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FULL-LENGTH PAPER

An efficient three-component synthesis of highly functionalized tetrahydroacenaphtho[1,2-*b*]indolone derivatives catalyzed by L-proline

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Abstract An efficient and diastereoselective synthetic procedure for highly functionalized tetrahydroacenaphtho[1,2-*b*]indolone derivatives was successfully developed by the three-component reaction of acenaphthequinone, enaminones, and barbituric acid in the presence of a catalytic amount of L-proline. This method has the advantages of convenient operation, excellent yields, mild reaction conditions, and environmental friendliness.

Keywords Tetrahydroacenaphtho[1, 2-*b*]indolone · Multicomponent reactions (MCRs) · Proline catalyst

Introduction

The development of a simple and highly efficient protocol for the synthesis of structurally complex, biologically active organic molecules from readily available starting materials is an attractive area of research in both academia and the pharmaceutical industry. One of the most promising approaches to this type of efficient synthesis relies on the use of multicomponent reactions (MCRs). MCRs have been widely used in organic synthesis and combinatorial chemistry due to their atom economy, excellent yields, easy execution, and productivity [1,2]. In the past decade, new MCRs (three- and four-component reactions) have been developed and used for the construction of important complex molecules [3–8].

Nitrogen-containing heterocycles remain part of many useful scaffolds holding pharmacophoric features that can act as potent and selective drugs for several diseases [9,10]. Among these heterocycles, the indole unit is one of the most important and abundant nitrogen-containing heterocycles in medicinal agents and natural products. Compounds containing an indole moiety display a broad range of biological activities including antitumor, antiviral, and anti-inflammatory activity [11–15]. The indole unit is also an important skeleton in organic and medicinal chemistry [16–18]. Some synthetic methodologies have been used for the construction of these important derivatives [19–22]. Recently, MCRs have been also used in the synthesis of several functionalized indole derivatives [23–25].

In recent years, L-proline has been widely used as a catalyst in organic synthesis because it is commercially available and has good solubility in organic solvents and water. L-Proline has been found to be as an efficient catalyst in organic reactions, such as asymmetric aldol condensation [26,27], Mannich reaction [28], Diels–Alder reaction [29], Michael addition [30], and several multicomponent reactions [31–34]. As part of our program to develop new methods for the construction of important heterocycles using L-proline as catalyst [35–38], we report herein an efficient method for the construction of pyrimidyl-fused tetrahydro-acenaphtho[1,2-*b*] indolone derivatives in the presence of a catalytic amount of L-proline.

Results and discussion

The three-component reaction of acenaphthylene-1,2-dione (**1**), 5,5- dimethyl-3-(*p*-tolylamino) cyclohex-2-enone (**2a**), and 1,3-dimethylpyrimidine-2,4,6(1*H*, 3*H*, 5*H*)-trione (**3a**) was initially selected as a model reaction to optimize the reaction conditions. The reaction, which consisted of a 1:1:1 molar mixture of **1**, **2a** and **3a**, was conducted under a variety of different conditions (Table 1). We assessed that

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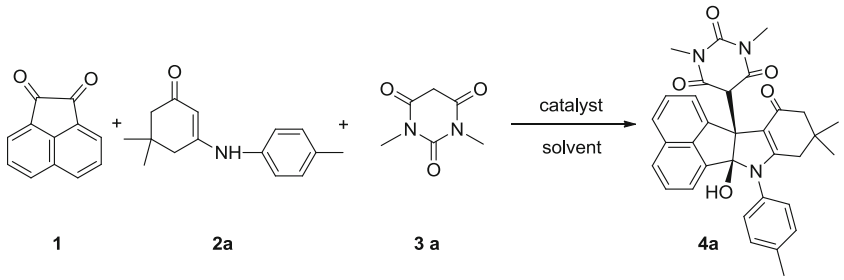
Table 1 Optimization study for the synthesis of **4a**



Entry	Solvent	Catalyst (mol%)	Temperature (°C)	Yield[a] (%)
1	Water	No	80	10
2	Water	L-proline (10)	80	22
3	$CHCl_3$	L-proline (10)	Reflux	13
4	1,4-Dioxane	L-proline (10)	Reflux	20
5	THF	L-proline (10)	Reflux	24
6	DMF	L-proline (10)	80	67
7	Toluene	L-proline (10)	80	28
8	Ethanol	L-proline (10)	Reflux	91
9	Ethanol	*p*-TSA (10)	Reflux	51
10	Ethanol	Piperidine (10)	Reflux	Trace
11	Ethanol	L-proline (5)	Reflux	46
12	Ethanol	L-proline (15)	Reflux	78
13	Ethanol	L-proline (20)	Reflux	53
14	Ethanol	L-proline (10)	r.t.	Trace
15	Ethanol	L-proline (10)	40	18
16	Ethanol	L-proline (10)	60	58

Reaction conditions: **1** (1 mmol), **2a** (1 mmol), **3a** (1 mmol), solvent (5 mL), 2h
[a] Isolated yield

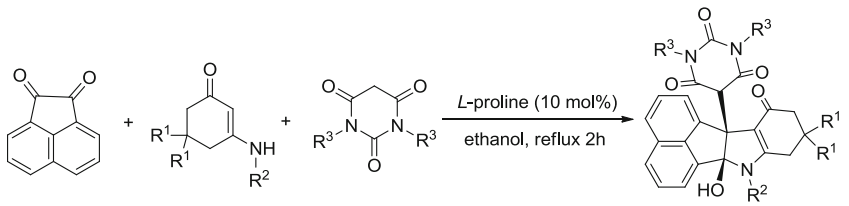
this reaction could not proceed when carried out in water under catalyst-free conditions at 80 °C (Table 1, entry 1). Pleasingly, the desired compound **4a** was obtained in 22 % yield when a catalytic amount of L-proline (10 mol%) was added (Table 1, entry 2). Various solvents were evaluated to determine their impact on the outcome of the reaction (Table 1, entries 3–8). The results of these screening experiments revealed that ethanol provided the best results from all the solvents tested. Other catalysts such as *p*-TSA and piperidine were evaluated; however, their catalytic efficiency was lower compared to L-proline (Table 1, entries 9–10).

Having identified L-proline as the best catalyst for this transformation, we proceeded to evaluate the amount of L-proline required to achieve optimum conversion. The results of these screening experiments showed that a 10 mol% loading of L-proline was sufficient to drive the reaction forward and provide the highest yield (Table 1, entries 8 and 11–13). The reaction was then conducted at a variety of different temperatures, including r.t., 40, 60 °C and refluxing temperature, to determine the optimum temperature for the transformation. The results indicated that when the reaction proceeded at reflux temperature, highest yields were obtained (Table 1, entries 8 and 14–16). Based on all our results, the optimum reaction conditions were determined to be 10 mol% L-proline in ethanol at reflux temperature.

To further explore the scope of this protocol, we examined the impact of substrate diversity on this three-component reaction using two barbituric acids and 17 enaminones. As shown in Table 2, electronic effects on the substrate had no significant influence on product yields. *n*-Butyl and phenyl groups bearing either electron-donating groups (e.g., methyl, ethyl, methoxy, and ethoxy groups) or electron-withdrawing groups (e.g., fluoro, chloro, bromo, and nitro groups), on the enaminone ring were tolerated under the reaction conditions, leading to the final products in good yields (81–93 %). Moreover, products were obtained in high purity by simply washing the crude products with cold ethanol, avoiding traditional purification via recrystallization or chromatography. This synthesis was confirmed to follow the group-assisted purification chemistry (GAP chemistry) process [39–41].

The structure of **4** was established by IR, ^{1}H NMR, and ^{13}C NMR spectroscopy, HRMS analysis, and it was further confirmed by X-ray diffraction analysis. The molecular structure of **4d** shown in Fig. 1 indicates that the hydroxy group at 2-position and the barbituric acid ring at 3-position all exist

Table 2 Synthesis of functionalized tetrahydroacenaphtho[1,2-*b*]indolone derivatives **4** via three-component reaction



1 **2** **3** **4**

Entry	Product	R^1	R^2	R^3	Isolated yield (%)
1	**4a**	CH_3	4-$CH_3C_6H_4$	CH_3	91
2	**4b**	CH_3	2-$C_2H_5C_6H_4$	CH_3	83
3	**4c**	CH_3	4-$CH_3OC_6H_4$	CH_3	89
4	**4d**	CH_3	4-BrC_6H_4	CH_3	90
5	**4e**	CH_3	2-ClC_6H_4	CH_3	82
6	**4f**	CH_3	4-FC_6H_4	CH_3	91
7	**4g**	CH_3	4-$NO_2C_6H_4$	CH_3	86
8	**4h**	CH_3	3-Cl-4-$CH_3C_6H_3$	CH_3	88
9	**4i**	CH_3	3-Cl-4-FC_6H_3	CH_3	89
10	**4j**	CH_3	*n*-C_4H_9	CH_3	90
11	**4k**	H	C_6H_5	CH_3	82
12	**4l**	H	4-BrC_6H_4	CH_3	84
13	**4m**	H	4-$C_2H_5OC_6H_4$	CH_3	80
14	**4n**	CH_3	4-$CH_3C_6H_4$	H	83
15	**4o**	CH_3	C_6H_5	H	81
16	**4p**	CH_3	4-$CH_3OC_6H_4$	H	84
17	**4q**	CH_3	3-ClC_6H_4	H	84
18	**4r**	CH_3	4-BrC_6H_4	H	84
19	**4s**	CH_3	4-$NO_2C_6H_4$	H	85
20	**4t**	CH_3	*n*-C_4H_9	H	90
21	**4u**	H	3,5-$(CH_3)_2C_6H_3$	H	92
22	**4v**	H	2,4-$(CH_3)_2C_6H_3$	H	91
23	**4w**	H	4-$C_2H_5OC_6H_4$	H	92
24	**4x**	H	4-BrC_6H_4	H	93

in *cis*-orientation justifying the high diastereoselectivity this three-component domino reaction exhibits.

Based on experimental observations, we have proposed a mechanism for this multicomponent domino reaction (Scheme 1). The initial reversible reaction of the acenaphthylene-1,2-dione **1** with L-proline would give iminum ion **5**. The intermediate **7** was formed by the Knoevenagel condensation of iminum ion **5** with barbituric acid **3**, and elimination of L-proline. Then the Michael addition of intermediate **7** with enaminones **2** would give the intermediate **8**, which would undergo intramolecular cyclization to give **4**.

In summary, we have developed an efficient and diastereoselective procedure for the construction of functionalized tetrahydroacenaphtho[1,2-*b*]indolone derivatives via the three- component domino reaction of acenaphthequinone, enaminones, and barbituric acid in the presence of a catalytic amount of L-proline (10 mol%). This method has the advantages of readily available starting materials, mild reaction conditions, and operational simplicity not requiring a product purification process.

Experimental section

General

All reagents and solvents were commercially available with analytical grade and used as received. All evaporations of organic solvents were carried out with a rotary evaporator in conjunction with a water aspirator. Melting points were determined on an electrothermal XT-5 apparatus and uncorrected. IR spectra were recorded on a Varian F-1000 spectrometer in KBr with absorption in cm^{-1}. ^1H NMR was recorded on a Varian Invoa-400 MHz spectrometer and ^{13}C NMR

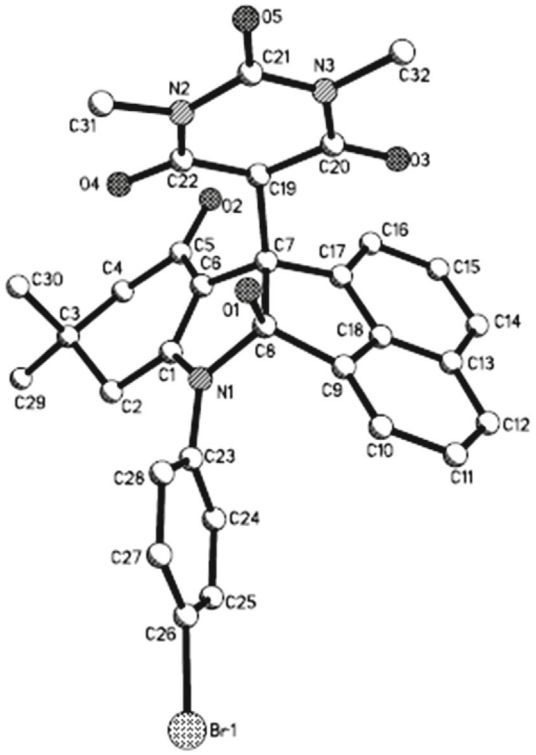


Fig. 1 Crystal structure of compound **4d**

was recorded on a Varian Invoa-300 MHz spectrometer in $CDCl_3$ or DMSO-d_6. J values are in Hz. Chemical shifts are expressed in ppm downfield from internal standard TMS. The abbreviations used for NMR signals are: s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. HRMS analyses were carried out using TOF-MS or GCT-TOF instrument. X-ray data were collected on a Bruker P4 diffractometer. Acenaphthylene-1,2-dione was obtained from HWRK company. 1,3-Dimethylbarbituric acid and barbituric acid were obtained from Alfa Aesar.

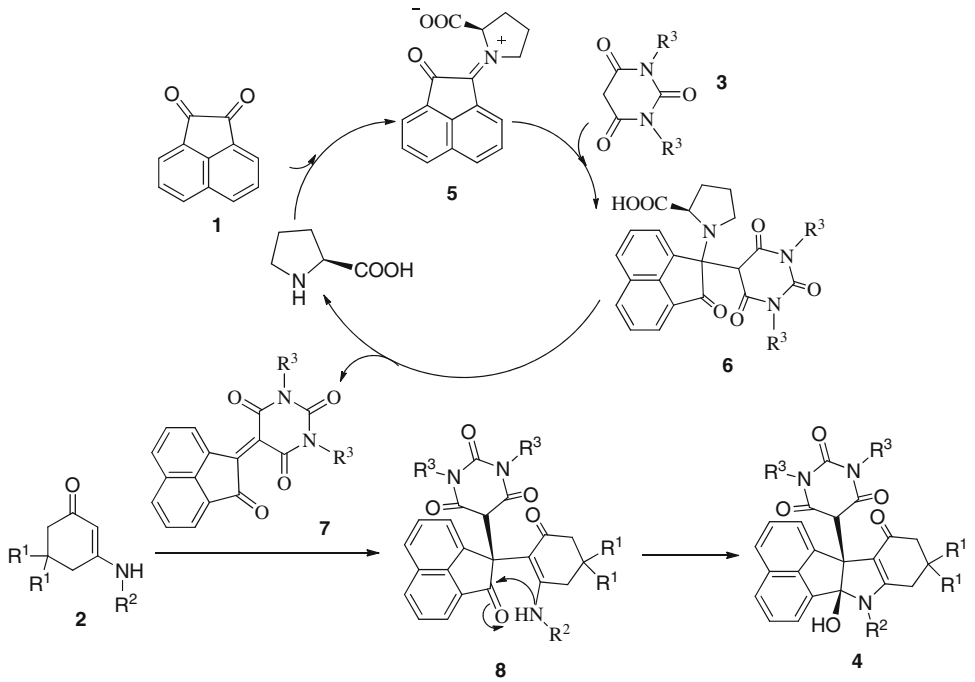
General procedure for the synthesis functionalized tetrahydroacenaphtho[1,2-*b*]indolone derivatives

A mixture of acenaphthylene-1,2-dione **1** (1 mmol), enaminone **2** (1 mmol), barbituric acid derivatives **3** (1 mmol), L-proline (0.1 mmol)m, and ethanol (2 mL) was refluxed for 2 h. After the completion of the reaction, the reaction mixture was then cooled to room temperature. The precipitate was collected by Büchner filtration and washed with a small portion of cold ethanol to give pure products **4a**–**4x** for analysis.

*5-(6b-Hydroxy-9,9-dimethyl-11-oxo-7-(p-tolyl)-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**4a**)*

White solid, yield: 91 %. m.p. 249–251 °C. IR (KBr): 3458, 2927, 1680, 1564, 1511, 1446, 1370, 1227, 1211, 1145, 1108, 1040, 1022, 984, 787, 737 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.71–7.63 (m, 4H, ArH), 7.48 (t, J = 7.2 Hz, 1H, ArH), 7.31–7.23 (m, 3H, ArH), 6.92 (s, 2H, ArH), 6.46 (d, J = 4.0 Hz, 1H, CH), 5.09 (s, 1H, OH), 3.15 (s, 3H, NCH_3), 2.87 (s, 3H, NCH_3), 2.18–1.94 (m, 3H, CH_2), 1.69 (d, J = 17.2 Hz, 1H, CH_2), 1.08 (s, 3H, CH_3), 0.80 (s, 3H,

Scheme 1 Proposed mechanism for the synthesis of **4**



CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 190.4, 170.6, 167.1, 164.9, 151.5, 129.7, 128.0, 127.1, 125.5, 124.0, 122.7, 119.8, 109.2, 107.1, 66.8, 50.8, 50.5, 37.5, 33.5, 29.6, 29.0, 28.8, 28.6, 27.3, 21.2. HRMS (ESI) Calcd. for $C_{33}H_{30}N_3O_5$ ([M−H]$^-$): 548.2185. Found: 548.2191.

5-(7-(2-Ethylphenyl)-6b-hydroxy-9,9-dimethyl-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**4b**)

Light pink solid, yield 83 %. m.p. 236–239 °C. IR (KBr): 3629, 3102, 2957, 1680, 1560, 1489, 1434, 1368, 1323, 1276, 1181, 1167, 1142, 1040, 1122, 979, 798, 757, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.75–7.41 (m, 9H, ArH), 7.04 (m, 2H, ArH + CH), 6.04 (s, 1H, OH), 3.42 (s, 3H, NCH_3), 3.23 (s, 3H, NCH_3), 3.03 (s, 1H, CH_2), 2.91 (s, 1H, CH_2), 2.14–2.00 (m, 2H, CH_2), 1.72 (s, 2H, CH_2), 1.43 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 0.80 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 199.8, 166.0, 165.8, 150.9, 142.1, 135.4, 132.6, 132.1, 131.7, 130.6, 130.4, 128.6, 128.4, 128.1, 126.1, 125.8, 122.7, 122.0, 121.9, 58.7, 52.8, 50.8, 36.3, 28.8, 28.7, 23.17, 22.0. HRMS (ESI) Calcd. for $C_{34}H_{32}N_3O_5$ ([M−H]$^-$): 562.2342. Found: 562.2341.

5-(6b-Hydroxy-7-(4-methoxyphenyl)-9,9-dimethyl-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**4c**)

White solid, yield 89 %. m.p. 210–212 °C. IR (KBr): 3416, 3100, 2955, 1693, 1609, 1561, 1511, 1448, 1383, 1248, 1143, 1023, 786, 755, 665 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.72–7.63 (m, 4H, ArH), 7.48 (t, J = 7.2 Hz, 1H, ArH), 7.32 (t, J = 6.8 Hz, 1H, ArH), 6.98 (s, 4H, ArH), 6.48 (d, J= 5.6 Hz, 1H, CH), 5.09 (s, 1H, OH), 3.80 (s, 3H, OCH_3), 3.15 (s, 3H, NCH_3), 2.87 (s, 3H, NCH_3), 2.12 (d, J = 17.2 Hz, 1H, CH_2), 1.99 (s, 2H, CH_2), 1.69 (d, J = 17.2 Hz, 1H, CH_2), 1.09 (s, 3H, CH_3), 0.79 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 190.1, 170.6, 167.4, 165.0, 160.0, 151.4, 140.8, 138.6, 135.8, 131.1, 127.9, 127.1, 125.5, 123.9, 122.7, 119.5, 114.2, 109.2, 107.0, 66.6, 55.4, 50.8, 50.4, 37.4, 33.4, 29.5, 29.0, 28.5, 27.3. HRMS (ESI) Calcd. for $C_{33}H_{30}N_3O_6$ ([M−H]$^-$):564.2135. Found: 564.2138.

5-(7-(4-Bromophenyl)-6b-hydroxy-9,9-dimethyl-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**4d**)

White solid, yield 90 %. m.p. 244–247 °C. IR (KBr): 3471, 3077, 2923, 1677, 1555, 1503, 1447, 1360, 1287, 1146, 1041, 1037, 789, 750, 681 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.88–7.02 (m, 10H, ArH), 6.49 (s, 1H, CH), 5.15 (s, 1H, OH), 3.16 (s, 3H, NCH_3), 2.86 (s, 3H, NCH_3), 2.24−1.72 (m, 4H, 2 × CH_2), 1.12 (s, 3H, CH_3), 0.82 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 190.8, 170.5, 167.0, 164.1, 151.4, 132.4, 131.5, 131.2, 128.1, 127.2, 125.8, 119.6, 109.9, 107.1, 66.9, 50.7, 50.5, 37.6, 33.6, 29.7, 29.1, 28.6, 27.2. HRMS (ESI) Calcd. for $C_{32}H_{27}BrN_3O_5$ ([M−H]$^-$): 612.1134, Found: 612.1144.

5-(7-(2-Chlorophenyl)-6b-hydroxy-9,9-dimethyl-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**4e**)

Light pink solid, yield 82 %. m.p. 248–250 °C. IR (KBr): 3450, 3080, 2929, 1688, 1563, 1501, 1449, 1371, 1299, 1041, 1023, 788, 745, 669 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.83–7.26 (m, 10H, ArH), 6.37 (s, 1H, CH), 5.09 (s, 1H, OH), 3.15 (s, 3H, NCH_3), 2.87 (s, 3H, NCH_3), 2.11–1.67 (m, 4H, 2 × CH_2), 1.04 (s, 3H, CH_3), 0.73 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 191.0, 170.9, 166.8, 165.2, 151.4, 135.1, 133.4, 131.0, 130.3, 130.0, 128.0, 127.7, 127.3, 125.6, 124.1, 122.5, 118.8, 66.9, 50.7, 50.6, 36.9, 33.7, 29.0, 28.9, 28.6, 28.1. HRMS (ESI) Calcd. for $C_{32}H_{27}ClN_3O_5$([M−H]$^-$): 568.1639, Found: 568.1630.

5-(7-(4-Fluorophenyl)-6b-hydroxy-9,9-dimethyl-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**4f**)

White solid, yield 91 %. m.p. 236–239 °C. IR (KBr): 3459, 3069, 2956, 2829, 1693, 1675, 1603, 1561, 1510, 1442, 1371, 1222, 1146, 1040, 1022, 982, 809, 781, 698 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.78–7.73 (m, 4H, ArH), 7.49 (t, J = 7.6 Hz, 1H, ArH), 7.33–7.27 (m, 3H, ArH), 7.07 (s, 2H, ArH), 6.44 (d, J = 6.0 Hz, 1H, CH), 5.09 (s, 1H, OH), 3.15 (s, 3H, NCH_3), 2.85 (s, 3H, NCH_3), 2.19 (d, J = 17.2 Hz, 1H, CH_2), 2.01 (s, 2H, CH_2), 1.70 (d, J = 17.2 Hz, 1H, CH_2), 1.11 (s, 3H, CH_3), 0.81 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 190.6, 170.4, 167.0, 164.3, 162.3 (d, J_{CF} = 239.3 Hz), 151.3, 140.7, 138.6, 135.6, 131.8 (d, J_{CF} = 8.3 Hz), 131.5, 131.2, 128.1, 127.0, 125.6, 124.1, 122.8, 119.6, 116.1 (d, J_{CF} = 22.5 Hz), 109.5, 107.1, 66.8, 50.7, 50.4, 37.5, 33.6, 29.6, 29.1, 28.6, 27.3. HRMS (ESI) Calcd. for $C_{32}H_{27}FN_3O_5$([M−H]$^-$): 552.1935, Found: 552.1940.

5-(6b-Hydroxy-9,9-dimethyl-7-(4-nitrophenyl)-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**4g**)

Yellow solid, yield 86 %. m.p. 256–259 °C. IR (KBr): 3458, 3067, 2929, 1695, 1672, 1601, 1573, 1493, 1439, 1417, 1372, 1351, 1278, 1143, 1017, 982, 798, 724 cm^{-1}. ^{1}H NMR (400

MHz, DMSO-d_6) δ (ppm): 8.28 (d, J = 8.4 Hz, 2H, ArH), 8.19 (s, 1H, ArH), 7.72–7.63 (m, 3H, ArH), 7.51 − 7.42 (m, 3H, ArH), 7.26 (t, J = 7.2 Hz, 1H, ArH), 6.50 (s, 1H, ArH), 5.19 (s, 1H, OH), 3.16 (s, 3H, NCH_3), 2.85 (s, 3H, NCH_3), 2.45 (d, J = 17.2 Hz, 1H, CH_2), 2.13–2.01 (m, 2H, CH_2), 1.80 (d, J = 17.2 Hz, 1H, CH_2), 1.15 (s, 3H, CH_3), 0.88 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 191.4, 170.4, 166.8, 162.8, 151.3, 146.9, 142.3, 138.4, 131.2, 129.8, 128.2, 127.2, 126.0, 124.5, 123.3, 122.9, 119.2, 111.5, 107.6, 50.4, 38.0, 33.9, 29.9, 29.1, 28.6, 26.9. HRMS (ESI) Calcd. for $C_{32}H_{27}N_4O_7$([M−H]$^-$): 579.1880, Found: 579.1866.

*5-(7-(3-Chloro-4-methylphenyl)-6b-hydroxy-9,9-dimethyl-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (***4h***)*

White solid, yield 88 %. m.p. 236–237 °C. IR (KBr): 3448, 2952, 1692, 1673, 1571, 1493, 1438, 1420, 1370, 1276, 1142, 1043, 1017, 984, 790, 757, 731 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.86–7.24 (m, 8H, ArH), 6.83 (s, 1H, ArH), 6.49 (s, 1H, CH), 5.13 (s, 1H, OH), 3.16 (s, 3H, NCH_3), 2.86 (s, 3H, NCH_3), 2.38 (s, 3H, CH_3), 2.25 (d, J = 16.4 Hz, 1H, CH_2), 2.01 (s, 2H, CH_2), 1.73 (d, J = 16.0 Hz, 1H, CH_2), 1.12 (s, 3H, CH_3), 0.82 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 190.7, 170.5, 167.0, 164.3, 151.4, 131.1, 128.0, 127.2, 125.7, 124.1, 122.8 119.7, 109.7, 107.1, 66.8, 50.7, 50.4, 37.6, 33.6, 29.7, 29.1, 28.6, 27.2, 19.9. HRMS (ESI) Calcd. for $C_{33}H_{30}ClN_3O_5$ ([M]$^+$): 583.1874, Found: 583.1864.

*5-(7-(3-Chloro-4-fluorophenyl)-6b-hydroxy-9,9-dimethyl-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (***4i***)*

White solid, yield 89 %. m.p. 228–232 °C. IR (KBr): 3485, 2957, 1707, 1690, 1553, 1496, 1442, 1406, 1256, 1222, 1145, 1060, 1017, 983, 780, 753, 712 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.91 (s, 1H,ArH), 7.74–7.64 (m, 3H, ArH), 7.51–7.31 (m, 4H, ArH), 6.99 (s, 1H, ArH), 6.48 (d, J = 5.6 Hz, 1H, CH), 5.14 (s, 1H, OH), 3.16 (s, 3H, NCH_3), 2.85 (s, 3H, NCH_3), 2.29 (d, J = 17.2 Hz, 1H, CH_2), 2.02 (s, 2H, CH_2), 1.74 (d, J = 17.2 Hz, 1H, CH_2), 1.13 (s, 3H, CH_3), 0.84 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 190.9, 170.4, 166.9, 163.8, 157.9 (d, J_{CF} = 252.0 Hz), 151.3, 140.3, 138.5, 135.7, 132.2, 131.1, 129.9(d, J_{CF} = 5.3 Hz), 128.1, 127.1, 125.8, 124.1, 122.8, 119.5, 116.8 (d, J_{CF} = 21.0 Hz), 110.0, 107.1, 66.8, 50.6, 50.4, 37.5, 33.6, 29.6, 29.0, 28.6, 27.2. HRMS (ESI) Calcd. for $C_{32}H_{27}ClFN_3O_5$([M]$^+$): 587.1623, Found: 587.1624.

*5-(7-Butyl-6b-hydroxy-9,9-dimethyl-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (***4j***)*

White solid, yield 90 %. m.p. 216–217 °C. IR (KBr): 3450, 2958, 2872, 1742, 1681, 1549, 1480, 1428, 1368, 1276, 1180, 1139, 1025, 939, 806, 787, 756 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.78–7.46 (m, 7H, ArH + CH), 4.90 (s, 1H, OH), 3.43 (s, 2H, CH_2), 3.09 (s, 3H, NCH_3), 2.91 (s, 3H, NCH_3), 2.27–2.11 (m, 2H, CH_2), 2.00–1.87 (m, 2H, CH_2), 1.51–1.12 (m, 7H, 2 × CH_2 + CH_3), 0.89 (s, 3H, CH_3), 0.78 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 189.1, 170.7, 166.8, 165.0, 151.5, 131.2, 128.2, 127.2, 125.8, 123.9, 122.7, 118.7, 108.0, 106.6, 66.2, 50.8, 50.1, 41.9, 36.8, 33.4, 33.1, 29.5, 28.9, 28.5, 27.7, 20.3, 13.8. HRMS (ESI) Calcd. for $C_{30}H_{33}N_3O_5$[M]$^+$): 515.2420, Found: 515.2416.

*5-(6b-Hydroxy-11-oxo-7-phenyl-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (***4k***)*

White solid, yield 82 %. m.p. 241–242 °C. IR (KBr): 3424, 2955, 1682, 1566, 1493, 1456, 1419, 1372, 1320, 1189, 1150, 1019, 981, 828, 791, 781, 695 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.76–7.63 (m, 4H, ArH), 7.52 − 7.43 (m, 4H, ArH), 7.28 (t, J = 7.2 Hz, 1H, ArH), 7.11 (s, 2H, ArH), 6.42 (d, J = 6.0 Hz, CH), 5.06 (s, 1H, OH), 3.17 (s, 3H, NCH_3), 2.88 (s, 3H, NCH_3), 2.28–1.75 (m, 6H, 3 × CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) : δ (ppm): 191.0, 170.4, 167.0, 165.8, 151.3, 131.0, 129.8, 128.9, 128.5, 127.8, 127.0, 125.5, 110.1, 106.7, 66.8, 51.0, 36.2, 28.7, 28.4, 24.0, 21.9. HRMS (ESI) Calcd. for $C_{30}H_{24}N_3O_5$([M−H]$^-$): 506.1716, Found: 506.1753.

*5-(7-(4-Bromophenyl)-6b-hydroxy-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (***4l***)*

Light gray solid, yield 84 %. m.p. 181–184 °C. IR (KBr): 3394, 2948, 2880, 1681, 1601, 1578, 1561, 1491, 1420, 1362, 1326, 1190, 1139, 1069, 1011, 844, 786, 755 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.87–7.50 (m, 7H, ArH), 7.32 (s, 1H, ArH), 7.07 (s, 2H, ArH), 6.48 (s, 1H, CH), 5.08 (s, 1H, OH), 3.16 (s, 3H, NCH_3), 2.87 (s, 3H, NCH_3), 2.25–1.76 (m, 6H, 3 × CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 191.3, 170.3, 167.0, 165.3, 151.2, 132.2, 131.4, 131.0, 128.0, 127.1, 125.7, 124.0, 123.0, 122.6, 119.5, 106.7, 66.9, 58.1, 50.9, 36.2, 28.8, 28.4, 24.0, 21.9, 18.3. HRMS (ESI) Calcd. for $C_{30}H_{24}BrN_3O_5$ ([M]$^+$): 585.0899, Found: 585.0859.

*5-(7-(4-Ethoxyphenyl)-6b-hydroxy-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (***4m***)*

Light yellow solid, yield 80 %. m.p. 219–221 °C. IR (KBr): 3428, 2954, 1701, 1686, 1560, 1509, 1453, 1432, 1380, 1247, 1141, 1021, 923, 788, 757 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.73–7.63 (m, 4H, ArH), 7.51 (d, J = 6.4Hz, 1H, ArH), 7.33 (s, 1H, ArH), 6.98 (s, 4H, ArH), 6.50 (s, 1H, CH), 5.04 (s, 1H, OH), 4.05 (d, J = 5.2 Hz, 2H, CH_2), 3.17 (s, 3H, NCH_3), 2.90 (s, 3H, NCH_3), 2.14–1.72 (m, 6H, 3 × CH_2), 1.36 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 191.0, 170.6, 167.2, 166.4, 159.0, 151.5, 139.0, 136.1, 131.1, 128.0, 127.8, 127.1, 125.6, 124.0, 123.1, 119.9, 114.8, 106.8, 66.9, 63.7, 51.2, 36.3, 28.8, 28.5, 24.0, 22.0, 14.8. HRMS (ESI) Calcd. for $C_{32}H_{28}N_3O_6$ ($[M-H]^-$): 550.1978, Found: 550.1975.

*5-(6b-Hydroxy-9,9-dimethyl-11-oxo-7-(p-tolyl)-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (***4n***)*

Light yellow solid, yield 83 %. m.p. 242–247 °C. IR (KBr): 3467, 3000, 2026, 1631, 1557, 1511, 1480, 1404, 1385, 1120, 1032, 845, 774, 722, 672 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.92 (s, 1H, NH), 10.56 (s, 1H, NH), 7.95 (s, 1H, ArH), 7.74–7.58 (m, 3H, ArH), 7.46 (s, 1H, ArH), 7.22 (s, 3H, ArH), 6.92 (s, 2H, ArH), 6.44 (s, 1H, CH), 4.95 (s, 1H, OH), 2.35 (s, 3H, CH_3), 2.18 (d, J = 16.0 Hz, 1H, CH_2), 2.08–1.93 (m, 2H, CH_2), 1.64 (d, J = 16.0 Hz, 1H, CH_2), 1.13 (s, 3H, CH_3), 0.82 (s, 3H, CH_3). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm): 190.0, 168.6, 168.5, 159.9, 151.3, 146.7, 141.4, 137.4, 136.2, 134.2, 131.1, 129.9, 129.5, 128.7, 126.7, 124.9, 122.2, 119.5, 119.2, 112.0, 104.9, 66.4, 50.9, 47.9, 37.2, 34.0, 30.2, 27.8, 21.2. HRMS (ESI) Calcd. for $C_{31}H_{28}N_3O_5$ ($[M+H]^+$): 522.2029, Found: 522.2037.

*5-(6b-Hydroxy-9,9-dimethyl-11-oxo-7-phenyl-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (***4o***)*

Light pink solid, yield 81 %. m.p. 228–233 °C. IR (KBr): 3527, 3197, 3056, 2962, 2843, 1741, 1721, 1686, 1608, 1561, 1496, 1421, 1402, 1355, 1180, 925, 795, 780, 724 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.93 (s, 1H, NH), 10.56 (s, 1H, NH), 8.00 (s, 1H, ArH), 7.74–7.59 (m, 3H, ArH), 7.45 (t, J = 8.0 Hz, 4H, ArH), 7.22 (t, J = 6.4 Hz, 1H, ArH), 7.04 (s, 2H, ArH), 6.39 (d, J = 6.4 Hz, 1H, CH), 4.97 (s, 1H, OH), 2.23 (d, J = 16.8 Hz, 1H, CH_2), 2.08–1.95 (m, 2H, CH_2), 1.66 (d, J = 17.2 Hz, 1H, CH_2), 1.14 (s, 3H, CH_3), 0.83 (s. 3H, CH_3). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm): 189.9, 168.2, 159.4, 150.8, 146.3, 141.0, 136.7, 135.6, 130.7, 129.3, 128.4, 127.6, 126.4, 124.4, 121.8, 119.3, 118.8, 112.1, 104.8, 66.2, 56.2, 50.6, 47.6, 37.0, 33.8, 30.00, 27.4, 18.7. HRMS (ESI) Calcd. for $C_{30}H_{24}N_3O_5$ ($[M-H]^-$): 506.1716, Found: 506.1729.

*5-(6b-Hydroxy-7-(4-methoxyphenyl)-9,9-dimethyl-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (***4p***)*

Yellow solid, yield 84 %. m.p. 214–217 °C. IR (KBr): 3422, 2897, 1715, 1644, 1511, 1442, 1371, 1164, 1112, 1060, 1033, 896, 664 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.92 (s, 1H, NH), 10.55 (s, 1H, NH), 7.89 (s, 1H, ArH), 7.40–7.59 (m, 3H, ArH), 7.47 (t, J = 7.6 Hz, 1H, ArH), 7.27 (t, J = 7.2 Hz, 1H, ArH), 6.97 (d, J = 6.0 Hz, 4H, ArH), 6.46 (d, J = 9.2 Hz, 1H, CH), 4.95 (s, 1H, OH), 3.79 (s, 1H, CH_3), 2.13 (d, J = 16.8 Hz, 1H, CH_2), 2.05–1.93 (m, 2H, CH_2), 1.64 (d, J = 16.8 Hz, 1H, CH_2), 1.13 (s, 3H, CH_3), 0.81 (s, 3H, CH_3). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm): 189.9, 168.6, 160.3, 158.9, 151.5, 147.1, 141.8, 136.3, 131.4, 129.2, 128.4, 126.9, 124.9, 122.1, 119.5, 114.5, 112.3, 104.9, 66.3, 56.2, 51.4, 47.6, 36.8, 34.0, 31.2, 30.3, 27.8. HRMS (ESI) Calcd. for $C_{31}H_{28}N_3O_6$ ($[M+H]^+$): 538.1978, Found: 538.1994.

*5-(7-(3-Chlorophenyl)-6b-hydroxy-9,9-dimethyl-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (***4q***)*

White solid, yield 84 %. m.p. 243–245 °C. IR (KBr): 3416, 3239, 3098, 2956, 2869, 1702, 1562, 1478, 1420, 1404, 1346, 1119, 1026, 823, 792, 779, 731 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.97 (s, 1H, NH), 10.60 (s, 1H, NH), 8.16 (s, 1H, ArH), 7.73–7.60 (m, 3H, ArH), 7.50–7.40 (m, 3H, ArH), 7.27 (t, J = 6.0 Hz, 2H, ArH), 6.91 (d, J = 6.8 Hz, 1H, ArH), 6.45 (d, J = 6.8 Hz, 1H, ArH), 4.98 (s, 1H, OH), 2.32 (d, J = 16.8 Hz, 4H, CH_2), 2.12-1.96 (m, 2H, CH_2), 1.68 (d, J = 16.8 Hz, 1H, CH_2), 1.16 (s, 3H, CH_3), 0.86 (s, 3H, CH_3). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm): 190.4, 168.3, 168.1, 158.8, 151.0, 146.1, 140.8, 138.3, 135.8, 133.2, 130.9, 130.6, 128.9, 128.4, 127.9, 127.6, 126.4, 124.9, 122.0, 119.3, 118.6, 112.7, 104.9, 66.2, 50.7, 47.6, 36.8, 33.9, 30.1, 27.2. HRMS (ESI) Calcd. for $C_{30}H_{26}N_3O_5$ ($[M+H]^+$): 508.1872, Found: 508.1906.

*5-(7-(4-Bromophenyl)-6b-hydroxy-9,9-dimethyl-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (***4r***)*

Light gray solid, yield 84 %. m.p. 237–241 °C. IR (KBr): 3530, 3209, 3103, 2957, 2868, 1714, 1575, 1561, 1491, 1429, 1397, 1342, 1282, 1012, 823, 790, 776 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.96 (s, 1H, NH), 10.60 (s, 1H, NH), 8.16 (s, 1H, ArH), 7.73–7.60 (m, 3H, ArH), 7.50–7.40 (m, 3H, ArH), 7.27 (t, J = 7.6 Hz, 2H, ArH), 6.91 (d, J = 6.8 Hz, 1H, ArH), 6.68 (d, J = 6.8 Hz, 1H, CH), 4.98 (s, 1H,

OH), 2.32 (d, J = 16.8 Hz, 1H, CH_2), 2.12–1.96 (m, 2H, CH_2), 1.68 (d, J = 17.2 Hz, 1H, CH_2), 1.14 (s, 3H, CH_3), 0.84 (s, 3H, CH_3). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm): 190.3, 168.2, 159.0, 150.8, 146.2, 140.9, 136.1, 132.2, 131.3, 130.9, 128.5, 126.5, 124.6, 122.1, 120.5, 119.3, 118.6, 112.6, 104.8. HRMS (ESI) Calcd. for $C_{30}H_{23}BrN_3O_5$ ([M−H]$^-$): 584.0821, Found: 584.0812.

*5-(6b-Hydroxy-9,9-dimethyl-7-(4-nitrophenyl)-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (***4s***)*

Yellow solid, yield 85 %. m.p. 232–235 °C. IR (KBr): 3442, 3020, 2989, 1761, 1716, 1695, 1579, 1523, 1495, 1421, 1395, 1348, 1284, 1114, 1022, 828, 788 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.97 (s, 1H, NH), 10.63 (s, 1H, NH), 8.43 (s, 1H, ArH), 8.26 (d, J = 8.0 Hz, 2H, ArH), 7.71–7.60 (m, 3H, ArH), 7.49−7.40 (m, 3H, ArH), 7.23 (t, J = 6.8 Hz, 1H, ArH), 6.47 (d, J = 6.0 Hz, 1H, CH), 5.01 (s, 1H, OH), 2.14–1.72 (m, 2H, 2 × CH_2), 1.16 (s, 3H, CH_3), 0.89 (s, 3H, CH_3). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm): 191.2, 168.6, 167.7, 157.8, 151.1, 146.0, 145.42, 143.6, 140.6, 135. 6, 131.0, 129.0, 126.6, 124.3, 122.2, 119.3, 118. 6, 114.3, 105.4, 66.3, 50.7, 47.7, 37.1, 34.2, 30.3, 27.0. HRMS (ESI) Calcd. for $C_{30}H_{23}N_4O_7$ ([M−H]$^-$): 551.1567, Found: 551.1571.

*5-(7-Butyl-6b-hydroxy-9,9-dimethyl-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (***4t***)*

Light gray solid, yield 90 %. m.p. 238–241 °C. IR (KBr): 3215, 3109, 2958, 2871, 1731, 1545, 1487, 1434, 1340, 1280, 1135, 1114, 1020, 881, 794, 779 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.80 (s, 1H, NH), 10.50 (s, 1H, NH), 7.81–7.44 (m, 7H, ArH + CH), 4.83 (s, 1H, OH), 2.16 (d, J = 14.8 Hz, 2H, CH_2), 1.93 (d, J = 16.8 Hz, 2H, CH_2), 1.59–0.84 (m, 15H, 3 × CH_2 + 3 × CH_3). ^{13}C NMR (75MHz, DMSO-d_6) δ (ppm): 188.1, 168.2, 160.9, 151.2, 146.5, 142.2, 136.9, 130.9, 128.6, 126.9, 124.7, 121.9, 119.3, 118.3, 109. 8, 103.8, 65.9, 50.5, 47.5, 35.8, 33.5, 32.6, 29.4, 28.1, 19.8, 13.9. HRMS (ESI) Calcd. for $C_{28}H_{29}N_3O_5$ ([M]$^+$): 487.2107, Found: 487.2092.

*5-(7-(3,5-Dimethylphenyl)-6b-hydroxy-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (***4u***)*

Light gray olid, yield 92 %. m.p. 229–230 °C. IR (KBr): 3217, 3096, 3002, 2943, 2899, 1710, 1555, 1453, 1407, 1328, 1192, 1025, 827, 784 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.89 (s, 1H, NH), 10.56 (s, 1H, NH), 7.95 (s, 1H, ArH), 7.77–7.46 (m, 4H, ArH), 7.25 (t, J = 7.2 Hz, 1H, ArH), 7.01 (s, 1H, ArH), 6.72 (s, 2H, ArH), 6.46 (d, J = 6.0 Hz, 1H, CH), 4.91 (s, 1H, OH), 2.25 (s, 6H, 2 × CH_3), 2.14 − 1.74 (m, 6H, 3 × CH_2). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm): 190.7, 168.4, 168.1, 160.5, 151.1, 140.8, 138.1, 136.6, 136.0, 130.8, 129.0, 128.3, 126.4, 124.8, 121.9, 119.7, 119.0, 112.9, 104.5, 66.7, 47.2, 36.7, 23.8, 22.1, 20.9. HRMS (ESI) Calcd. for $C_{30}H_{24}N_3O_5$ ([M−H]$^-$): 506.1716, Found: 506.1740.

*5-(7-(2,4-Dimethylphenyl)-6b-hydroxy-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (***4V***)*

Gray solid, yield 91 %. m.p. 232–235 °C. IR (KBr): 3218, 3086, 2925, 2876, 1710, 1550, 1459, 1400, 1328, 1025, 833, 789 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.90 (s, 1H, NH), 10.57 (s, 1H, NH), 7.91–6.97 (m, 9H, ArH), 6.43 (s, 1H, CH), 4.97 (s, 1H, OH), 2.32–0.87 (m, 12H, 2 × CH_3 + 3 × CH_2). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm): 190.4, 168.3, 168.1, 161.6, 151.1, 146.3, 140.4, 137.9, 137.2, 136.3, 132.0, 131.3, 130.7, 128.6, 127.4, 126.5, 124.7, 122.0, 119.4, 118.7, 112.0, 104.4, 66.6, 47.2, 36.6, 23.2, 21.8, 20.9, 16.3. HRMS (ESI) Calcd. for $C_{30}H_{26}N_3O_5$ ([M+H]$^+$): 508.1872, Found: 508.1906.

*5-(7-(4-Ethoxyphenyl)-6b-hydroxy-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (***4w***)*

Light gray solid, yield 92 %. m.p. 258–261 °C. IR (KBr): 3226, 3086, 2944, 2879, 1764, 1740, 1717, 1698, 1606, 1581, 1547, 1509, 1439, 1404, 1357, 1245, 1195, 1146, 1022, 826, 781 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.90 (s, 1H, NH), 10.56 (s, 1H, NH), 7.88–7.46 (m, 5H, ArH), 7.29 (t, J = 7.2 Hz, 1H, ArH), 6.96 (s, 4H, ArH), 6.49 (d, J = 6.4 Hz, 1H, CH), 4.91 (s, 1H, OH), 4.08–4.03 (m, 2H, OCH_2), 2.20–1.72 (m, 6H, 3 × CH_2), 1.35 (t, J = 6.8 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm): 190.4, 168.1, 161.1, 158.0, 151.1, 141.0, 136.0, 130.8, 130.7, 128.9, 128.3, 126.5, 124.7, 121.8, 119.8, 119.1, 114.6, 112.4, 104.3, 66.5, 63.4, 47.1, 36.6, 23.5, 21.9, 14.8. HRMS (ESI) Calcd. for $C_{30}H_{24}N_3O_6$ ([M−H]$^-$): 522.1665, Found: 522.1679.

*5-(7-(4-Bromophenyl)-6b-hydroxy-11-oxo-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (***4x***)*

Light gray solid, yield 93 %. m.p. >300 °C. IR (KBr): 3213, 3093, 1716, 1698, 1554, 1491, 1434, 1406, 1344, 1189, 1141, 1113, 1021, 1012, 824, 786, 776 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.93 (s, 1H, NH), 10.60 (s, 1H, NH), 7.79 (s, 1H, ArH), 7.70–7.09 (m, 9H, ArH), 6.49 (s, 1H, CH), 4.94 (s, 1H, OH), 2.28–1.76 (m, 6H, 3 × CH_2). ^{13}C(75 MHz, DMSO-d_6) δ (ppm): 191.1, 168.2, 160.0, 151.0, 145.7,

140.7, 136.3, 135.9, 132.1, 131.0, 128.4, 126.5, 125.0, 122.0, 121.0, 119.8, 118.8, 113.6, 104.6, 66.7, 47.2, 36.7, 23.6, 22.0. HRMS (ESI) Calcd. for $C_{28}H_{20}BrN_3O_5$ ($[M]^+$): 557.0586, Found: 557.0564.

Supporting information

^1H NMR and ^{13}C NMR spectra for all compounds. The detailed experiments are available.

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