Regioselective one-pot synthesis of functionalised 6,7-dihydro-1*H*-indol-4(5*H*)-ones

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A one-pot two-step synthesis of functionalised 6,7-dihydro-1*H*-indol-4(5*H*)-ones from 1,3-cyclohexanediones, benzylamines, and 2-(2-oxo-2-phenylethylidene)-1*H*-indene-1,3(2*H*)-dione has been achieved. The advantages of this approach are operational simplicity, good yields of the products and avoidance of the use of any ligands, metal catalysts, acidic media, or column chromatography.

Keywords: 6,7-dihydro-1*H*-indol-4(5*H*)-one, 2-(2-oxo-2-phenylethylidene)-1*H*-indene-1,3(2*H*)-dione, benzylamine, 1,3-cyclohexanedione, one-pot reaction

Heterocycles containing the indole and pyrrole rings are significant targets for synthetic and medicinal chemists as these fragments are key structures in various biologically active compounds such as atorvastatin and mitomycin.[1–3] They also exhibit a range of biological properties including anti-tubulin,[4] antifouling, antibacterial,[5] and antifungal activity.[6] They can also act as potent inhibitors of AKT[7] and fructose-1,6-bisphosphatase[8] and are apoptosis protein antagonists.[9] Moreover, appropriately functionalised 6,7-dihydro-1*H*-indol-4(5*H*)-ones have been identified as anti-psychotic agents,[10] inhibitors of heat-shock protein 90 (scaffolds A and B in Fig. 1),[11,12] and inhibitors of aurora kinase (scaffold C in Fig. 1).[13] These structures are commonly employed as building blocks for the synthesis of indole-based scaffolds.[14,15]

Most of the syntheses of 6,7-dihydro-1*H*-indol-4(5*H*)-ones involve multistep synthetic transformations and consequently they suffer from tedious isolation steps.[16,17] Despite the importance of the 6,7-dihydro-1*H*-indol-4(5*H*)-ones, known approaches for obtaining them based on multicomponent reactions are scarce. In this area, Shi recently reported the three-component reaction of 1,3-dicarbonyl compounds, arylglyoxal monohydrate, and enaminones leading to functionalised 6,7-dihydro-1*H*-indol-4(5*H*)-ones.[18] These structures were also synthesised by reaction of alkenoyl bis(ketene dithioacetals) and tosylmethyl isocyanide.[19] Batra synthesised 2-(substituted) phenyl-6,7-dihydro-1*H*-indol-4(5*H*)-ones from adducts of the Morita–Baylis–Hillman reaction between 2-oxo-(substituted) phenylacetaldehydes and cyclohex-2-enone.[20]

Enaminones as active intermediates have shown good reactivity in MCRs for they readily attack electrophiles to give interesting bioactive N-heterocyclic compounds.[21–23] Based on these findings and as part of our program aimed at construction of new heterocyclic compounds,[24–30] here we report the reaction of 1,3-cyclohexanediones, benzylamines, and 2-(2-oxo-2-phenylethylidene)-1*H*-indene-1,3(2*H*)-dione for construction of 6,7-dihydro-1*H*-indol-4(5*H*)-ones.

Results and discussion

We started our study with the optimisation of the condensation of 1,3-cyclohexanedione **1a** (R^1=H) and benzylamine **2a** (R^2=H). Although this condensation occurred well under solvent-free conditions at 100 °C in 30 min, the reaction did not proceed well in various solvents at reflux temperature (Table 1, entries 1–6). Then we investigated the one-pot sequential reaction of the enamine **3a** (R^1, R^2=H), the product of the solvent-free condensation of 1,3-cyclohexanedione **1a** (R^1=H) and benzylamine **2a** (R^2=H), with 2-(2-oxo-2-

Table 1 Optimisation of the reaction conditions for converting cyclohexanedione **1a** (R^1=H) and benzylamine **2a** (R^2=H) to 2-(1-benzyl-4-oxo-2-phenyl-4,5,6,7-tetrahydro-1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione **4a** (R^1, R^2=H)

Entry	Solvent 1[a]/ Temp/°C	Solvent 2[a]/ Temp/°C	Yield of **4a**/%
1	CH_3CN/rf	CH_3CN/rf	10
2	MeOH/rf	MeOH/rf	20
3	EtOH/rf	EtOH/rf	17
4	DMF/rf	DMF/rf	14
5	DCM/rf	DCM/rf	0
6	THF/rf	THF/rf	0
7	SF/100 °C	SF/100 °C	0
8	SF/100 °C	MeOH/rf	67
9	SF/100 °C	EtOH/rf	64
10	SF/100 °C	CH_3CN/rf	45
11	SF/100 °C	DCM/rf	20
12	SF/100 °C	DMF/rf	30
13	SF/100 °C	H_2O/rf	10

[a]SF, solvent-free conditions.

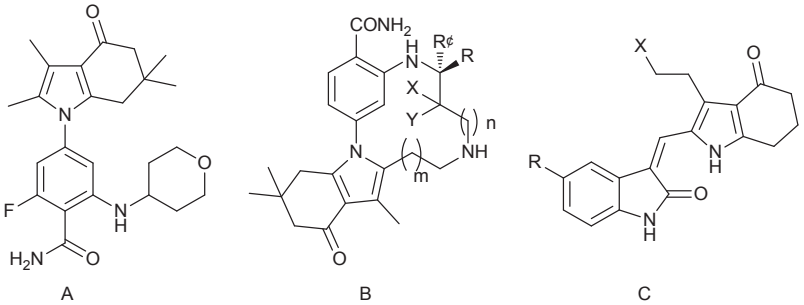

Fig. 1 Examples of biologically active 6,7-dihydro-1*H*-indol-4(5*H*)-one scaffolds.

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phenylethylidene)-1*H*-indene-1,3(2*H*)-dione. The results are also shown in Table 1. Following trials with other solvents at reflux (entries 9–13) we found that the highest yield of the desired functionalised 6,7-dihydro-1*H*-indol-4(5*H*)-one **4a** (R^1, R^2=H) could be achieved using MeOH at the reflux temperature (entry 8).

With optimal conditions established (Scheme 1), we then explored the scope of this reaction by varying the structures of 1,3-cyclohexanedione **1** and benzylamine **2**. The results are shown in Table 2. As can be seen, yields were in the range 63–82%.

The newly synthesised products **4a–j** were fully characterised by their IR, ^{1}H NMR, ^{13}C NMR and mass spectra and their elemental analysis. Some selected spectral data are discussed below.

The mass spectrum of **4f** displayed the molecular ion peak at *m/z*=473, which is in agreement with the proposed structure. In the IR spectrum of **4f** absorption bands at 3054 (aromatic C–H), 2931 and 2865 (alkyl C–H), 1714 (C=O), and 1649 (C=C) cm^{-1} are most significant stretching frequencies. In the ^{1}H NMR spectrum of **4f**, two methyl groups appeared as a singlet at δ 0.94 ppm as expected. Three singlets at δ 2.05, 2.59 and 5.18 ppm are attributed to three CH_2 groups. The singlet at δ 4.35 ppm is ascribed to the CH group, and the 14 aromatic hydrogen atoms gave rise to characteristic resonances in the aromatic region of the spectrum. Observation of 23 distinct signals in the ^{1}H-decoupled ^{13}C NMR spectrum of **4f** is in agreement with the proposed structure.

Based on these results, a plausible mechanism for the construction of 6,7-dihydro-1*H*-indol-4(5*H*)-ones is proposed (Scheme 2). The formation of enaminone **3** occurs through condensation of 1,3-cyclohexanedione **1** and benzylamine **2**. Then, the enaminone **3** attacks 2-(2-oxo-2-phenylethylidene)-1*H*-indene-1,3(2*H*)-dione in a Michael-type addition to generate intermediate **5** which tautomerises to the enamine form **6**. Then the NH group of **6** attacks the carbonyl group, through an intramolecular 5-*exo-trig* cyclisation to form **7**. This is followed by loss of one molecule of H_2O from **7** which effects aromatisation to form product **4**.

Table 2 Yields for the conversion of cyclohexanediones **1** and various benzylamines **2** to the enamines **3** (R^1=H, Me; R^2=various), and thence to 2-(1-R^2-benzyl-4-oxo-2-phenyl-4,5,6,7-tetrahydro-1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-diones **4** (R^1=H, Me; R^2=various) (Scheme 1)

Entry	R^1	R^2	Product	Yield/%
1	H	H	**4a**	67
2	H	2-Cl	**4b**	63
3	H	4-Cl	**4c**	72
4	H	4-OCH_3	**4d**	65
5	H	4-CH_3	**4e**	82
6	CH_3	H	**4f**	66
7	CH_3	2-Cl	**4g**	70
8	CH_3	4-Cl	**4h**	69
9	CH_3	4-OCH_3	**4i**	80
10	CH_3	4-CH_3	**4j**	78

Experimental

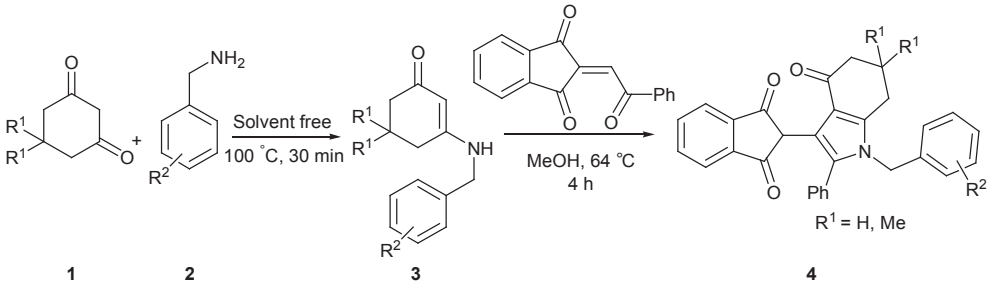
Elemental analyses for C, H and N were performed using a Heraeus CHN–O–Rapid analyser. Mass spectra were recorded on a Finnigan-Mat 8430 mass spectrometer operating at an ionisation potential of 70 eV. NMR spectra were obtained on a Bruker DRX-400 Avance spectrometer (^{1}H NMR at 400 Hz, ^{13}C NMR at 100 Hz) in DMSO-d_6 using tetramethylsilane as internal standard. Chemical shifts (δ) are given in ppm and coupling constants (*J*) in Hz. IR spectra were recorded as KBr pellets on a NICOLET FTIR 100 spectrometer; absorbencies are reported in cm^{-1}. Melting points were measured on an Electrothermal 9100.

Synthesis of 2-(1-R²-benzyl-4-oxo-2-phenyl-6,7-dihydro-1H-indol-4(5H)-one derivatives **4a–j** *(R¹=H, Me; R²=various); general procedure*

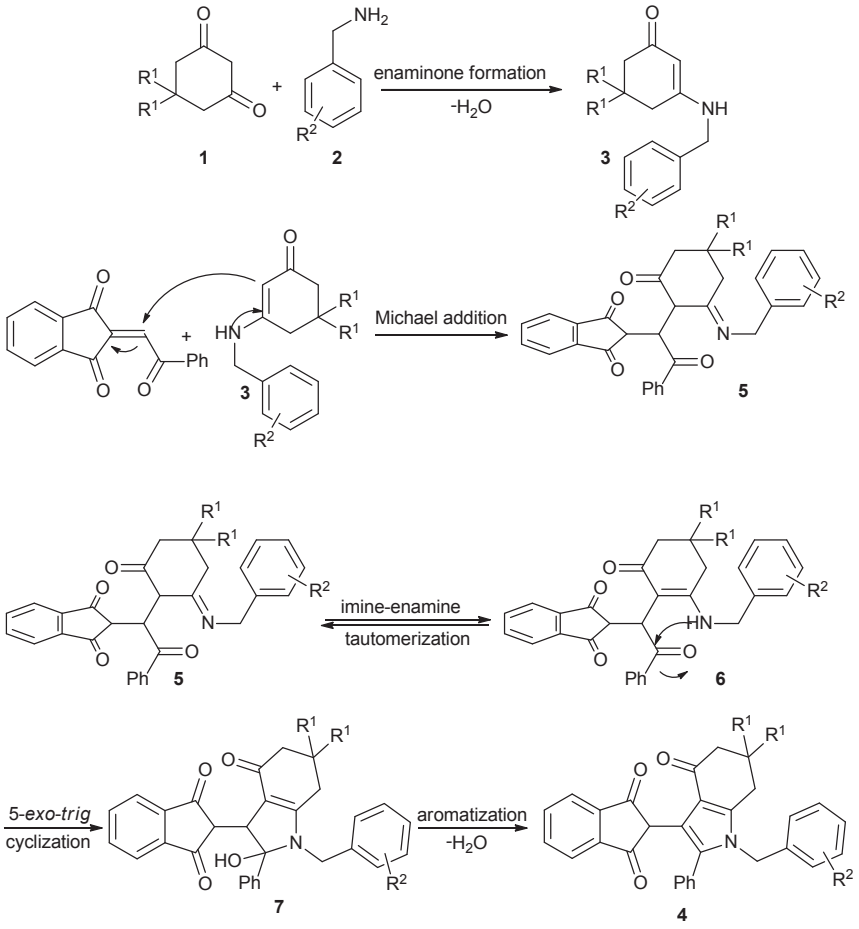
A mixture of 1,3-cyclohexanedione **1** (1 mmol) and a benzylamine **2** (1 mmol) was heated at 100 °C for 30 min and cooled. Then a solution of 2-(2-oxo-2-phenylethylidene)-1*H*-indene-1,3(2*H*)-dione (1 mmol) in MeOH (3 mL) was added. The mixture was stirred at reflux temperature for another 4 h, during which time precipitation of the product occurred. Progress of reaction was monitored by TLC, and upon completion (4 h) the mixture was filtered and the precipitate was washed with MeOH (4 mL) to afford the pure product **4a–j** (R^1=H, Me; R^2=various). NMR and IR spectra were recorded and a sample was recrystallised for elemental analysis.

*2-(1-Benzyl-4-oxo-2-phenyl-4,5,6,7-tetrahydro-1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione* (**4a**): White powder, yield 0.30 g (67%); m.p. 226–228 °C; IR (KBr): 3059 (aromatic C–H), 2926 and 2861 (alkyl C–H), 1711 (C=O), 1645 (C=C), 1600 and 1475 (Ar), 1252 (C–N) cm^{-1}; ^{1}H NMR: δ 1.92–2.01 (m, 2 H, CH_2), 2.14 (t, $^3J_{HH}$=5.6 Hz, 2 H, CH_2), 2.70 (t, $^3J_{HH}$=6.0 Hz, 2 H, CH_2), 4.29 (s, 1 H, CH), 5.18 (s, 2 H, CH_2Bn), 6.91 (d, $^3J_{HH}$=7.2 Hz, 2 H, 2×CH_{ortho} of Ph), 7.27 (t, $^3J_{HH}$=6.8 Hz, 1 H, CH_{para} of Ph), 7.32 (t, $^3J_{HH}$=7.2 Hz, 2 H, 2×CH_{meta} of Ph), 7.35–7.45 (m, 5 H, 5×CH of Ph), 7.85–7.95 (m, 4 H, 4×CH of Ar); ^{13}C NMR: δ 21.5 ($CH_2CH_2CH_2$), 23.0 (CH_2), 36.7 (CH_2–CO), 47.3 (CH_2Ar), 53.4 (CH), 110.2 (C^3 of pyrrole), 116.9 (C^{3a} of pyrrole), 122.4 (2×CH of Ar), 125.9 (2×CH of Ph), 127.3 (CH of Ph), 128.5 (CH of Ph), 128.7 (4×CH of Ph), 129.4 (C_{ipso} of Ph), 130.4 (2×CH of Ph), 134.9 (2×CH of Ar), 137.1 (C^{7a} of pyrrole), 137.3 (C_{ipso} of Ph), 141.8 (2×C_{ipso}–CO), 144.3 (C^2 of pyrrole). 192.7 (2×C=O), 198.4 (C=O); MS (EI, 70 eV): *m/z* (%)=445 [M$^+$], 401, 354, 298, 270, 139, 91. Anal. calcd for $C_{30}H_{23}NO_3$ (445.51): C, 80.88; H, 5.20; N, 3.14; found: C, 80.81; H, 5.26; N, 3.05%.

*2-(1-(2-Chlorobenzyl)-4-oxo-2-phenyl-4,5,6,7-tetrahydro-1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione* (**4b**): White powder, yield 0.30 g (63%); m.p. 201–203 °C; IR (KBr): 3060 (aromatic C–H), 2926 and 2862 (alkyl C–H), 1713 (C=O), 1644 (C=C), 1602 and 1466 (Ar), 1255 (C–N) cm^{-1}; ^{1}H NMR: δ 1.90–2.05 (m, 2 H, CH_2), 2.10–2.25 (m, 2 H, CH_2), 2.59–2.75 (m, 2 H, CH_2), 4.34 (s, 1 H, CH), 5.21 (s, 2 H, CH_2Bn), 6.46–6.62 (m, 1 H, CH of Ar), 7.20–7.52 (m, 8 H, 8×CH of Ar),



Scheme 1



Scheme 2 Mechanistic rationale for the synthesis of **4**.

7.82–8.02 (m, 4 H, 4×CH of Ar);. ^{13}C NMR: δ 21.2 ($CH_2CH_2CH_2$), 23.0 (CH_2), 36.7 (CH_2–CO), 45.5 (CH_2Ar), 53.3 (CH), 110.5 (C^3 of pyrrole), 117.0 (C^{3a} of pyrrole), 122.4 (2×CH of Ar), 126.5 (CH of Ar), 127.8 (CH of Ar), 128.6 (CH of Ph), 128.7 (2×CH of Ph), 129.1 (C_{ipso} of Ph), 129.2 (CH of Ar), 129.4 (CH of Ar), 130.1 (2×CH of Ph), 130.7 (C_{ipso} of Ar), 134.5 (C_{ipso} of Ar), 135.0 (2×CH of Ar), 137.1 (C^{7a} of pyrrole), 141.8 (2×C_{ipso}–CO), 144.5 (C^2 of pyrrole). 192.8 (2×C=O), 198.3 (C=O); MS (EI, 70 eV): *m/z* (%)=479 [M^+], 354, 326, 298, 165, 139, 125, 89. Anal. calcd for $C_{30}H_{22}ClNO_3$ (479.96): C, 75.07; H, 4.62; N, 2.92; found: C, 75.14; H, 4.68; N, 2.88%.

*2-(1-(4-Chlorobenzyl)-4-oxo-2-phenyl-4,5,6,7-tetrahydro-1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione* (**4c**): White powder, yield 0.35 g (72%); m.p. 205–207 °C; IR (KBr): 3051 (aromatic C–H), 2939 and 2855 (alkyl C–H), 1712 (C=O), 1641 (C=C), 1590 and 1481 (Ar), 1254 (C–N) cm^{-1}; ^{1}H NMR: δ 1.90–2.03 (m, 2 H, CH_2), 2.10–2.20 (m, 2 H, CH_2), 2.65–2.76 (m, 2 H, CH_2), 4.31 (s, 1 H, CH), 5.18 (s, 2 H, CH_2Bn), 6.92 (d, $^3J_{HH}$=7.2 Hz, 2 H, 2×CH of Ar), 7.38–7.50 (m, 7 H, 7×CH of Ar), 7.85–7.95 (m, 4 H, 4×CH of Ar); ^{13}C NMR: δ 21.4 ($CH_2CH_2CH_2$), 23.0 (CH_2), 36.7 (CH_2–CO), 46.7 (CH_2Ar), 53.3 (CH), 110.3 (C^3 of pyrrole), 116.9 (C^{3a} of pyrrole), 122.4 (2×CH of Ar), 127.8 (2×CH of Ph), 128.6 (CH of Ph), 128.7 (2×CH of Ar), 128.8 (2×CH of Ph), 129.3 (C_{ipso} of Ph), 130.4 (2×CH of Ar), 131.9 (C_{ipso}–Cl), 135.0 (2×CH of Ar), 136.3 (C_{ipso} of Ar), 137.0 (C^{7a} of pyrrole), 141.8 (2×C_{ipso}–CO), 144.3 (C^2 of pyrrole). 192.7 (2×C=O), 198.4 (C=O); MS (EI, 70 eV): *m/z* (%)=479 [M^+], 354, 298, 165, 139, 125, 89. Anal. calcd for $C_{30}H_{22}ClNO_3$ (479.96): C, 75.07; H, 4.62; N, 2.92; found: C, 75.13; H, 4.56; N, 2.99%.

*2-(1-(4-Methoxybenzyl)-4-oxo-2-phenyl-4,5,6,7-tetrahydro-1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione* (**4d**): White powder, yield 0.31 g (65%); m.p. 223–224 °C; IR (KBr): 3059 (aromatic C–H), 2926 and 2850 (alkyl C–H), 1713 (C=O), 1642 (C=C), 1600, 1509 and 1473 (Ar), 1252 (C–N) cm^{-1}; ^{1}H NMR: δ 1.82–2.02 (m, 2 H, CH_2), 2.06–2.22 (m, 2 H, CH_2), 2.64–2.85 (m, 2 H, CH_2), 3.71 (s, 3 H, OCH_3), 4.30 (s, 1 H, CH), 5.10 (s, 2 H, CH_2Bn), 6.70–6.98 (m, 4 H, 4×CH of Ar), 7.34–7.54 (m, 5 H, 5×CH of Ph), 7.80–8.00 (m, 4 H, 4×CH of Ar); ^{13}C NMR: δ 21.5 ($CH_2CH_2CH_2$), 23.0 (CH_2), 36.7 (CH_2–CO), 46.7 (CH_2Ar), 53.4 (CH), 55.0 (OCH_3), 110.1 (C^3 of pyrrole), 114.1 (2×CH of Ar), 116.8 (C^{3a} of pyrrole), 122.4 (2×CH of Ar), 127.4 (2×CH of Ph), 128.5 (CH of Ph), 128.7 (2×CH of Ph), 129.0 (C_{ipso} of Ar), 129.5 (C_{ipso} of Ph), 130.4 (2×CH of Ar), 134.9 (2×CH of Ar), 137.0 (C^{7a} of pyrrole), 141.8 (2×C_{ipso}–CO), 144.2 (C^2 of pyrrole). 158.4 (C_{ipso}–OMe), 192.7 (2×C=O), 198.5 (C=O); MS (EI, 70 eV): *m/z* (%)=475 [M^+], 354, 298, 139, 121, 91, 77. Anal. calcd for $C_{31}H_{25}NO_4$ (475.54): C, 78.30; H, 5.30; N, 2.95; found: C, 78.36; H, 5.39; N, 2.89%.

*2-(1-(4-Methylbenzyl)-4-oxo-2-phenyl-4,5,6,7-tetrahydro-1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione* (**4e**): White powder, yield 0.38 (82%); m.p. 237–239 °C; IR (KBr): 3023 (aromatic C–H), 2939 and 2854 (alkyl C–H), 1713 (C=O), 1639 (C=C), 1600 and 1476 (Ar), 1253 (C–N) cm^{-1}; ^{1}H NMR: δ 1.87–2.01 (m, 2 H, CH_2), 2.07–2.18 (m, 2 H, CH_2), 2.26 (s, 3 H, CH_3), 2.60–2.75 (m, 2 H, CH_2), 4.32 (s, 1 H, CH), 5.13 (s, 2 H, CH_2Bn), 6.80 (d, $^3J_{HH}$=6.8 Hz, 2 H, 2×CH of Ar), 7.13 (d, $^3J_{HH}$=6.8 Hz, 2 H, 2×CH of Ar), 7.35–7.46 (m, 5 H, 5×CH of Ph), 7.84–8.00 (m, 4 H, 4×CH of Ar); ^{13}C NMR: δ 20.6 (CH_3), 21.5 ($CH_2CH_2CH_2$), 23.0 (CH_2), 36.7 (CH_2–CO), 47.1 (CH_2Ar), 53.3 (CH), 110.0 (C^3 of pyrrole), 116.8 (C^{3a} of pyrrole), 122.4 (2×CH of Ar), 125.9 (2×CH of Ar), 128.5 (CH of Ph), 128.7 (2×CH of Ph), 129.3 (2×CH of Ar), 129.4 (C_{ipso} of Ph), 130.4 (2×CH of Ph), 134.2 (C_{ipso}–Me), 135.0 (2×CH of Ar), 136.5 (C_{ipso} of Ar), 137.1 (C^{7a} of pyrrole), 141.8 (2×C_{ipso}–CO), 144.2 (C^2 of pyrrole). 192.7 (2×C=O), 198.5 (C=O); MS (EI, 70 eV): *m/z* (%)=459 [M^+], 354, 298, 165, 139, 105, 77. Anal. calcd for $C_{31}H_{25}NO_3$ (459.54): C, 81.02; H, 5.48; N, 3.05; found: C, 80.97; H, 5.41; N, 3.12%.

*2-(1-Benzyl-6,6-dimethyl-4-oxo-2-phenyl-4,5,6,7-tetrahydro-1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione* (**4f**): White powder, yield 0.31 (66%); m.p. 217–219 °C; IR (KBr): 3054 (aromatic C–H), 2931

and 2865 (alkyl C–H), 1714 (C=O), 1649 (C=C), 1603 and 1467 (Ar), 1252 (C–N) cm^{-1}; ^1H NMR: δ 0.94 (s, 6 H, 2×CH_3), 2.05 (s, 2H, CH_2), 2.59 (s, 2 H, CH_2), 4.35 (s, 1H, s, CH), 5.18 (s, 2H, CH_2Bn), 6.89 (d, $^3J_{HH}$=6.8 Hz, 2 H, 2×CH_{ortho} of Ph), 7.27 (t, $^3J_{HH}$=6.0 Hz, 1 H, CH_{para} of Ph), 7.33 (, t, $^3J_{HH}$=6.4 Hz, 2 H, 2×CH_{meta} of Ph), 7.37–7.45 (m, 5 H, 5×CH of Ph), 7.85–7.95 (m, 4 H, 4×CH of Ar); ^{13}C NMR: δ 28.0 (2×CH_3), 35.0 (CH_2), 35.2 (*C*Me_2), 47.2 (CH_2Ph), 50.7 (*C*H_2–CO), 53.4 (CH), 110.1 (C^3 of pyrrole), 115.8 (C^{3a} of pyrrole), 122.4 (2×CH of Ar), 125.7 (2×CH of Ph), 127.3 (CH of Ph), 128.5 (CH of Ph), 128.6 (2×CH of Ph), 128.7 (2×CH of Ph), 129.4 (C_{ipso} of Ph), 130.3 (2×CH of Ph), 135.0 (2×CH of Ar), 137.3 (C^{7a} of pyrrole), 137.4 (C_{ipso} of Ph), 141.8 (2×C_{ipso}–CO), 143.1 (C^2 of pyrrole). 192.1 (2×C=O), 198.5 (C=O); MS (EI, 70 eV): *m/z* (%)=473 [M^+], 382, 326, 298, 167, 139, 91, 65. Anal. calcd for $C_{32}H_{27}NO_3$ (473.57): C, 81.16; H, 5.75; N, 2.96; found: C, 81.23; H, 6.00; N, 2.92%.

*2-(1-(2-Chlorobenzyl)-6,6-dimethyl-4-oxo-2-phenyl-4,5,6,7-tetrahydro-1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione* (**4g**): White powder, yield 0.36 (70%); m.p. 217–219 °C; IR (KBr): 3049 (aromatic C–H), 2952 and 2924 (alkyl C–H), 1714 (C=O), 1645 (C=C), 1602 and 1467 (Ar), 1254 (C–N) cm^{-1}; ^1H NMR: δ 0.95 (s, 6 H, 2×CH_3), 2.07 (s, 2 H, CH_2), 2.57 (s, 2 H, CH_2), 4.37 (s, 1 H, CH), 5.19 (s, 2 H, CH_2Bn), 6.50 (d, $^3J_{HH}$=6.8 Hz, 2 H, 2×CH of Ar), 7.30–7.42 (m, 7 H, 7×CH of Ar), 7.46 (d, $^3J_{HH}$=7.2 Hz, 1 H, CH of Ar), 7.85–7.95 (m, 4 H, 4×CH of Ar); ^{13}C NMR: δ 28.0 (2×CH_3), 34.9 (*C*Me_2), 35.1 (CH_2), 45.5 (CH_2Ar), 50.8 (*C*H_2–CO), 53.3 (CH), 110.5 (C^3 of pyrrole), 116.0 (C^{3a} of pyrrole), 122.4 (2×CH of Ar), 126.4 (CH of Ar), 127.7 (CH of Ar), 128.6 (CH of Ph), 128.7 (2×CH of Ph), 129.1 (C_{ipso} of Ph), 129.2 (CH of Ar), 129.4 (CH of Ar), 130.0 (2×CH of Ph), 130.6 (C_{ipso}–Cl), 134.7 (C_{ipso} of Ar), 135.0 (2×CH of Ar), 137.3 (C^{7a} of pyrrole), 141.8 (2×C_{ipso}–CO), 143.3 (C^2 of pyrrole).192.2 (2×C=O), 198.54 (C=O); MS (EI, 70 eV): *m/z* (%)=508 [M^+], 507, 416, 382, 326, 298, 167, 139, 125, 89. Anal. calcd for $C_{32}H_{26}ClNO_3$ (508.01): C, 75.66; H, 5.16; N, 2.76; found: C, 75.58; H, 5.11; N, 2.83%.

*2-(1-(4-chlorobenzyl)-6,6-dimethyl-4-oxo-2-phenyl-4,5,6,7-tetrahydro-1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione* (**4h**): White powder, yield 0.35 (69%); m.p. 276–278 °C; IR (KBr): 3052 (aromatic C–H), 2952, 2931 and 2866 (alkyl C–H), 1713 (C=O), 1643 (C=C), 1604 and 1478 (Ar), 1253 (C–N) cm^{-1}; ^1H NMR: δ 0.95 (s, 6 H, 2×CH_3), 2.05 (s, 2 H, CH_2), 2.59 (s, 2 H, CH_2), 4.34 (s, 1H, CH), 5.17 (s, 2 H, CH_2Bn), 6.90 (d, $^3J_{HH}$=7.6 Hz, 2 H, 2×CH of Ar), 7.35–7.46 (m, 7 H, 7×CH of Ar), 7.85–7.95 (m, 4 H, 4×CH of Ar); ^{13}C NMR: δ 28.0 (2×CH_3), 35.0 (CH_2), 35.1 (*C*Me_2), 46.6 (CH_2Ar), 50.7 (*C*H_2–CO), 53.3 (CH), 110.2 (C^3 of pyrrole), 115.9 (C^{3a} of pyrrole), 122.4 (2×CH of Ar), 127.6 (2×CH of Ph), 128.5 (CH of Ph), 128.7 (2×CH of Ar), 128.8 (2×CH of Ph), 129.3 (C_{ipso} of Ph), 130.3 (2×CH of Ar), 131.9 (C_{ipso}–Cl), 135.0 (2×CH of Ar), 136.5 (C_{ipso} of Ar), 137.2 (C^{7a} of pyrrole), 141.8 (2×C_{ipso}–CO), 143.0 (C^2 of pyrrole). 192.1 (2×C=O), 198.4 (C=O);. MS (EI, 70 eV): *m/z* (%)=507 [M^+], 382, 326, 298, 167, 139, 125, 83. Anal. calcd for $C_{32}H_{26}ClNO_3$ (508.01): C, 75.66; H, 5.16; N, 2.76; found: C, 75.71; H, 5.08; N, 2.71%.

*2-(1-(4-Methoxybenzyl)-6,6-dimethyl-4-oxo-2-phenyl-4,5,6,7-tetrahydro-1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione* (**4i**): White powder, yield 0.40 (80%); m.p. 254–246 °C;. IR (KBr): 3057 (aromatic C–H), 2951 and 2873 (alkyl C–H), 1713 (C=O), 1642 (C=C), 1582 and 1481 (Ar), 1249 (C–N) cm^{-1}; ^1H NMR: δ 0.95h (s, 6 H, 2×CH_3), 2.04 (s, 2 H, CH_2), 2.61 (s, 2 H, CH_2), 3.72 (s, 3 H, OCH_3), 4.32 (s, 1 H, CH), 5.10 (s, 2 H, CH_2Bn), 6.81 (d, $^3J_{HH}$=8.0 Hz, 2 H, 2×CH of Ar), 6.88 (d, $^3J_{HH}$=7.6 Hz, 2 H, 2×CH of Ar), 7.34–7.54 (m, 5H, 5×CH of Ph), 7.82–8.00 (m, 4 H, 4×CH of Ar); ^{13}C NMR: δ 28.1 (2×CH_3), 35.0 (CH_2), 35.2 (*C*Me_2), 46.7 (CH_2Ar), 50.8 (*C*H_2–CO), 53.4 (CH), 55.0 (OCH_3), 110.0 (C^3 of pyrrole), 114.1 (2×CH of Ar), 115.8 (C^{3a} of pyrrole), 122.4 (2×CH of Ar), 127.1 (2×CH of Ph), 128.4 (CH of Ph), 128.7 (2×CH of Ph), 129.2 (C_{ipso} of Ar), 129.5 (C_{ipso} of Ph), 130.3 (2×CH of Ar), 135.0 (2×CH of Ar), 137.2 (C^{7a} of pyrrole), 141.8 (2×C_{ipso}–CO), 143.0 (C^2 of pyrrole). 192.1 (2×C=O), 198.4 (C=O); MS (EI, 70 eV): *m/z* (%)=503 [M^+], 382, 326, 139, 121, 91, 77. Anal. calcd for $C_{33}H_{29}NO_4$ (503.59): C, 78.71; H, 5.80; N, 2.78; found: C, 78.75; H, 5.73; N, 2.83%.

*2-(6,6-Dimethyl-1-(4-methylbenzyl)-4-oxo-2-phenyl-4,5,6,7-tetrahydro-1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione* (**4j**): White powder, yield 0.38 (78%); m.p. 272–274 °C; IR (KBr): 3024 (aromatic C–H), 2927 and 2861 (alkyl C–H), 1714 (C=O), 1644 (C=C), 1606 and 1470 (Ar), 1251 (C–N) cm^{-1}; ^1H NMR: δ 0.94 (s, 6 H, 2×CH_3), 2.04 (s, 2 H, CH_2), 2.26 (s, 3 H, CH_3), 2.58 (s, 2 H, CH_2), 4.33 (s, 1 H, CH), 5.12 (s, 2 H, CH_2Bn), 6.78 (d, $^3J_{HH}$=6.8 Hz, 2 H, 2×CH of Ar), 7.13 (d, $^3J_{HH}$=7.2 Hz, 2 H, 2×CH of Ar), 7.36–7.46 (m, 5 H, 5×CH of Ph), 7.86–7.96 (m, 4H, 4×CH of Ar); ^{13}C NMR: δ 20.6 (CH_3), 28.1 (2×CH_3), 35.0 (CH_2), 35.2 (*C*Me_2), 47.0 (CH_2Ar), 50.8 (*C*H_2–CO), 53.4 (CH), 110.1 (C^3 of pyrrole), 115.8 (C^{3a} of pyrrole), 122.4 (2×CH of Ar), 125.6 (2×CH of Ar), 128.4 (CH of Ph), 128.7 (2×CH of Ph), 129.2 (2×CH of Ar), 129.4 (C_{ipso} of Ph), 130.3 (2×CH of Ph), 134.4 (C_{ipso} of Ar) 135.0 (2×CH of Ar), 136.4 (C_{ipso} of Ar), 137.2 (C^{7a} of pyrrole), 141.8 (2×C_{ipso}–CO), 143.0 (C^2 of pyrrole). 192.1 (2×C=O), 198.5 (C=O); MS (EI, 70 eV): *m/z* (%)=487 [M^+], 382, 326, 298, 133, 105, 83. Anal. calcd for $C_{33}H_{29}NO_3$ (487.59): C, 81.29; H, 5.99; N, 2.87; found: C, 81.21; H, 6.59; N, 2.78%.

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