Catalyst-free Synthesis of Tetrahydroacenaphtho[1,2-*b*]indolone Derivatives *via* One-pot Four-component Reaction

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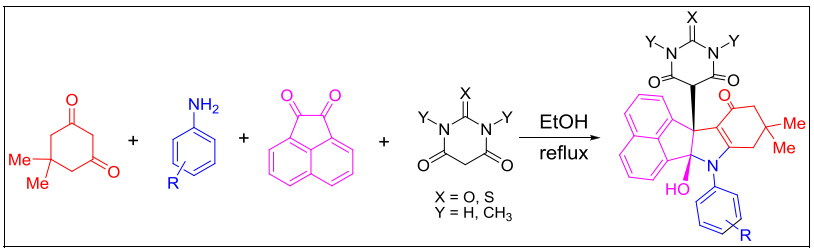

A simple and efficient one-pot synthesis of tetrahydroacenaphtho[1,2-*b*]indolone derivatives via four-component reaction of 5,5-dimethylcyclohexane-1,3-dione (dimedone), arylamines, acenaphthoquinone, and active methylene compounds under catalyst-free conditions is described. The reactions were carried out under mild conditions using ethanol as solvent. Advantages of this method include simple experimental and workup procedure, readily available starting materials, and high yields.

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INTRODUCTION

Multicomponent reactions have emerged as an efficient and powerful tool in modern synthetic organic chemistry because of their valued features. Multicomponent reactions, leading to interesting heterocyclic scaffolds, are particularly useful for the construction of diverse chemical libraries of "drug-like" molecules [1,2]. Heterocyclic compounds are of great importance in the discovery of pharmaceutical reagents, organic synthesis, and synthetic materials [3,4]. Nitrogen-containing heterocycles, in particular, are one of the most significant classes of heterocycles because of their molecular functions and wide spectrum of biological activities [5]. These heterocycles are able to insert into DNA and disrupt undesirable cellular processes [6], which result in this wide range of biological properties that include antitumor [7], antibacterial [8], antiparasitic [9], antiviral [10], antifungal [11], and anti-HIV activities [12]. Between these heterocycles, the indole unit is one of the most important and profuse nitrogen-containing heterocycles in medicinal agents and natural products. Compounds containing an indole moiety display a wide range of biological activities including antitumor, antiviral, and anti-inflammatory activities [13–17]. The indole unit is also an important skeleton in organic and medicinal chemistry [18–20]. Therefore, the preparation of polycyclic indole moiety could potentially lead to a series of biologically and structurally interesting compounds. Recently, several methods for the synthesis of functionalized nitrogen-containing heterocycles and acenaphtho[1,2-*b*]indole derivatives have been reported [21]. Zhang and coworker reported synthesis of tetrahydroacenaphtho[1,2-*b*]indolone derivatives by using L-proline as catalyst [22].

RESULTS AND DISCUSSION

The reaction between arylamines, 5,5-dimethylcyclohexane-1,3-dione (dimedone), under melt condition at 80°C for 10 min led to enaminone **1**, and then addition of acenaphthoquinone **2** and barbituric acid **3** in ethanol at reflux for 2 h led to tetrahydroacenaphtho[1,2-*b*]indolone derivatives **4a**-**p**, in high yields (Scheme 1).

The effects of solvents and catalyst were evaluated for this model reaction, and the results are summarized in (Table 1).

Initially, this reaction was carried out in EtOH at room temperature without the addition of catalyst. In this case, target compound **4a** was observed but with low yield (Table 1, entry 1). When Et_3N/*para*-toluenesulfonic acid (*p*-TSA) was added to the mixture respectively at room temperature and reflux, the product was observed with low yield. But when this reaction was employed in EtOH at reflux without catalyst, we found that the reaction swiftly reached completion within 2 h to give the desirable product **4a**

Scheme 1. Synthesis of the tetrahydroacenaphtho[1,2-*b*]indolone derivatives **4**.

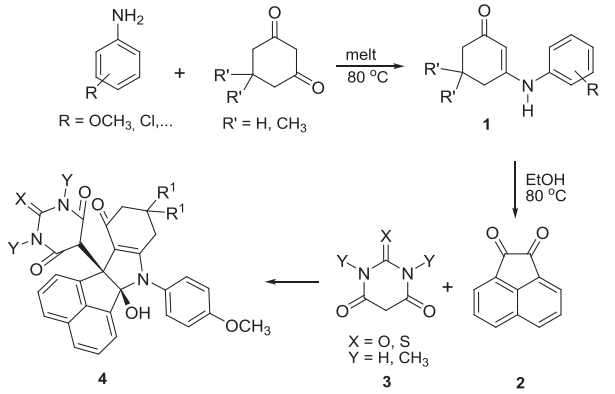


Table 1

Synthesis of the tetrahydroacenaphtho[1,2-*b*]indolone derivatives under different conditions[a].

Entry	Solvent	Temperature (°C)	Catalyst	Time (h)	Yield (%)[b]
1	EtOH	r.t.	—	15	40
2	EtOH	80	*p*-TSA	6	45
3	EtOH	r.t.	Et_3N	12	55
4	EtOH[c]	80	—	2	95
5	MeOH	65	—	6	Trace
6	CH_3CN	80	—	6	58
7	CH_3CN	80	*p*-TSA	6	—
8	CH_3CN	r.t.	—	12	55
9	H_2O	80	—	10	54
10	H_2O	80	*p*-TSA	10	35
11	H_2O	r.t.	—	15	25

[a]Dimedone (1 mmol), 4-methoxyaniline (1 mmol), acenaphthoquinone (1 mmol), and *N,N*-dimethylbarbituric acid (1 mmol), solvent 5 mL.
[b]Yield of isolated **4a**.
[c]The best condition.

in excellent yield (Table 1, entry 4). Next, with catalyst *p*-TSA and without catalyst in different solvents such as MeOH, CH_3CN and H_2O were employed (Table 1, entries 5–11), and results show that except CH_3CN in reflux with *p*-TSA and MeOH without catalyst that failed the others, almost all were successful but with low yields. As a result, EtOH was determined to be the appropriate solvent. In refluxing EtOH, reaction not only occurred over a shorter period of time but also provided a higher yield than that obtained by using any of the other examined solvents such as MeOH, CH_3CN, and H_2O (Table 1, entries 5–11). Accordingly, it could be concluded that the best reaction condition is catalyst free in EtOH at reflux. In these experiments, procedure is very simple and the products do not require further purification. Then a mixture of **4** and without any catalytic at 80°C for about 2 h under refluxing ethanol conditions led to the formation of tetrahydroacena phtho[1,2-*b*]indolone derivatives **4** in excellent yields (Scheme 1). The yields were excellent without formation of any side products, and products are obtained in very good purity (Table 2).

Plausible mechanism for the formation of tetrahydroacenaphtho[1,2-*b*]indolone derivatives is proposed in Scheme 2. The structures of products were deduced from their IR and ^1H and ^{13}C NMR spectra. The mass spectra of these products displayed molecular ion peaks at the appropriate *m/z* values. The present procedure has the advantage that not only the reaction is performed under neutral conditions but also the reactants can be mixed without any activation or modification. The simplicity of the present procedure makes it an interesting alternative to complex multistep approaches.

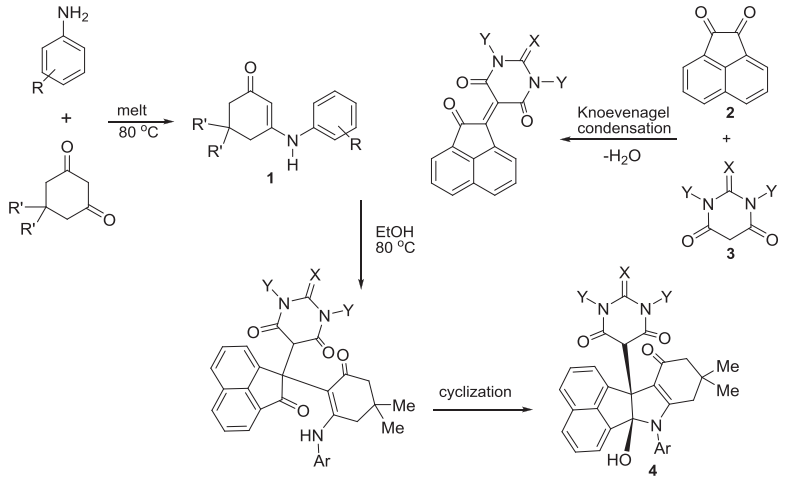
Table 2

Compounds **4a**-**p**.

Entry	Product	R	X	Y	Time (h)	Yields (%)	Mp (°C)
1	**4a**	4-OCH_3	O	CH_3	2	93	244–245
2	**4b**	4-H	O	CH_3	2	89	257–258
3	**4c**	4-Cl	O	CH_3	2	91	258–259
4	**4d**	4-Br	O	CH_3	2	92	255–256
5	**4e**	4-NO_2	O	CH_3	2	90	217–218
6	**4f**	2-CH_3	O	CH_3	2	92	265–266
7	**4g**	4-OCH_3	S	H	2	91	237–238
8	**4h**	4-Cl	S	H	2	89	237–239
9	**4i**	4-H	S	H	2	91	227–229
10	**4j**	4-Br	S	H	2	93	229–230
11	**4k**	4-OCH_3	O	H	2	92	260–261
12	**4l**	4-Cl	O	H	2	91	246–247
13	**4m**	4-H	O	H	2	90	238–240
14	**4n**	2-Cl	O	CH_3	2	93	180–182
15	**4o**	3-Cl	O	CH_3	2	91	280–281
16	**4p**	3,4-Cl	O	CH_3	2	89	254–256

Reagents and conditions: **1–3** (1 mmol), EtOH (5 mL), 80°C, catalyst free.
Isolated yield based on arylamines and barbituric acids.

Scheme 2. Proposed mechanism for the synthesis of tetrahydroacenaphtho[1,2-*b*]indolone derivatives.



CONCLUSIONS

In summary, we have described a facile and highly efficient route for the synthesis of novel tetrahydroacenaphtho[1,2-*b*]indolone derivatives via four-component reaction between aniline derivatives, dimedone, acenaphthoquinone, and barbiturates in ethanol at reflux. Advantages of this route include catalyst-free reaction conditions, short reaction time, simple workup procedure, and excellent yields. In this method, reactants can be mixed without any activation or modification.

EXPERIMENTAL

General. All of the chemicals used in this work were purchased from Merck and Aldrich Chemical Companies. Melting points were measured on an Electrothermal 9100 apparatus. IR spectra were measured with Bruker Tensor 27 spectrometer; absorbencies are reported in cm^{-1}. ^1H and ^{13}C NMR spectra were measured with a Bruker DRX-300 AVANCE spectrometer at 299.87 MHz. NMR spectra were obtained in solutions of DMSO-d_6. Mass spectra were recorded on an Agilent Technologies 5975C VL MSD with Tripe-Axis Detector mass spectrometer operating at an ionization potential of 70 eV.

General procedure for the synthesis of product 4a. Typical procedure for preparation of 5-(6*bS*,11*bR*)-6*b*-hydroxy-7-(4-methoxyphenyl)-9,9-dimethyl-11-oxo-7,8,9,10,11,11*b*-hexahydro-6*bH*-acenaphtho[1,2-*b*]indol-11*b*-yl)-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (**4a**): A mixture of 4-methoxyaniline (0.123 g, 1 mmol), 5,5-dimethylcyclohexane-1,3-dione (0.140 g, 1 mmol), under solvent-free condition for 10 min at 80°C, then acenaphthoquinone **2** (0.182 g, 1 mmol), and 1,3-dimethylbarbituric acid **3** (0.156 g, 1 mmol) in EtOH (5 mL) was added and was heated at reflux for 2 h. The progress of the reaction was monitored by TLC using EtOAc/*n*-hexane (1 : 1) as eluent. After reaction completion, the solid was washed with ethanol (5 mL) to obtain the product **4a**.

5-(6bS,11bR)-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 (4a). Gray solid, yield, (93%). Mp: 244–246°C, IR (KBr), ν_{max}: 3424, 3051, 2951, 1685, 1563, 1510, 1445, 1248, 1148, 789, 671, 602 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 0.77 (s, 3 H, CH_3), 1.06 (s, 3 H, CH_3), 1.64–2.07 (m, 4 H, $2CH_2$), 2.70 (s, 3 H, N-CH_3), 3.10 (s, 3 H, N-CH_3), 3.71 (s, 3 H, O-CH_3), 5.02 (s, 1 H, OH), 6.46 (d, $^2J_{HH}$ = 6 Hz, 1 H, CH), 6.96 (s, 3 H, Ar), 7.29 (t, $^3J_{HH}$ = 8 Hz, 1 H, Ar), 7.45 (t, $^3J_{HH}$ = 8 Hz, 1 H, Ar), 7.62 (d, $^2J_{HH}$ = 8 Hz, 2 H, Ar), 7.69 (d, $^2J_{HH}$ = 8 Hz, 2 H, Ar). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 28.6, 29.9, 33.7, 37.1, 50.8, 55.8, 66.9, 114.6, 119.5, 125.3, 127.1, 128.6, 131.2, 131.3, 136.1, 152.3, 159.1, 167.1, 189.8 (C═O). *Anal*. Calcd for $C_{33}H_{31}N_3O_6$ (565.62): C, 70.07; H, 5.52; N, 7.43. Found C, 70.5; H, 5.2; N, 7.8. MS (EI) *m/z* (%): 565 (M^+, 0.2), 547 (9), 409 (17), 393 (35), 325 (100), 278 (20), 265 (13), 41 (10).

5-(6bS,11bR)-6b-Hydroxy-9,9-dimethyl-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 (4b). Gray solid, yield, (89%). Mp: 257–259°C, IR (KBr), ν_{max}: 3409, 2946, 2883, 2659, 1680, 1557, 1431, 1369, 1275, 1141, 1032, 787, 706, 598, 459 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 0.79 (s, 3 H, CH_3), 1.08 (s, 3 H, CH_3), 1.66–2.21 (m, 4 H, $2CH_2$), 2.8 (s, 3 H, N-

CH_3), 3.1 (s, 3 H, N-CH_3), 5.02 (s, 1 H, OH), 6.46 (d, $^2J_{HH}$ = 6 Hz, 1 H, CH), 6.38 (s, 1 H, Ar), 7.03 (s, 2 H, Ar), 7.29 (t, $^3J_{HH}$ = 6 Hz, 1 H, Ar), 7.41–7.49 (m, 3 H, Ar), 7.62 (d, $^2J_{HH}$ = 6 Hz, 2 H, Ar), 7.68 (d, $^2J_{HH}$ = 6 Hz, 2 H, Ar). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 27.7, 28.6, 30.0, 33.9, 37.2, 49.0, 50.8, 67.0, 105.3, 119.3, 120.1, 122.7, 125.3, 127.0, 128.3, 128.6, 129.5, 129.9, 131.2, 136.1, 136.7, 152.3, 167.1, 190.4 (C═O). *Anal*. Calcd for $C_{33}H_{29}N_3O_5$ (535.59): C, 71.76; H, 5.46; N, 7.85. Found C, 71.4; H, 5.8; N, 7.6. MS (EI) *m/z* (%): 535 (M^+, 73), 443 (10), 380 (100), 296 (36), 215 (12), 187 (13), 151 (19), 117 (15), 83 (87), 42 (17).

5-(6bS,11bR)-7-(4-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 (4c). Gray powder, yield, (91%). Mp: 258–259°C, IR (KBr), ν_{max}: 3417, 2943, 1679, 1560, 1488, 1435, 1276, 1144, 792, 600 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 0.80 (s, 3 H, CH_3), 1.08 (s, 3 H, CH_3), 1.67–2.23 (m, 4 H, 2CH_2), 2.86 (s, 3 H, N-CH_3), 3.12 (s, 3 H, N-CH_3), 5.06 (s, 1 H, OH), 6.45 (d, $^2J_{HH}$ = 6 Hz, 1 H, CH), 7.07 (s, 1 H, Ar), 7.29 (t, $^3J_{HH}$ = 6 Hz, 1 H, Ar), 7.44–7.50 (m, 3 H, Ar), 7.62 (d, $^2J_{HH}$ = 6 Hz, 2 H, Ar), 7.69 (d, $^2J_{HH}$ = 6 Hz, 1 H, Ar), 7.81 (s, 1 H, Ar). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 28.6, 30.1, 33.9, 37.0, 49.0, 50.8, 67.0, 87.2, 108.3, 119.2, 122.7, 125.4, 127.1, 128.4, 128.6 (2 C), 129.5, 131.2, 131.5 (2 C), 132.7, 136.5, 136.7, 152.3, 167.3, 190.4 (C═O). MS (EI) *m/z* (%): 571 (M^++1, 23), 570 (M^+, 23), 569 (M^+−1, 60), 415 (25), 414 (64), 330 (23), 294 (10), 191 (18), 150 (30), 83 (100), 42 (18).

5-(6bS,11bR)-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). Gray powder, yield, (92%). Mp: 255–256°C, IR (KBr), ν_{max}: 3538, 3051, 2956, 1690, 1613, 1424, 1369, 1274, 1208, 1144, 788, 670 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 0.80 (s, 3 H, CH_3), 1.09 (s, 3 H, CH_3), 1.67–2.24 (m, 4 H, 2CH_2), 2.83 (s, 3 H, N-CH_3), 3.12 (s, 3 H, N-CH_3), 5.11 (s, 1 H, OH), 6.45 (s, 1 H, CH), 7.00 (s, 2 H, Ar), 7.29 (s, 1 H, Ar), 7.46–7.85 (m, 6 H, Ar). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 27.6, 28.6, 30.0, 34, 37.0, 49.3, 50.8, 66.9, 105.4, 119.2, 121.3, 122.7, 125.4, 127.1, 128.7, 131.2, 131.8 (2 C), 132.5(2 C), 136.0, 152.3, 167.1, 190.4 (C═O). MS (EI) *m/z* (%): 615 (M^+, 44), 458 (40), 359 (15), 294 (16), 150 (20), 83 (100), 42 (20).

5-(6bS,11bR)-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 (4e). Gray powder, yield, (90%). Mp: 217–218°C, IR (KBr), ν_{max}: 3415, 3010, 2943, 1679, 1561, 1486, 1434, 1374, 1276, 1143, 792, 599 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 0.75 (s, 3 H, CH_3), 1.14 (s, 3 H, CH_3), 2.02–2.25 (m, 4 H, 2CH_2), 2.80 (s, 3 H, N-CH_3), 3.09 (s, 3 H, N-CH_3), 4.86 (s, 1 H, OH), 7.48–7.64 (m, 7 H, ArH, CH), 7.79 (d, $^2J_{HH}$ = 6 Hz, 2 H, Ar), 9.15 (s, 1 H, Ar). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 28.6, 28.9, 33.7, 37.2, 48.5, 51.1, 56.5, 65.6, 105.3, 119.5, 120.0, 123.2, 126.3, 128.0, 128.8, 135.7, 139.1, 152.3, 166.8, 193.6 (C═O). *Anal*. Calcd for $C_{32}H_{28}N_4O_7$ (580.59): C, 66.20; H, 4.86; N, 9.65. Found C, 66.8; H, 4.5; N, 9.3.

5-(6bS,11bR)-6b-Hydroxy-9,9-dimethyl-11-oxo-7-(o-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 (4f). Gray powder, yield, (92%). Mp: 265–266°C, IR (KBr), ν_{max}: 3412, 2954, 1679, 1557, 1437, 1373, 1275, 1146, 787, 595 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 0.71 (s, 3 H, CH_3), 1.12 (s, 3 H, CH_3), 1.46–1.97 (m, 4 H, 2CH_2), 2.27 (s, 3 H, *o*-CH_3), 2.74 (s, 3 H, N-CH_3), 3.12 (s, 3 H, N-CH_3), 5.02 (s, 1 H, OH), 6.38 (s, 1 H, CH), 6.81 (d, $^2J_{HH}$ = 6 Hz, 1 H, Ar), 7.18 (t, $^3J_{HH}$ = 6 Hz, 1 H, Ar), 7.36–7.49 (m, 3 H, Ar), 7.63 (d, $^2J_{HH}$ = 6 Hz, 2 H, Ar), 7.76 (d, $^2J_{HH}$ = 6 Hz, 2 H, Ar). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 28.5, 29.7, 33.6, 33.7, 36.6, 36.8, 49.1, 50.9, 67.0, 105.3, 119.1, 120.1, 122.7, 125.2, 126.5, 127.2, 128.8, 129.4, 131.0, 131.1, 131.3, 131.8, 132.3, 134.3, 134.9, 136.5, 138.1, 152.3, 167.0, 190.0 (C═O). *Anal*. Calcd for $C_{33}H_{31}N_3O_5$ (549.62): C, 72.11; H, 5.69; N, 7.65. Found C, 72.5; H, 5.2; N, 7.4.

5-(6bS,11bR)-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)-2-thioxodihydropyrimidine-4,6(1H,5H)-dione (4g). Gray powder, yield, (91%). Mp: 237–238°C, IR (KBr), ν_{max}: 3158, 2943, 1693, 1548, 1513, 1429, 1338, 1244, 1157, 782, 600 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 0.79 (s, 3 H, CH_3), 1.10 (s, 3 H, CH_3), 1.59–2.14 (m, 4 H, 2CH_2), 3.77 (s, 3 H, O-CH_3), 5.02 (s, 1 H, OH), 6.46 (s, 1 H, CH), 6.93 (s, 4 H, Ar), 7.24 (s, 3 H, Ar), 7.44–7.57 (m, 3 H, Ar), 7.63–7.69 (m, 2 H, Ar), 8.02 (s, 1 H, Ar), 11.64 (s, 1 H, NH), 11.97 (s, 1 H, NH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 27.9, 30.2, 33.9, 37.1, 48.6, 50.9, 55.7, 104.7, 114.5, 119.5, 122.3, 124.9, 126.7, 128.7, 129.1, 131.2, 136.3, 158.9, 160.4, 166.5, 189.2 (C═O). *Anal*. Calcd for $C_{31}H_{27}N_3O_5S$ (553.63): C, 67.25; H, 4.92; N, 7.59. Found C, 67.7; H, 4.5; N, 7.3.

5-(6bS,11bR)-7-(4-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 (4h). Gray powder, yield, (89%). Mp: 237–238°C, IR (KBr), ν_{max}: 3378, 3173, 2957, 2882, 2694, 1716, 1548, 1436, 1392, 1315, 1203, 1149, 964, 790, 737, 599 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 0.79 (s, 3 H, CH_3), 1.12 (s, 3 H, CH_3), 1.62–2.25 (m, 4 H, 2CH_2), 5.04 (s, 1 H, OH), 6.45 (d, $^2J_{HH}$ = 6 Hz, 1 H, CH), 7.05 (d, $^2J_{HH}$ = 6 Hz, 2 H, Ar), 7.25 (t, $^3J_{HH}$ = 6 Hz, 1 H, A), 7.46 (d, $^2J_{HH}$ = 6 Hz, 3 H, Ar), 7.58–7.68 (m, 4 H, Ar), 8.22 (s, 1 H, Ar), 11.67 (s, 1 H, NH), 11.98 (s, 1 H, NH). ^{13}C

NMR (75 MHz, DMSO-d_6) δ: 19.0, 27.7, 30.3, 34.2, 37.1, 48.7, 51.0, 56.5, 67.2, 104.9, 105.0, 115.2, 118.0, 119.2, 119.7, 122.5, 125.1, 126.8, 128.8, 129.5, 131.3, 132.5, 135.9, 136.2, 141.1, 145.2, 159.4, 166.5, 190.5 (C═O). *Anal*. Calcd for $C_{30}H_{24}ClN_3O_4S$ (558.05): C, 64.57; H, 4.33; N, 7.53. Found C, 65.1; H, 4.8; N, 7.2.

5-(6bS,11bR)-6b-Hydroxy-9,9-dimethyl-11-oxo-7-phenyl-7,8,9,10,11,11b-hexahydro-6bH-acenaphtho[1,2-b]indol-11b-yl)-2-thioxodihydropyrimidine-4,6(1H,5H)-dione (4i). Gray powder, yield, (91%). Mp: 227–229°C, IR (KBr), ν_{max}: 3374, 3284, 3050, 2951, 1796, 1701, 1500, 1407, 1268, 1163, 1015, 875, 784, 600 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 0.79 (s, 3 H, CH_3), 0.81 (s, 3 H, CH_3), 1.08 (s, 3 H, CH_3), 1.12 (s, 3 H, CH_3), 1.81–2.41 (m, 8 H, $4CH_2$), 4.68 (s, 1 H, OH), 4.67 (s, 1 H, OH),6.51–6.73 (m, 3 H, ArH, 2CH), 7.28–7.91 (m, 21 H, Ar), 8.80 (s, 1 H, Ar), 9.32 (s, 1 H, Ar), 9.51 (s, 1 H, NH), 9.69 (s, 1 H, NH), 11.56 (s, 1 H, NH), 11.78 (s, 1 H, NH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 26.3, 27.2, 29.4, 30.1, 34.0, 35.4, 36.6, 37.8, 50.3, 50.4, 56.5, 57.3, 65.9, 67.1, 110.1, 112.9, 113.0, 113.4, 120.4, 120.5, 121.7, 122.2, 124.8, 125.1, 127.2, 127.9, 128.2, 128.4, 128.9, 129.4, 129.7, 130.3, 131.6, 131.7, 135.7, 135.8, 135.9, 136.1, 136.2, 137.5, 140.0, 142.8, 163.8, 164.1, 166.7, 167.7, 171.9, 172.5, 181.0, 181.7, 191.3 (C═O), 191.5 (C═O).

5-(6bS,11bR)-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)-2-thioxodihydropyrimidine-4,6(1H,5H)-dione (4j). Gray powder, yield, (93%). Mp: 229–230°C, IR (KBr), ν_{max}: 3375, 3204, 3047, 2956, 2358, 1716, 1547, 1489, 1436, 1393, 1315, 1149, 791, 736, 676, 599 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 0.78 (s, 3 H, CH_3), 1.05 (s, 3 H, CH_3), 1.63–2.26 (m, 4 H, $2CH_2$), 5.04 (s, 1 H, OH), 6.44 (d, $^2J_{HH}$ = 6 Hz, 1 H, CH), 6.99 (d, $^2J_{HH}$ = 6 Hz, 2 H, Ar), 7.25–7.58 (m, 2 H, Ar), 7.60–7.67 (m, 5 H, Ar), 8.23 (s, 1 H, Ar), 11.67 (s, 1 H, NH), 11.99 (s, 1 H, NH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 19.0, 27.7, 30.3, 31.2, 34.2, 37.1, 48.0, 51.0, 56.5, 67.0, 104.9, 112.5, 119.2, 119.7, 121.0, 122.5, 125.1, 126.8, 128.7, 131.2, 131.6, 132.5, 136.2, 136.4, 141.8, 146.4, 159.3, 166.5, 166.7, 190.4 (C═O).

5-(6bS,11bR)-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 (4k). Gray powder, yield, (92%). Mp: 260–261°C, IR (KBr), ν_{max}: 3403, 3211, 3096, 2963, 2873, 2742, 1700, 1552, 1506, 1425, 1286, 1137, 1028, 837, 782, 672, 601 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 0.79 (s, 3 H, CH_3), 1.11 (s, 3 H, CH_3), 1.58–2.25 (m, 4 H, $2CH_2$), 3.77 (s, 3 H, O-CH_3), 4.91 (s, 1 H, OH), 6.43 (d, $^2J_{HH}$ = 6 Hz, 1 H, CH), 6.93 (s, 2 H, Ar), 7.25 (t, $^3J_{HH}$ = 6 Hz, 1 H, Ar), 7.44 (t, $^3J_{HH}$ = 6 Hz, 2 H, Ar), 7.58 (d, $^2J_{HH}$ = 6 Hz, 1 H, Ar), 7.63–7.72 (m, 3 H, Ar), 7.88 (s, 1 H, Ar), 10.53 (s, 1 H, NH), 10.91 (s, 1 H, NH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 27.8, 30.3, 31.2, 34.0, 37.1, 39.1, 47.9, 51.0, 55.8(2C), 66.4, 104.9, 111.7, 114.5, 119.3, 119.6, 122.2, 124.9, 126.8, 128.7, 129.2, 131.2, 136.3, 141.5, 146.7, 151.4, 158.9, 160.2, 168.5, 168.7, 189.9 (C═O).

5-(6bS,11bR)-7-(4-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 (4l). Gray powder, yield, (91%). Mp: 246–247°C, IR (KBr), ν_{max}: 3219, 3100, 2953, 2867, 1713, 1567, 1492, 1427, 1136, 788, 673, 600, 508 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 0.81 (s, 3 H, CH_3), 1.11 (s, 3 H, CH_3), 1.60–2.06 (m, 4 H, $2CH_2$), 4.93 (s, 1 H, OH), 6.41 (d, $^2J_{HH}$ = 6 Hz, 1 H, CH), 7.06 (d, $^2J_{HH}$ = 6 Hz, 2 H, Ar), 7.25 (t, $^3J_{HH}$ = 6 Hz, 1 H, Ar), 7.46 (d, $^2J_{HH}$ = 6 Hz, 3 H, Ar), 7.58 (d, $^2J_{HH}$ = 6 Hz, 3 H, Ar), 7.66 (d, $^2J_{HH}$ = 6 Hz, 3 H, Ar), 8.08 (s, 1 H, Ar), 10.56 (s, 1 H, NH), 10.92 (s, 1 H, NH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 27.6, 30.4, 31.2, 34.2, 37.1, 39.1, 47.9, 49.2, 50.8, 66.5, 105.1, 112.8, 119.1, 119.6, 122.3, 125.1, 126.8, 128.8, 129.5, 131.3, 132.3, 136.0, 141.2, 146.5, 151.3, 159.3, 168.4, 168.7, 190.5 (C═O). *Anal*. Calcd for $C_{30}H_{24}ClN_3O_5$ (541.98): C, 66.48; H, 4.46; N, 7.75. Found C, 66.0; H, 4.9; N, 7.5.

5-((6bS,11bR)-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 (4m). Gray powder, yield, (90%). Mp: 238–240°C, IR (KBr), ν_{max}: 3401, 3016, 2956, 2864, 1708, 1557, 1490, 1424, 1272, 1127, 1026, 779, 669, 600 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 0.81 (s, 3 H, CH_3), 1.12 (s, 3 H, CH_3), 1.60–2.25 (m, 4 H, $2CH_2$), 4.94 (s, 1 H, OH), 6.36 (d, $^2J_{HH}$ = 6 Hz, 1 H, CH), 7.02 (s, 1 H, Ar), 7.20 (s, 1 H, Ar), 7.37–7.49 (m, 3 H, Ar), 7.56–7.69 (m, 3 H, Ar), 7.99 (s, 1 H, Ar), 10.55 (s, 1 H, NH), 10.92 (s, 1 H, NH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 19.0, 27.7, 30.4, 34.1, 37.3, 39.1, 47.9, 51.0, 56.5, 66.5, 105.1, 112.4, 119.1, 119.6, 122.3, 125.0, 126.7, 128.0, 128.7, 129.4, 129.7, 131.2, 136.2, 137.0, 146.7, 151.4, 159.6, 168.5, 168.7, 190.2 (C═O).

5-(6bS,11bR)-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 (4n). Gray powder, yield, (93%). Mp: 180–182°C, IR (KBr), ν_{max}: 3377, 3052, 2958, 2880, 1683, 1610, 1426, 1374, 1273, 1210, 1146, 783, 669, 615 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 0.75 (s, 3 H, CH_3), 1.11 (s, 3 H, CH_3), 1.96–2.19 (m, 4 H, $2CH_2$), 2.78 (s, 3 H, N-CH_3), 3.08 (s, 3 H, N-CH_3), 4.86 (s, 1 H, OH), 7.54–7.79 (m, 11 H, ArH, CH), 9.16 (s, 1 H, Ar). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 19.0, 28.4, 28.6, 28.9, 33.7, 37.2, 48.4, 51.0, 56.5, 65.6, 119.5, 119.9, 123.2, 126.2, 128.0, 128.8, 131.2, 135.7, 140.8, 152.3, 166.7, 193.6 (C═O). *Anal*. Calcd for $C_{32}H_{28}ClN_3O_5$ (570.03): C, 67.42; H, 4.95; N, 7.37. Found C, 67.8; H, 5.4; N, 7.2.

5-(6bS,11bR)-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)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (4o). Gray powder, yield, (91%). Mp: 280–281°C, IR (KBr), ν_{max}: 3413, 2950, 2709, 1670, 1558, 1430, 1376, 1275, 1143, 1038, 784, 726, 674, 596 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 0.81 (s, 3 H, CH_3), 1.11 (s, 3 H, CH_3), 1.67–2.32 (m, 4 H, $2CH_2$), 2.80 (s, 3 H, N-CH_3), 3.12 (s, 3 H, N-CH_3), 5.10 (s, 1 H, OH), 6.39 (s, 1 H, CH), 6.90 (s, 1 H, Ar), 7.26–7.67 (m, 8 H, Ar), 7.91 (s, 1 H, Ar). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 27.5, 28.6, 30.2, 34.1, 37.0, 50.9, 66.9, 106.2, 113.4, 119.1, 120.1, 122.6, 125.5, 127.1, 128.2, 128.4, 128.7, 129.3, 131.0, 131.2, 133.5, 136.0, 138.4, 152.3, 167.1, 190.6 (C═O). *Anal*. Calcd for $C_{32}H_{28}ClN_3O_5$ (570.03): C, 67.42; H, 4.95; N, 7.37. Found C, 70.0; H, 4.5; N, 7.1.

5-(6bS,11bR)-7-(3,4-Dichlorophenyl)-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 (4p). Gray solid, yield, (89%). Mp: 254–256°C, IR (KBr), ν_{max}: 3363, 2946, 2700, 1678, 1563, 1466, 1425, 1370, 1271, 1198, 1134, 1030, 787, 738, 672, 602 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 0.82 (s, 3 H, CH_3), 1.10 (s, 3 H, CH_3), 1.70–2.35 (m, 4 H, $2CH_2$), 2.79 (s, 3 H, N-CH_3), 3.12 (s, 3 H, N-CH_3), 5.12 (s, 1 H, OH),6.46 (s, 1 H, CH), 6.96 (s, 1 H, Ar), 7.30–7.67 (m, 7 H, Ar), 7.98 (s, 1 H, Ar). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 19.0, 27.5, 28.2, 28.6, 28.7, 30.3, 34.1, 36.9, 48.9, 50.9, 56.5, 66.9, 105.2, 119.1, 120.1, 121.7, 122.8, 125.5, 127.2, 128.7, 128.9, 129.8, 130.7, 131.1, 131.3, 131.4, 131.7, 132.7, 136.0, 137.1, 152.3, 167.0, 190.9 (C═O). *Anal*. Calcd for $C_{32}H_{27}Cl_2N_3O_5$ (604.48): C, 63.58; H, 4.50; N, 6.95. Found C, 64.1; H, 4.9; N, 6.5.

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