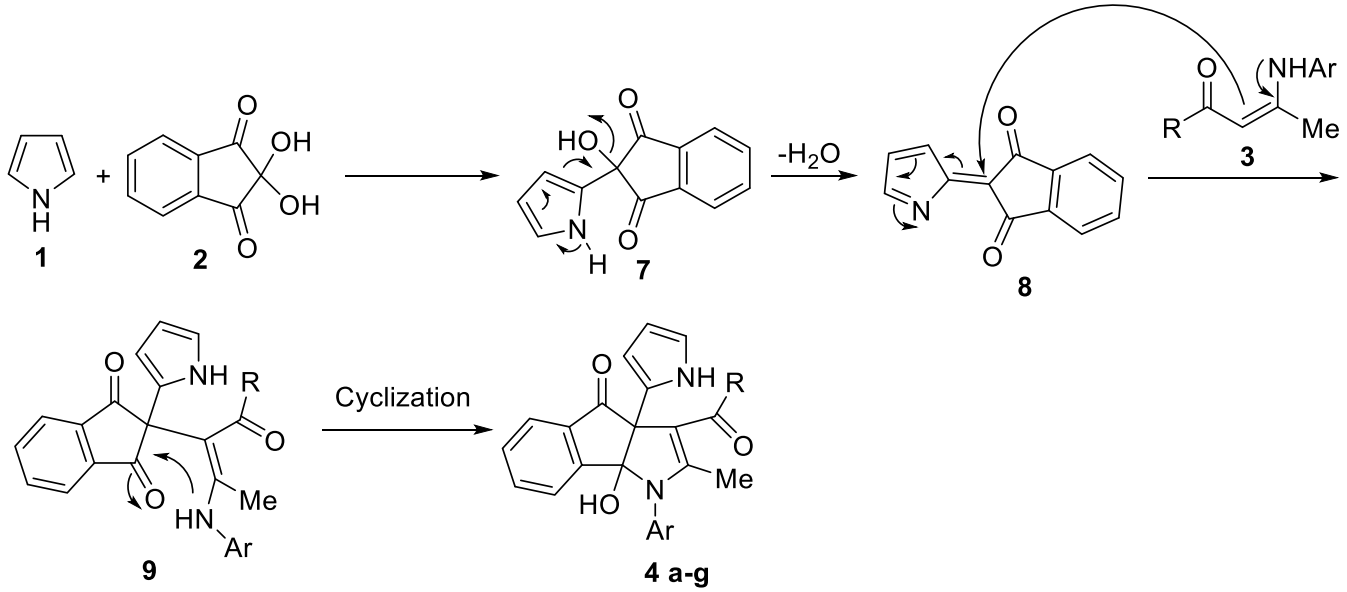


Ar = C_6H_5, 4-ClC_6H_4, 4-MeC_6H_4, 4-IC_6H_4, $CH_2C_6H_5$
R = Me, OMe

Scheme 3. Reaction between indole, ninhydrin and β-enaminocarbonyls

Scheme 4 displays a plausible mechanism by which 8b-hydroxy-3a-(1*H*-pyrrol-2-yl)-3a,8b-dihydroindeno[1,2-*b*]pyrrol-4(1*H*)-one derivatives **4a-g** can be produced by the reaction between pyrrole, ninhydrin and β-enaminocarbonyls. First pyrrole undergoes electrophilic aromatic substitution with ninhydrin in aqueous media in the absence of any catalyst to generate 2-hydroxy-2-(1*H*-pyrrol-2-yl)-1*H*-indene-1,3(2*H*)-dione intermediate **7**. The removal of a molecule of water from intermediate **7** promoted the formation of intermediate **8**, then the nucleophilic addition of

β-enaminocarbonyls **3** to intermediate **8** afforded intermediate **9**, which underwent intramolecular nucleophilic addition of nitrogen to the ketonic carbonyl carbon affording the desired products **4a-g**. This mechanism was also used in the reaction of indole in lieu of pyrrole with ninhydrin and β-enaminocarbonyls to afford 8b-hydroxy-3a-(1*H*-indol-3-yl)-3a,8b-dihydroindeno[1,2-*b*]-pyrrol-4(1*H*)-one **6a-f** derivatives.



Scheme 4. The suggested mechanism for the formation of (1*H*-pyrrol-2-yl)dihydroindenopyrrole derivatives **4a-g**

It is concluded that a simple and efficient method was found to produce highly functionalized (1*H*-pyrrol-2-yl) or (1*H*-indol-3-yl)dihydroindenopyrrole from one pot, three-component reaction of pyrrole or indole with ninhydrin and β-enaminocarbonyls in aqueous media in the absence of any catalyst. This method has many benefits, including the availability of the starting materials, neutral reaction conditions, the use of water as an environmentally green solvent, and good yields in the absence of any catalyst. Furthermore, these products can play an important role as valuable intermediates for further transformations into more complex heterocycles. They are not only environmentally friendly, but also economically useful since toxic wastes can be minimized or eliminated. All these facts have led us to achieve the multi-component synthesis of a new class of highly functionalized (1*H*-pyrrol-2-yl) or (1*H*-indol-3-yl)dihydroindenopyrrole derivatives (**4a–g** and **6a–f**) in water under reflux conditions in the absence of any catalyst.

EXPERIMENTAL PROCEDURES AND MATERIALS

All chemicals were procured from Fluka (Buchs, Switzerland) with high-grade quality, and were employed without purification. The reactions were monitored by TLC and all yields were reported for

isolated products. IR spectra were determined with a Shimadzu IR-470 spectrometer with absorption in cm^{-1}. A Bruker DRX-400 Avance spectrometer was used to record the proton and carbon-13 NMR spectra at 400 and 100 MHz, respectively with Me_4Si as an internal standard in d_6-DMSO. All the products were characterized using the NMR and IR spectral and analytical data.

General procedure for synthesis of compounds 4a-g and 6a-f:

A mixture of pyrrole (1 mmol, for preparation of **4a–g**) or indole (1 mmol, for preparation of **6a–f**) and ninhydrin (1.3 mmol) in water (15 mL) as a green solvent was stirred at 100 ˚C under reflux conditions. After 10 min stirring, the β-enaminocarbonyl derivatives (1.3 mmol) were added to the reaction mixture. The solution was stirred for 8 h under reflux conditions. After the completion of reaction (indicated by TLC), the solvent was removed under reduced pressure and the viscous residue was purified by plate chromatography (20 × 20 cm) using *n*-hexane–EtOAc (2:1) as eluent to give the pure compounds.

3-Acetyl-8b-hydroxy-2-methyl-1-phenyl-3a-(1*H*-pyrrol-2-yl)-3a,8b-dihydroindeno[1,2-*b*]pyrrol-4(1*H*)-one (4a) Yield: 82%; yellow oil. IR (KBr) ($\bar{\upsilon}_{max}$, cm^{-1}): 3440 (NH), 1648 (C=O). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.98 (3H, s, CH_3), 2.38 (3 H, s, CH_3), 5.94 (1H, s, OH), 7.03 - 7.68 (12H, m, aromatic hydrogens), 8.97 (1H, s, NH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.01 (CH_3), 31.35 (CH_3), 67.98, 94.66 (C-8b and C-3a), 94.01, 149.16 (C=C), 112.50, 122.06, 123.14, 125.88, 127.37, 128.05, 128.23, 128.61, 129.87, 132.14, 132.78, 132.93, 136.14, 137.53 (aromatic carbons), 190.01, 197.72 (2 C=O) ppm. Anal. Calcd for ($C_{24}H_{20}N_2O_3$) (384.15): C, 74.98; H, 5.24; N, 7.29%. Found: C, 74.69; H, 5.13; N, 7.08%.

Methyl 1-benzyl-8b-hydroxy-2-methyl-4-oxo-3a-(1*H*-pyrrol-2-yl)-1,3a,4,8b-tetrahydroindeno[1,2-*b*]pyrrole-3-carboxylate (4b) Yield: 83%; orange oil. IR (KBr) ($\bar{\upsilon}_{max}$, cm^{-1}): 3343 (NH), 1691 (C=O). ^{1}H NMR (d_6-DMSO, 400 MHz): δ = 2.34 (3 H, s, CH_3), 3.69 (3 H, s, OCH_3), 5.00 (2H, s, NCH_2), 5.06 (1H, s, OH), 6.85 - 7.38 (12H, m, aromatic hydrogens), 11.21 (1H, s, NH) ppm. ^{13}CNMR (d_6-DMSO, 100 MHz): δ = 12.01 (CH_3), 47.06 (NCH_2), 50.82 (OCH_3), 63.64, 95.46 (C-8b and C-3a), 98.47, 140.17 (C=C), 107.64, 109.79, 115.13, 123.57, 125.41, 127.11, 128.15, 128.34, 128.59, 131.12, 131.23, 132.22, 135.35, 137.54 (aromatic carbons), 166.22, 194.13 (2 C=O) ppm. Anal. Calcd for ($C_{25}H_{22}N_2O_4$) (414.16): C, 72.45; H, 5.35; N, 6.76%. Found: C, 72.09; H, 5.56; N, 6.34%.

Ethyl 1-benzyl-8b-hydroxy-2-methyl-4-oxo-3a-(1*H*-pyrrol-2-yl)-1,3a,4,8b-tetrahydroindeno[1,2-*b*]-pyrrole-3-carboxylate (4c) Yield: 80%; orange oil. IR (KBr) ($\bar{\upsilon}_{max}$, cm^{-1}): 3360 (NH), 1682 (C=O). ^{1}H NMR (d_6-DMSO, 400 MHz): δ = 1.16 ((3H, t, CH_3, J = 7.4 Hz), 2.38 (3 H, s, CH_3), 4.16 (2H, q, OCH_2, J = 7.4 Hz), 4.99 (2H, s, NCH_2), 5.05 (1H, s, OH), 6.83 - 7.31 (12H, m, aromatic hydrogens), 11.11 (1H, s, NH) ppm. ^{13}C NMR (d_6-DMSO, 100 MHz): δ = 13.15 (CH_3), 15.21 (CH_3), 49.01 (NCH_2), 59.81 (OCH_2), 69.12, 89.57 (C-8b and C-3a), 98.21, 143.12 (C=C), 108.21, 109.88, 114.02, 122.81, 125.38, 127.12, 128.15,

128.34, 129.48, 131.02, 131.24, 132.23, 135.21, 137.46 (aromatic carbons), 165.20, 194.61 (2 C=O) ppm. Anal. Calcd for ($C_{26}H_{24}N_2O_4$) (428.17): C, 72.88; H, 5.65; N, 6.54%. Found: C, 72.59; H, 5.39; N, 6.04%.

3-Acetyl-1-(4-chlorophenyl)-8b-hydroxy-2-methyl-3a-(1*H*-pyrrol-2-yl)-3a,8b-dihydroindeno[1,2-*b*]-pyrrol-4(1*H*)-one (4d) Yield: 76%; orange oil. IR (KBr) ($\bar{\upsilon}_{max}$, cm^{-1}): 3293 (NH), 1651 (C=O). ^1H NMR ($CDCl_3$, 400 MHz): δ = 2.16 (3H, s, CH_3), 2.37 (3 H, s, CH_3), 5.90 (1H, s, OH), 6.88 - 7.39 (11H, m, aromatic hydrogens), 9.22 (1H, s, NH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz,): δ = 13.72 (CH_3), 30.53 (CH_3), 55.16, 86.47 (C-8b and C-3a), 95.87, 145.86 (C=C), 111.43, 115.73, 122.58, 124.22, 128.01, 128.49, 128.57, 129.25, 130.15, 131.68, 131.79, 131.82, 132.87, 136.24 (aromatic carbons), 197.54, 198.12 (2 C=O) ppm. Anal. Calcd for ($C_{24}H_{19}ClN_2O_3$) (418.11): C, 68.82; H, 4.57; N, 6.69%. Found: C, 68.47; H, 4.76; N, 6.38%.

3-Acetyl-8b-hydroxy-1-(4-methoxybenzyl)-2-methyl-3a-(1*H*-pyrrol-2-yl)-3a,8b-dihydroindeno[1,2-*b*]pyrrol-4(1*H*)-one (4e) Yield: 78%; yellow oil. IR (KBr) ($\bar{\upsilon}_{max}$, cm^{-1}): 3438 (NH), 1645 (C=O). ^1H NMR (*d*$_6$-DMSO, 400 MHz): δ = 2.38 (3 H, s, CH_3), 2.52 (3 H, s, CH_3), 3.64 (3 H, s, OCH_3), 4.99 (2H, s, NCH_2), 5.06 (1H, s, OH), 6.83 - 7.84 (12H, m, aromatic hydrogens), 11.25 (1H, s, NH) ppm. ^{13}CNMR (*d*$_6$-DMSO, 100 MHZ): δ = 12.15 (CH_3), 28.76 (CH_3), 46.91 (NCH_2), 51.34 (OCH_3), 60.23, 81.75 (C-8b and C-3a), 93.65, 137.12 (C=C), 126.25, 126.42, 127.14, 127.17, 127.39, 127.61, 127.78, 128.57, 128.92, 129.59, 130.12, 132.25, 132.58, 135.46 (aromatic carbons), 190.18, 194.13 (2 C=O) ppm. Anal. Calcd for ($C_{26}H_{24}N_2O_4$) (428.17): C, 72.88; H, 5.65; N, 6.54%. Found: C, 72.53; H, 5.48; N, 6.18%.

Ethyl 8b-hydroxy-2-methyl-4-oxo-1-phenyl-3a-(1*H*-pyrrol-2-yl)-1,3a,4,8b-tetrahydroindeno[1,2-*b*]-pyrrole-3-carboxylate (4f) Yield: 73%; orange oil. IR (KBr) ($\bar{\upsilon}_{max}$, cm^{-1}): 3358 (NH), 1684 (C=O). ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.30 ((3H, t, CH_3, *J* = 7.4 Hz), 2.46 (3 H, s, CH_3), 4.30 (2H, q, OCH_2, *J* = 7.4 Hz), 5.30 (1H, s, OH), 6.86 - 7.33 (12H, m, aromatic hydrogens), 11.26 (1H, s, NH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 12.39 (CH_3), 14.28 (CH_3), 59.94 (OCH_2), 62.18, 92.26 (C-8b and C-3a), 98.31, 138.18 (C=C), 108.67, 110.89, 116.22, 123.92, 125.53, 128.74, 128.82, 130.01, 131.32, 132.85, 134.01, 135.92, 137.41, 137.45 (aromatic carbons), 166.63, 195.11 (2 C=O) ppm. Anal. Calcd for ($C_{25}H_{22}N_2O_4$) (414.16): C, 72.45; H, 5.35; N, 6.76%. Found: C, 72.28; H, 5.62; N, 6.44%.

3-Acetyl-8b-hydroxy-2-methyl-3a-(1*H*-pyrrol-2-yl)-1-(*p*-tolyl)-3a,8b-dihydroindeno[1,2-*b*]pyrrol-4(1*H*)-one (4g) Yield: 84%; yellow oil. IR (KBr) ($\bar{\upsilon}_{max}$, cm^{-1}): 3370 (NH), 1685 (C=O). ^1H NMR (*d*$_6$-DMSO, 400 MHz): δ = 1.18 (3H, s, CH_3), 2.23 (3 H, s, CH_3), 2.33 (3 H, s, CH_3), 5.11 (1H, s, OH), 6.82 - 7.36 (11H, m, aromatic hydrogens), 11.12 (1H, s, NH) ppm. ^{13}C NMR (*d*$_6$-DMSO, 100 MHz): δ = 11.91 (CH_3), 27.35 (CH_3), 28.72 (CH_3), 50.71, 81.66 (C-8b and C-3a), 91.22, 137.54 (C=C), 107.91, 110.22, 115.58, 123.56, 125.18, 127.14, 128.46, 128.73, 130.56, 131.19, 132.56, 132.83, 135.62, 137.54 (aromatic carbons), 193.12, 195.10 (2 C=O) ppm. Anal. Calcd for ($C_{25}H_{22}N_2O_3$) (398.16): C, 75.36; H, 5.57; N, 7.03%. Found: C, 75.15; H, 5.31; N, 6.82%.

3-Acetyl-8b-hydroxy-3a-(1*H*-indol-3-yl)-2-methyl-1-phenyl-3a,8b-dihydroindeno[1,2-*b*]pyrrol-4(1*H*) -one (6a) yield: 80%; yellow oil. IR (KBr) ($\bar{\upsilon}_{max}$, cm^{-1}): 3376 (NH), 1602 (C=O). ^1H NMR ($CDCl_3$, 400 MHz): δ = 2.07 (3H, s, CH_3), 2.37 (3 H, s, CH_3), 4.53 (1H, s, NH), 5.68 (1H, s, OH), 6.63 - 7.58 (14H, m, aromatic hydrogens) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 15.39 (CH_3), 29.04 (CH_3), 48.62, 70.59 (C-8b and C-3a), 93.82, 147.34 (C=C), 115.13, 120.49, 121.52, 124.92, 125.14, 126.42, 127.71, 127.91, 128.34, 128.52, 128.76, 129.16, 130.23, 130.76, 131.03, 133.01, 136.52, 139.71 (aromatic carbons), 190.12, 193.20 (2 C=O) ppm. Anal. Calcd for ($C_{28}H_{22}N_2O_3$) (434.16): C, 77.40; H, 5.10; N, 6.45%. Found: C, 77.15; H, 5.32; N, 6.17%.

3-Acetyl-1-(4-chlorophenyl)-8b-hydroxy-3a-(1*H*-indol-3-yl)-2-methyl-3a,8b-dihydroindeno[1,2-*b*]-pyrrol-4(1*H*)-one (6b) yield: 74%; yellow oil. IR (KBr) ($\bar{\upsilon}_{max}$, cm^{-1}): 3276 (NH), 1601 (C=O). ^1H NMR (*d*$_6$-DMSO, 400 MHz): δ = 1.94 (3H, s, CH_3), 2.23 (3 H, s, CH_3), 4.38 (1H, s, NH), 6.04 (1H, s, OH), 7.03 - 7.35 (13H, m, aromatic hydrogens) ppm. ^{13}C NMR (*d*$_6$-DMSO, 100 MHz): δ = 14.58 (CH_3), 28.59 (CH_3), 50.25, 67.59 (C-8b and C-3a), 97.25, 148.49 (C=C), 115.59, 120.61, 126.64, 126.90, 128.43, 128.52, 128.72, 129.12, 129.54, 129.66, 130.14, 130.58, 130.73, 131.14, 131.43, 132.56, 133.76, 140.14 (aromatic carbons), 190.16, 192.14 (2 C=O) ppm. Anal. Calcd for ($C_{28}H_{21}ClN_2O_3$) (468.12): C, 71.72; H, 4.51; N, 5.97%. Found: C, 71.65; H, 4.32; N, 5.65%.

3-Acetyl-8b-hydroxy-3a-(1*H*-indol-3-yl)-2-methyl-1-(*p*-tolyl)-3a,8b-dihydroindeno[1,2-*b*]pyrrol-4(1*H*)-one (6c) yield: 80%; orange oil. IR (KBr) ($\bar{\upsilon}_{max}$, cm^{-1}): 3274 (NH), 1600 (C=O). ^1H NMR (*d*$_6$-DMSO, 400 MHz): δ = 1.89 (3H, s, CH_3), 2.21 (3 H, s, CH_3), 2.34 (3H, s, CH_3), 4.38 (1H, s, NH), 6.21 (1H, s, OH), 7.01 - 7.37 (13H, m, aromatic hydrogens) ppm. ^{13}C NMR (*d*$_6$-DMSO, 100 MHz): δ = 14.69 (CH_3), 20.68 (CH_3), 28.56 (CH_3), 49.55, 68.13 (C-8b and C-3a), 94.43, 148.64 (C=C), 111.90, 113.52, 117.14, 124.68, 125.71, 126.08, 126.79, 126.89, 127.90, 127.93, 128.03, 128.07, 128.25, 128.34, 128.65, 129.00, 136.74, 136.95 (aromatic carbons), 190.44, 192.14 (2 C=O) ppm. Anal. Calcd for ($C_{29}H_{24}N_2O_3$) (448.18): C, 77.66; H, 5.39; N, 6.25%. Found: C, 77.43; H, 5.48; N, 6.07%.

3-Acetyl-8b-hydroxy-3a-(1*H*-indol-3-yl)-1-(4-iodophenyl)-2-methyl-3a,8b-dihydroindeno[1,2-*b*]-pyrrol-4(1*H*)-one (6d) yield: 75%; yellow oil. IR (KBr) ($\bar{\upsilon}_{max}$, cm^{-1}): 3440 (NH), 1605 (C=O). ^1H NMR (*d*$_6$-DMSO, 400 MHz): δ = 2.15 (3H, s, CH_3), 2.19 (3 H, s, CH_3), 4.97 (1H, s, NH), 6.35 (1H, s, OH), 6.95 – 7.43 (13H, m, aromatic hydrogens) ppm. ^{13}C NMR (*d*$_6$-DMSO, 100 MHZ): δ = 13.85 (CH_3), 19.54 (CH_3), 51.49, 78.23 (C-8b and C-3a), 97.54, 154.13 (C=C), 123.82, 125.24, 126.83, 127.12, 127.43, 128.13, 128.40, 128.45, 128.47, 128.53, 129.23, 129.53, 130.15, 130.54, 130.76, 132.38, 132.48, 133.53 (aromatic carbons), 190.13, 192.60 (2 C=O) ppm. Anal. Calcd for ($C_{28}H_{21}IN_2O_3$) (560.06): C, 60.01; H, 3.78; N, 5.00%. Found: C, 59.82; H, 3.92; N, 4.82%.

Methyl 8b-hydroxy-3a-(1*H*-indol-3-yl)-2-methyl-4-oxo-1-phenyl-1,3a,4,8b-tetrahydroindeno[1,2-*b*]-

pyrrole-3-carboxylate (6e) yield: 78%; yellow oil. IR (KBr) ($\bar{\upsilon}_{max}$, cm^{-1}): 3378 (NH), 1654 (C=O). ^1H NMR (d_6-DMSO, 400 MHz): δ = 2.23 (3H, s, CH_3), 3.50 (3 H, s, OCH_3), 4.38 (1H, s, NH), 6.50 (1H, s, OH), 7.00 - 7.41 (13H, m, aromatic hydrogens) ppm. ^{13}C NMR (d_6-DMSO, 100 MHz): δ = 14.05 (CH_3), 49.90, 67.94 (C-8b and C-3a), 55.98 (OCH_3), 94.04, 149.14 (C=C), 112.03, 113.99, 117.34, 123.16, 124.89, 125.76, 125.84, 126.12, 126.58, 127.76, 127.84, 127.85, 128.38, 128.41, 128.49, 128.54, 137.25, 143.52 (aromatic carbons), 165.84, 192.14 (2 C=O) ppm. Anal. Calcd for ($C_{28}H_{22}N_2O_4$) (450.16): C, 74.65; H, 4.92; N, 6.22%. Found: C, 74.32; H, 5.01; N, 6.09%.

3-Acetyl-1-benzyl-8b-hydroxy-3a-(1*H*-indol-3-yl)-2-methyl-3a,8b-dihydroindeno[1,2-*b*]pyrrol-4(1*H*)-one (6f) yield: 80%; yellow oil. IR (KBr) ($\bar{\upsilon}_{max}$, cm^{-1}): 3367 (NH), 1600 (C=O). ^1H NMR ($CDCl_3$, 400 MHz): δ = 2.12 (3H, s, CH_3), 2.43 (3 H, s, CH_3), 4.01 (2H, s, NCH_2), 4.61 (1H, s, NH), 6.64 (1H, s, OH), 7.14 - 7.92 (14H, m, aromatic hydrogens) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 15.54 (CH_3), 28.98 (CH_3), 47.39, 70.62 (C-8b and C-3a), 93.79, 147.29 (C=C), 115.12, 120.53, 122.78, 124.26, 124.63, 126.42, 126.53, 127.66, 127.72, 128.71, 128.85, 128.90, 129.50, 129.54, 132.01, 133.34, 133.52, 136.31 (aromatic carbons), 190.16, 192.82 (2 C=O) ppm. Anal. Calcd for ($C_{29}H_{24}N_2O_3$) (448.18): C, 77.66; H, 5.39; N, 6.25%. Found: C, 77.34; H, 5.14; N, 5.88%.

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