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An Efficient Catalyst-free Chemoselective Multicomponent Reaction for the Synthesis of Pyrimidine Functionalized Pyrrolo-annelated Derivatives

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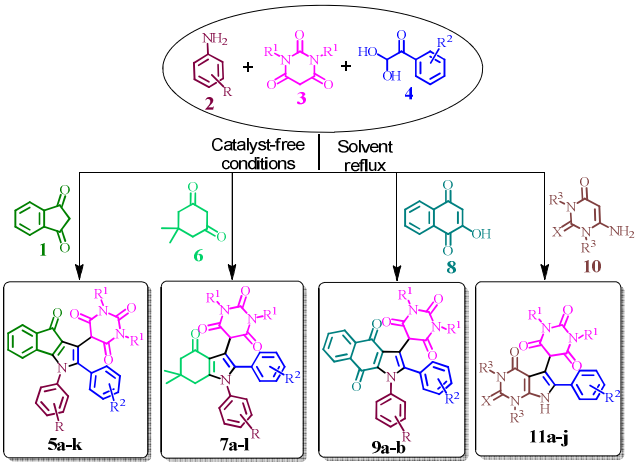
An efficient method for the synthesis of pyrimidine functionalized pyrrolo-annelated derivatives has been developed *via* a catalyst-free, one-pot chemoselective multicomponent domino reaction. The method offers ease of execution, easy and column free separation, mild reaction conditions and high yields.

Introduction

Multicomponent reactions (MCRs) are alternate green techniques to multistep processes. Application of MCRs in the synthesis of natural products and building blocks are well documented in the literature.[1] MCRs have remarkable impact in the field of medicinal chemistry, combinatorial synthesis and pharmaceutical industry due to their loftier gains like simplistic execution, convergence, less energy consumption, more productivity with excellent chemo and regio-selectivities.[2] Therefore, the design of new chemo- and regio-selective multicomponent reactions for easy and efficient synthesis is an ongoing challenge to synthetic chemists.[3] In recent literature the number of reports regarding reagent and substrate based multicomponent reactions are quite high.[4] Especially isocyanide based multicomponent reactions (IMCRs)[5] and arylglyoxal based multicomponent[6] reactions are well established for the construction of diverse molecular libraries in easy and efficient way.

Moreover, pyrrole core unit is present in many natural products, its analogues are renowned in medicine[7] and many reports were published in recent literature[8] to produce their novel analogues of indoles,[9] carbazoles,[10] pyrrolo pyrimidines,[11] indeno pyrroles[12] and pyrrolo naphthoquinones.[13] Pyrimidinylpyrrole motif appears in several natural and bioactive products like meridianins, variolins, psammopemmins, hyrtinadine, aplicyanins etc.[14] and therefore, cyclic systems with this structural motif drew considerable attention in the field of combinatorial chemistry and drug discovery.[15] In continuation to our studies towards the synthesis of pyrimidine heterocycles and drug intermediates *via* multicomponent reactions,[16] herein we report an efficient chemoselective multicomponent one-pot strategy for the construction of novel pyrimidinylpyrrole fused cyclic systems under catalyst-free conditions using different cyclic 1,3-dicarbonyl compounds (Scheme 1).

Scheme 1. Synthesis of pyrimidine functionalized pyrrolo-annelated derivatives.

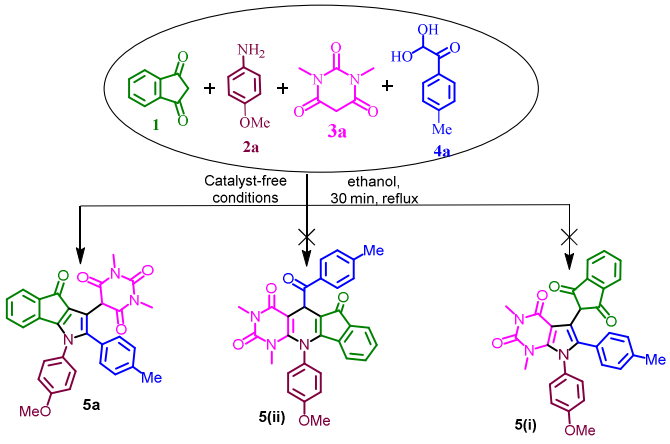


Results and discussion

We initiated our study by performing a one-pot reaction of 1,3-indanedione **1**, 4-methoxy aniline **2a**, 1,3-dimethyl barbituric acid **3a** and 4-methyl phenylglyoxal hydrate **4a** in equimolar quantities using different solvents. It was found that ethanolic

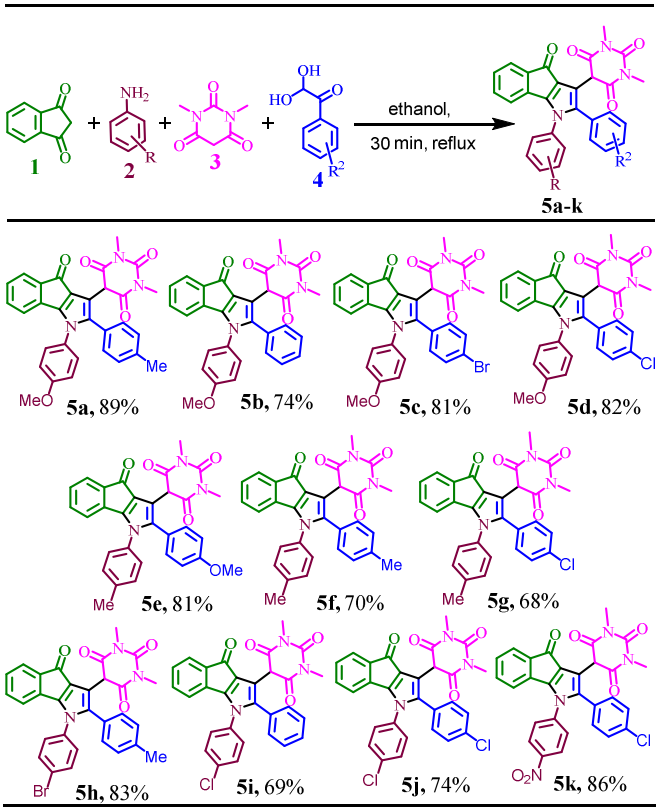
mixture of all the reactants under reflux conditions gave **5a** in 89% yield. Other solvents like water (24%), toluene (39%), acetonitrile (59%), dimethylformamide (56%), chloroform (42%), acetic acid (64%) and methanol (79%) are comparatively less effective towards this transformation. Moreover, it is remarkable to note here that the reaction occurred at room temperature also but with a lesser yield (10%). A variation in temperature revealed that reflux condition is the best reaction condition for synthesis of the desired product. It was observed that the product 5-(1-(4-methoxyphenyl)-4-oxo-2-(p-tolyl)-1,4-dihydroindeno[1,2-b]pyrrol-3-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione **5a** was formed exclusively without the formation of the other likely products **5(i)** or **5(ii)** (Scheme 2). The ^{1}H-NMR spectrum of **5a** showed a singlet with 6 protons at 3.38 ppm. The N-methyl signal at 28.81 ppm in ^{13}C-NMR clearly shows that methyl protons of barbituric acid are at the same chemical environment which indicates the formation of **5a**. The chemoselective formation of enamine of 1,3-diketones **1** and **3a** with aromatic amine **2a** can explain the formation of **5a** rather than **5(i)** or **5(ii)**. Due to resonance of the amide nitrogen towards the carbonyl group, the reactivity of barbituric acid amide ketone is less than the ketone group of **1** to form the enamine intermediate with aromatic amine **2a**, which lead to selective formation of **5a** but not **5(i)** or **5(ii)**.

Scheme 2. Chemoselective formation of pyrrolo-annelated derivative **5a**.



The scope of the reaction was examined under optimized reaction conditions, with different substituted aromatic amines **2** and aromatic phenylglyoxal hydrates **4**. The results obtained are summarized in Table 1. Generalization study reveals that the method is suitable with a wide variety of substituted aromatic amines and arylglyoxal hydrates with excellent yields (Table 1, entries **5a-k**). The reaction was also equally effective with aromatic amines and phenylglyoxal hydrates containing both the electron-withdrawing and donating groups. The products thus obtained were characterized by spectroscopic analyses.

Table 1. Chemoselective synthesis of 3-(pyrimidin-5-yl)indeno[1,2-b]pyrrol-4(1H)-one derivatives **5a-k**.[a]



[a]Reaction conditions: Indane-1,3-dione **1** (1 mmol), aromatic amine **2** (1 mmol), barbituric acid **3a** (1 mmol) and phenylglyoxal hydrate **4** (1 mmol) was refluxed in 8 mL of ethanol for 30 min.

Encouraged by the above results, we extended our study to find the feasibility of the method with other cyclic 1,3-dicarbonyl compounds *viz.* dimedone **6** and 2-hydroxy naphthoquinone **8** (Scheme 3). We found that under identical reaction condition the desired pyrimidylpyrrole fused derivatives **7** and **9** were obtained in good yields without the formation of any other products. The generalization study for the formation of **7** is listed in Table 2. The scope of the reaction scheme was well tolerated with various substituted aromatic amines **2**, barbituric acid **3** and arylglyoxal hydrate **4** and successfully furnished the corresponding pyrimidinylpyrrole fused analogues of **7a-l** in good to excellent yields. Furthermore, we observed that the free NH group of **3b** did not interrupt the reaction process, constructing the desired pyrimidinylpyrrole fused derivative in good yields (Scheme 3).

Scheme 3. Chemoselective formation of pyrrolo-annelated derivatives **7** & **9**.

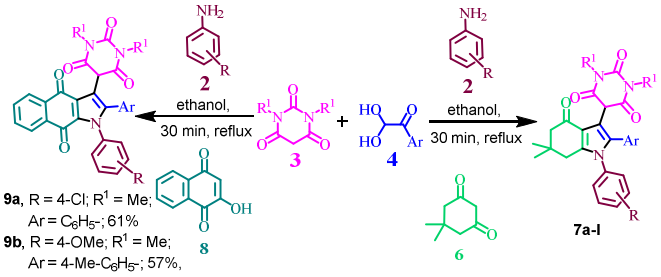
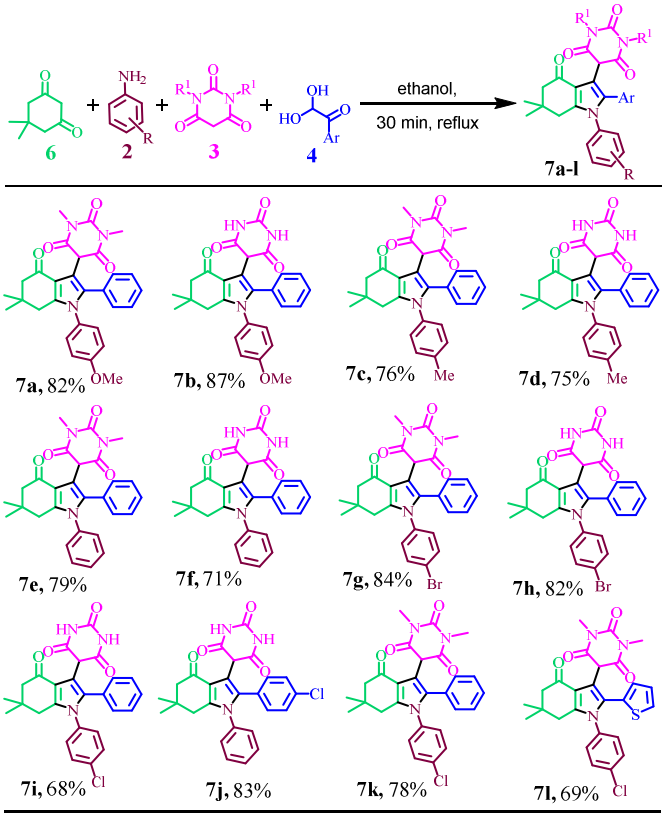


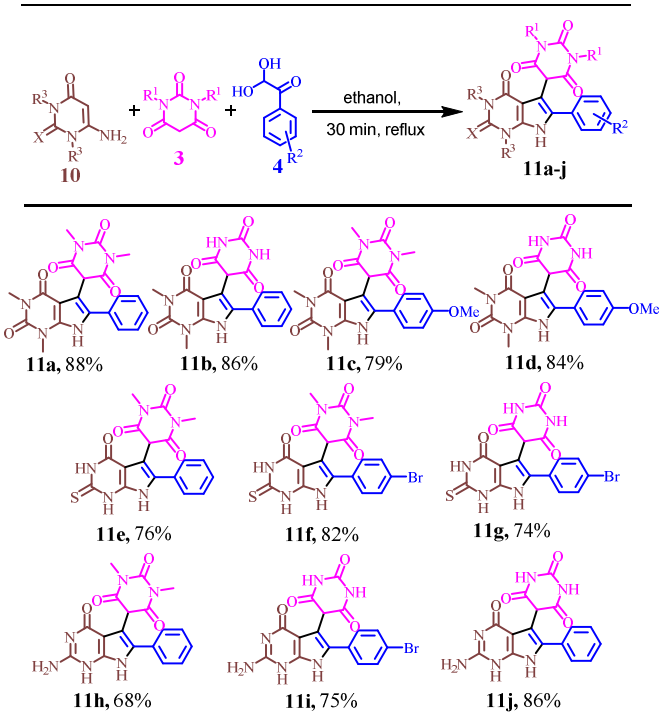
Table 2. Synthesis of 3-(pyrimidin-5-yl)-6,7-dihydro-1*H*-indol-4(5H)-one derivatives **7a-l**.[a]



[a]Reaction conditions: Dimedone **6** (1 mmol), aromatic amine **2** (1 mmol), barbituric acid **3** (1 mmol) and arylglyoxal hydrate **4** (1 mmol) was refluxed in 8 mL of ethanol for 30 min.

We then performed the same reaction using 6-amino-1,3-dimethyluracil as enamine instead of *in situ* generated enamine of an aromatic amine and cyclic 1,3-dicarbonyl compound which generates enamine and we observed the formation of pyrimidinylpyrrole fused pyrimidine derivative in good yields. In a typical case, a mixture of 1,3-dimethyl-6-amino uracil **10a**, 1,3-dimethyl barbituric acid **3a** and phenylglyoxal hydrate **4** in ethanol was refluxed with stirring for 30 min (monitored vide TLC). On completion, after usual work-up the desired pyrimidinylpyrrole fused pyrimidine derivative **11a** was obtained in 88% yield. The reaction was then generalized by using different 6-amino uracil **10a-c**, barbituric acid **3a,b** and arylglyoxal hydrates **4** to obtain the substrate scope of the reaction scheme (Table 3). The nature of substituent's in the substrates play no significant role towards the formation of the products and in all the cases reaction proceeds smoothly to give **11** as the product exclusively.

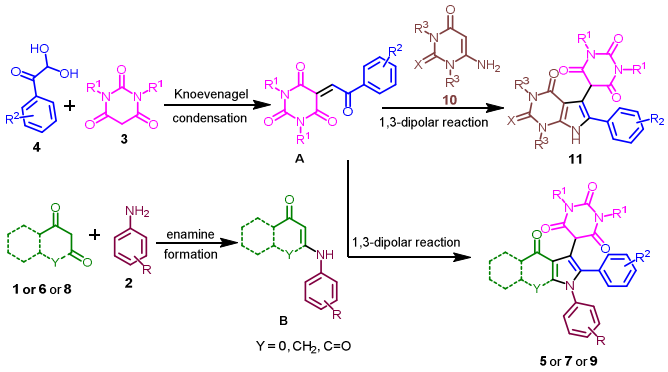
Table 3. Substrate scope for the synthesis of 3-(pyrimidin-5-yl)indeno[1,2-*b*]pyrrol-4(1*H*)-one derivatives **11a-j**.[a]



[a]Reaction conditions: 6-aminouracil **10** (1 mmol), barbituric acid **3a** (1 mmol) and phenylglyoxal hydrate **4** (1 mmol) was refluxed in 8 mL of ethanol for 30 min.

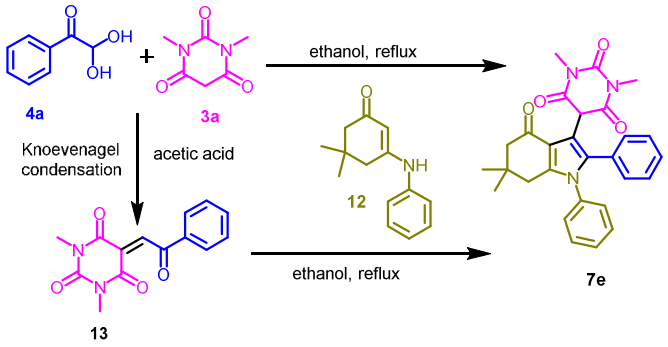
Although the detailed mechanistic studies are not performed, a possible mechanism for the formation of pyrimidinylpyrrolo fused cyclic compounds is shown in Scheme 4. It is assumed that under reflux conditions **3** and **4** form Knoevenagel product **A**, which undergoes 1,3-dipolar cyclization with 6-amino uracil **10**, leads to the formation of **11**. Similarly, 1,3-dipolar cyclization of **A** with *in situ* generated enaminones **B** from cyclic 1,3-dicarbonyl compounds and aromatic amines forms other pyrrole fused ring systems **5** or **7** or **9**.

Scheme 4. Plausible mechanism for the formation of pyrrolo-annelated derivatives.



To support our mechanistic postulate, we have carried out the reaction in three-component as well as two-component manner. In three component process, the reaction of 1,3-dimethylbarbituric acid **3a**, phenylglyoxal hydrate **4a** with enamine **12** (prepared from aromatic amine **2a** and dimedone **6**)[17] under reflux conditions in ethanol was performed and got the desired product **7e**. Moreover, the two component reaction of enamine **12** and Knoevenagel product **13** also resulted the product **7e** under similar reaction conditions. Compound **13** was prepared from **3a** and **4a** by using procedure reported in the earlier literature.[18] These experiments supports our assumption that the reaction was proceeded through *in situ* formation of an enamine and Knoevenagel products (Scheme 5).

Scheme 5. Mechanistic studies for the formation of **7e**.



Conclusions

In conclusion, we have developed a facile and efficient one-pot ecofriendly multicomponent reaction strategy for the construction of pyrimidinyl functionalized pyrrole fused heterocycles. A variety of arylglyoxal hydrates have been shown to participate in a clean reaction with barbituric acid and enaminones or *in situ* generated enaminones from cyclic 1,3-dicarbonyl compounds and several aromatic amines under catalyst-free conditions. The methodology provides a rapid access to pyrimidinyl functionalized pyrrolo-annelated derivatives with excellent yields without tedious workup and purification processes. Further, we believe that our developed methodology will be a good alternative for the synthesis of pyrrole fused heterocycles.

Experimental

General experimental methods:

Phenylglyoxal hydrates were prepared accordingly earlier reported procedure,[19] remaining all the other commercially available reagents were used as received. IR Spectra were recorded on a SHIMADZU FTIR-8400 instrument. NMR spectra were recorded on Avance DPX 300 MHz FT-NMR spectrometer and Avance DPX 500 MHz FT-NMR using tetramethyl silane (TMS) as an internal standard. Mass spectra were recorded on ESQUIRE 3000 Mass spectrometer. All the experiments were monitored by thin layer chromatography (TLC). TLC was performed on pre-coated silica gel plates (Merck).

Typical procedure for the synthesis of pyrrolo-annelated derivatives (5 or 7 or 9). 1,3-indanedione **1** (1 mmol), aromatic amine **2** (1 mmol), barbituric acid **3** (1 mmol), arylglyoxal hydrate **4** (1 mmol) and ethanol (8 mL) were taken in a 50 mL round bottom flask. The mixture was stirred at refluxing temperature for 30 min. After completion of the reaction, the reaction mixture was cooled, formed solids were filtered and washed with cold ethanol to obtain the products **5a-k**.
Similarly, the reaction was carried out by taking dimedone **6** or 2-hydroxy-1,4-naphthoquinone **8** in place of indane-1,3-dione **1** to obtain **7** or **9**.

5-(1-(4-methoxyphenyl)-4-oxo-2-(p-tolyl)-1,4-dihydroindeno[1,2-b]pyrrol-3-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (5a): black solid (yield 89%); mp: 275.6-276.4 ^{o}C; IR (KBr, υ/ cm^{-1}): 3431, 3052, 2966, 2845, 1693, 1633, 1605, 1519, 1446, 1374, 1287, 1253, 1118, 1029, 899, 868, 841, 828, 769, 751726, 654; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm), 7.28 (d, *J* = 7.2 Hz, 3H), 7.17 (d, *J* = 8.8 Hz, 2H), 7.09 (d, *J* = 7.9 Hz, 2H), 7.00 (dd, *J* = 5.2, 3.1 Hz, 2H), 6.88 (d, *J* = 8.9 Hz, 2H), 6.36 (dd, *J* = 5.2, 2.9 Hz, 1H), 4.52 (s, 1H), 3.83 (s, 3H), 3.38 (s, 6H), 2.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 186.09, 167.37, 159.54, 151.68, 151.37, 141.46, 139.08, 138.47, 135.82, 132.49, 130.56, 129.65, 129.25, 128.25, 128.14, 125.87, 123.46, 120.34, 117.48, 114.39, 112.47, 55.49, 46.59, 28.81, 21.32; MS (GCMS, m/z) 519.9 [M]+; Anal. Calcd. For $C_{31}H_{25}N_3O_5$: C, 71.67; H, 4.85; N, 8.09; O, 15.39. Found C, 71.64; H, 4.86; N, 8.08; O, 15.42.

5-(1-(4-methoxyphenyl)-4-oxo-2-phenyl-1,4-dihydroindeno[1,2-b]pyrrol-3-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (5b): black solid (yield 74%); mp: 295.0-295.8 ^{o}C; IR (KBr, υ/ cm^{-1}): 3423, 3062, 2997, 2956, 2932, 2840, 1752, 1683, 1607, 1516, 1445, 1376, 1291, 1246, 1119, 1023, 987, 898, 886, 785, 757, 725, 708, 686; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm), 7.45 – 7.35 (m, 2H), 7.30 (dd, *J* = 7.5, 5.0 Hz, 4H), 7.17 (d, *J* = 8.8 Hz, 2H), 7.01 (dd, *J* = 5.1, 3.1 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 6.43 – 6.33 (m, 1H), 4.53 (s, 1H), 3.83 (s, 3H), 3.39 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): 186.06, 167.32, 159.59, 151.65, 151.49, 141.28, 139.06, 135.75, 132.54, 130.71, 129.55, 128.86, 128.53, 128.23, 123.50, 120.39, 117.56, 114.42, 112.65, 55.49, 46.55, 28.82; MS (GCMS, m/z) 505.9 [M]+ ; Anal. Calcd. For $C_{30}H_{23}N_3O_5$: C, 71.28; H, 4.59; N, 8.31; O, 15.82. Found C, 71.26; H, 4.58; N, 8.33; O, 15.83.

5-(2-(4-bromophenyl)-1-(4-methoxyphenyl)-4-oxo-1,4-dihydroindeno[1,2-b]pyrrol-3-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (5c): red solid (yield 81%); mp: 299.8-300.6 ^{o}C; IR (KBr, υ/ cm^{-1}): 3420, 3075, 2966, 2908, 2833, 1692, 1605, 1519, 1448, 1375, 1286, 1254, 1185, 1117, 1089, 1030, 983, 898, 868, 834, 812, 768, 753, 725, 654; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm), 7.43 (d, *J* = 8.4 Hz, 2H), 7.33 – 7.27 (m, 3H), 7.16 (d, *J* = 8.8 Hz, 2H), 7.02 (dd, *J* = 4.8, 3.5 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 6.38 (dd, *J* = 5.4, 2.7 Hz, 1H), 4.46 (s, 1H), 3.85 (s, 3H),

3.39 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): 185.93, 167.18, 159.75, 151.73, 151.58, 139.93, 138.96, 135.54, 132.62, 132.19, 131.81, 129.24, 128.39, 128.21, 127.82, 123.62, 123.07, 120.37, 117.66, 114.61, 112.98, 55.54, 46.50, 28.86; MS (GCMS, m/z) 584.8 [M]+ ; Anal. Calcd. For $C_{30}H_{22}BrN_3O_5$: C, 61.66; H, 3.79; Br, 13.67; N, 7.19; O, 13.69. Found C, 61.64; H, 3.80; Br, 13.66; N, 7.18; O, 13.72.

5-(2-(4-chlorophenyl)-1-(4-methoxyphenyl)-4-oxo-1,4-dihydroindeno[1,2-b]pyrrol-3-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (5d): red solid (yield 82%); mp: 279.8-280.6 ^{o}C; IR (KBr, υ/ cm^{-1}): 3436, 2948, 2929, 1695, 1681, 1601, 1517, 1420, 1376, 1286, 1260, 1093, 1018, 840, 767, 726; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm), 7.38 – 7.25 (m, 5H), 7.16 (d, *J* = 8.8 Hz, 2H), 7.02 (dd, *J* = 5.0, 3.3 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.38 (dd, *J* = 5.5, 2.7 Hz, 1H), 4.46 (s, 1H), 3.85 (s, 3H), 3.39 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): 185.94, 167.20, 159.74, 151.70, 151.58, 139.93, 138.97, 135.56, 134.75, 132.61, 131.96, 129.26, 128.86, 128.38, 128.21, 127.35, 123.61, 120.35, 117.65, 114.59, 113.00, 55.53, 46.50, 28.85; MS (GCMS, m/z) 539.9 [M]+ ; Anal. Calcd. For $C_{30}H_{22}ClN_3O_5$: C, 66.73; H, 4.11; Cl, 6.57; N, 7.78; O, 14.81. Found C, 66.74; H, 4.12; Cl, 6.56; N, 7.76; O, 14.82.

5-(2-(4-methoxyphenyl)-4-oxo-1-(p-tolyl)-1,4-dihydroindeno[1,2-b]pyrrol-3-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (5e): red solid (yield 81%); mp: 298.6-299.4 ^{o}C; IR (KBr, υ/ cm^{-1}): 3435, 3075, 2966, 2833, 1694, 1678, 1606, 1516, 1453, 1376, 1291, 1257, 1178, 1114, 1032, 985, 898, 844, 800, 768, 727; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm), 7.31 (t, *J* = 7.9 Hz, 3H), 7.15 (dd, *J* = 18.9, 8.3 Hz, 4H), 6.99 (dt, *J* = 7.8, 3.9 Hz, 2H), 6.81 (d, *J* = 8.7 Hz, 2H), 6.37 (dd, *J* = 5.2, 3.0 Hz, 1H), 4.50 (s, 1H), 3.77 (s, 3H), 3.38 (s, 6H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 186.10, 167.41, 159.71, 151.68, 151.06, 141.13, 139.04, 138.81, 135.86, 134.33, 132.47, 132.11, 129.91, 128.10, 126.86, 123.43, 121.13, 120.39, 117.52, 113.94, 112.51, 55.22, 46.60, 28.81, 21.22; MS (GCMS, m/z) 519.9 [M]+ ;Anal. Calcd. For $C_{31}H_{25}N_3O_5$: C, 71.67; H, 4.85; N, 8.09; O, 15.39. Found C, 71.64; H, 4.86; N, 8.09; O, 15.41.

1,3-dimethyl-5-(4-oxo-1,2-di-p-tolyl-1,4-dihydroindeno[1,2-b]pyrrol-3-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (5f): black solid (yield 70%); mp: 189.2-190.0 ^{o}C; IR (KBr, υ/ cm^{-1}): 3428, 3023, 2960, 2925, 1694, 1679, 1633, 1603, 1516, 1495, 1453, 1417, 1373, 1286, 1261, 1187, 1117, 1088, 1022, 982, 898, 867, 837, 826, 767, 753, 727, 655; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm), 7.30 – 7.24 (m, 3H), 7.13 (dt, *J* = 10.9, 8.1 Hz, 6H), 6.99 (dd, *J* = 4.9, 3.2 Hz, 2H), 6.37 (dd, *J* = 4.9, 3.3 Hz, 1H), 4.52 (s, 1H), 3.38 (s, 6H), 2.38 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 186.12, 167.37, 151.69, 151.19, 141.31, 139.06, 138.82, 138.47, 135.84, 134.33, 132.49, 130.53, 129.90, 129.24, 128.13, 126.84, 125.89, 123.45, 120.50, 117.57, 112.57, 46.56, 28.81, 21.34, 21.23; MS (GCMS, m/z) 504.1 [M]+ ;Anal. Calcd. For $C_{31}H_{25}N_3O_4$: C, 73.94; H, 5.00; N, 8.34; O, 12.72. Found C, 73.94; H, 5.01; N, 8.33; O, 12.72.

5-(2-(4-chlorophenyl)-4-oxo-1-(p-tolyl)-1,4-dihydroindeno[1,2-b]pyrrol-3-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (5g): red solid (yield 68%); mp: 300.4-301.2 ^{o}C; IR (KBr, υ/ cm^{-1}): 3432, 3057, 2961, 2916, 1695, 1678, 1604, 1505, 1458, 1377, 1288, 1117, 1087, 1015, 899, 844, 829, 766, 753, 728, 659; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm), 7.39 – 7.28 (m, 3H), 7.27 (d, *J* = 3.6 Hz, 2H), 7.20 (d, *J* = 8.2 Hz, 2H), 7.11 (d, *J* = 8.2 Hz, 2H), 7.06 – 6.96 (m, 2H), 6.39 (dd, *J* = 5.4, 2.8 Hz, 1H), 4.46 (s, 1H), 3.39 (s, 6H), 2.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 185.95, 167.19, 151.58, 151.52, 139.80, 139.21, 138.96, 135.59, 134.75, 134.02, 132.59, 131.94, 130.11, 128.84, 128.37, 127.39, 126.80, 123.60, 120.51, 117.72, 113.10, 46.48, 28.85, 21.22; MS (GCMS, m/z) 523.9 [M]+ ; Anal. Calcd. For $C_{30}H_{22}ClN_3O_4$: C, 68.77; H, 4.23; Cl, 6.77; N, 8.02; O, 12.21. Found C, 68.74; H, 4.24; Cl, 6.78; N, 8.01; O, 12.23.

5-(1-(4-bromophenyl)-4-oxo-2-(p-tolyl)-1,4-dihydroindeno[1,2-b]pyrrol-3-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (5h): red solid (yield 83%); mp: 294.8-295.6 ^{o}C; IR (KBr, υ/ cm^{-1}): 3431, 3057, 2960, 2914, 1694, 1679, 1603, 1505, 1456, 1376, 1288, 1117, 1087, 1015, 899, 842, 827, 766, 752, 726, 656; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm), 7.53 (d, *J* = 8.6 Hz, 2H), 7.32 (dd, *J* = 5.5, 2.8 Hz, 1H), 7.25 (d, *J* = 8.8 Hz, 2H), 7.12 (t, *J* = 7.8 Hz, 4H), 7.03 (dd, *J* = 4.7, 3.6 Hz, 2H), 6.41 (dd, *J* = 5.4, 2.7 Hz, 1H), 4.51 (s, 1H), 3.38 (s, 6H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 185.99, 167.18, 151.61, 150.88, 141.18, 138.88, 138.85, 136.00, 135.54, 132.63, 132.58, 130.54, 129.46, 128.68, 128.38, 125.46, 123.67, 122.78, 120.99, 117.45, 112.93, 46.49, 28.84, 21.33; MS (GCMS, m/z) 568.8 [M]+ ; Anal. Calcd. For $C_{30}H_{22}BrN_3O_4$: C, 63.39; H, 3.90; Br, 14.06; N, 7.39; O, 11.26. Found C, 63.37; H, 3.91; Br, 14.05; N, 7.38; O, 11.29.

5-(1-(4-chlorophenyl)-4-oxo-2-phenyl-1,4-dihydroindeno[1,2-b]pyrrol-3-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (5i): red solid (yield 69%); mp: 272.8-273.6 ^{o}C; IR (KBr, υ/ cm^{-1}): 3435, 3059, 2960, 1693, 1680, 1605, 1505, 1445, 1378, 1291, 1262, 1192, 1093, 1017, 985, 926, 900, 867, 843, 809, 756, 727, 656; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm), 7.44 – 7.27 (m, 8H), 7.20 (d, *J* = 8.6 Hz, 2H), 7.08 – 6.99 (m, 2H), 6.49 – 6.33 (m, 1H), 4.52 (s, 1H), 3.37 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): 185.98, 167.15, 151.58, 151.08, 141.06, 138.84, 135.48, 135.39, 134.85, 132.67, 130.67, 129.64, 128.85, 128.74, 128.47, 128.37, 123.72, 120.98, 117.51, 113.06, 46.46, 28.86; MS (GCMS, m/z) 510.8 [M]+ ; Anal. Calcd. For $C_{29}H_{20}ClN_3O_4$: C, 68.31; H, 3.95; Cl, 6.95; N, 8.24; O, 12.55. Found C, 68.29; H, 3.94; Cl, 6.96; N, 8.23; O, 12.58.

5-(1,2-bis(4-chlorophenyl)-4-oxo-1,4-dihydroindeno[1,2-b]pyrrol-3-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (5j): dark tan solid (yield 74%); mp: 315.6-316.4 ^{o}C; IR (KBr, υ/ cm^{-1}): 3431, 3057, 2954, 2897, 1694, 1679, 1630, 1603, 1505, 1453, 1376, 1286, 1094, 1017, 984, 899, 868, 845, 836, 766, 754, 726, ; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm), 7.40 (d, *J* = 8.5 Hz, 2H), 7.31 (dd, *J* = 16.1, 9.6 Hz, 5H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.11 – 6.99 (m, 2H), 6.49 – 6.35 (m, 1H), 4.45 (s, 1H), 3.39 (s, 6H); MS (GCMS, m/z) 544.8 [M]+ ; Anal. Calcd. For $C_{29}H_{19}Cl_2N_3O_4$: C, 63.98; H, 3.52; Cl, 13.02; N, 7.72; O, 11.76. Found C, 63.96; H, 3.53; Cl, 13.01; N, 7.73; O, 11.77.

5-(2-(4-chlorophenyl)-1-(4-nitrophenyl)-4-oxo-1,4-dihydroindeno[1,2-b]pyrrol-3-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (5k): red solid (yield 86%); mp: 307.3-308.1 ^{o}C; IR (KBr, υ/ cm^{-1}): 3432, 3429, 3058, 2956, 2898, 1697, 1680, 1642, 1631, 1603, 1508, 1459, 1379, 1286, 1095, 1018, 985, 900, 868, 836, 768, 726, 755, 657; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm), 8.31 (d, *J* = 8.9 Hz, 2H), 7.45 (d, *J* = 8.8 Hz, 2H), 7.40 – 7.27 (m, 5H), 7.09 (dd, *J* = 5.1, 3.1 Hz, 2H), 6.46 (dd, *J* = 5.4, 2.7 Hz, 1H), 4.46 (s, 1H), 3.40 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): 185.70, 166.80, 151.42, 150.95, 147.50, 142.00, 139.60, 138.49, 135.57, 135.00, 132.91, 131.88, 129.35, 128.95, 127.98, 126.57, 125.00, 124.10, 121.80, 117.55, 114.12, 46.31, 28.95; MS (GCMS, m/z) 555.8 [M]+ ; Anal. Calcd. For $C_{29}H_{19}ClN_4O_6$: C, 62.77; H, 3.45; Cl, 6.39; N, 10.10; O, 17.29. Found C, 62.75; H, 3.46; Cl, 6.38; N, 10.11; O, 17.30.

5-(1-(4-methoxyphenyl)-6,6-dimethyl-4-oxo-2-phenyl-4,5,6,7-tetrahydro-1H-indol-3-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (7a): white solid (yield 82%); mp: 254.6-255.4 ^{o}C (260.0-261.0 ^{o}C)[6g]; IR (KBr, υ/ cm^{-1}): 3420, 3368, 3268, 3079, 3056, 3002, 2951, 2870, 1682, 1645, 1515, 1490, 1471, 1441, 1410, 1376, 1284, 1248, 1168, 1102, 1045, 1024, 983, 926, 847, 805, 795, 772, 754, 704, 651; ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm), 7.29 (d, J = 6.3 Hz, 3H), 7.17 (dd, J = 9.7, 5.5 Hz, 4H), 6.95 (d, J = 8.8 Hz, 2H), 4.84 (s, 1H), 3.76 (s, 3H), 3.16 (s, 6H), 2.52 (s, 2H), 2.21 (s, 2H), 0.99 (s, 6H); ^{13}C NMR (75 MHz, DMSO-d_6):

194.10, 168.18, 159.14, 152.46, 144.30, 136.88, 130.40, 130.07, 129.69, 129.31, 128.89, 128.30, 115.81, 114.87, 112.21, 55.78, 51.39, 47.85, 36.38, 35.73, 28.82, 28.53; MS (GCMS, m/z) 500.1 [M]+ ; Anal. Calcd. For $C_{29}H_{29}N_3O_5$: C, 69.72; H, 5.85; N, 8.41; O, 16.02. Found C, 69.73; H, 5.86; N, 8.39; O, 16.02.

5-(1-(4-methoxyphenyl)-6,6-dimethyl-4-oxo-2-phenyl-4,5,6,7-tetrahydro-1H-indol-3-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (7b): white solid (yield 87%); mp: 292.4-293.2 ^oC; IR (KBr, υ/ cm^{-1}): 3226, 3107, 2957, 2869, 2844, 1760, 1719, 1691, 1645, 1515, 1493, 1471, 1445, 1405, 1368, 1300, 1252, 1205, 1168, 1114, 1034, 931, 888, 843, 807, 772, 704, 653; ^1H NMR (300 MHz, DMSO-d_6): δ (ppm), 11.14 (s, 2H), 7.34 – 7.22 (m, 3H), 7.19 – 7.10 (m, 4H), 6.95 (d, *J* = 8.9 Hz, 2H), 4.68 (s, 1H), 3.76 (s, 3H), 2.53 (s, 2H), 2.22 (s, 2H), 1.00 (s, 6H); ^{13}C NMR (75 MHz, DMSO-d_6): 193.79, 169.72, 159.10, 151.69, 144.07, 137.06, 130.40, 130.10, 129.77, 129.30, 128.83, 128.20, 116.05, 114.86, 111.89, 55.79, 51.58, 47.57, 36.41, 35.72, 28.52; MS (GCMS, m/z) 471.9 [M]+ ; Anal. Calcd. For $C_{27}H_{25}N_3O_5$: C, 68.78; H, 5.34; N, 8.91; O, 16.97. Found C, 68.76; H, 5.35; N, 8.90; O, 16.99.

5-(6,6-dimethyl-4-oxo-2-phenyl-1-(p-tolyl)-4,5,6,7-tetrahydro-1H-indol-3-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (7c): white solid (yield 76%); mp: 282.6-283.4 ^oC (281.0-283.0 ^oC)[6g]; IR (KBr, υ/ cm^{-1}): 3421, 3075, 3043, 2956,2931, 2871, 2729, 1693, 1679, 1645, 1568, 1542, 1518, 1445, 1418, 1378, 1286, 1259, 1215, 1178, 1157, 1103, 1073, 1045, 982, 929, 894, 847, 774, 756, 706, 677,652; ^1H NMR (300 MHz, DMSO-d_6): δ (ppm), 7.32 – 7.06 (m, 9H), 4.84 (s, 1H), 3.15 (s, 6H), 2.53 (s, 2H), 2.31 (s, 3H), 2.21 (s, 2H), 0.99 (s, 6H).; ^{13}C NMR (75 MHz, DMSO-d_6): 194.02, 168.04, 152.34, 143.98, 138.08, 136.60, 134.36, 130.26, 130.18, 129.93, 128.79, 128.19, 127.72, 115.84, 112.29, 51.27, 47.71, 36.31, 35.63, 28.70, 28.39, 20.93; MS (GCMS, m/z) 484.1 [M]+ ; Anal. Calcd. For $C_{29}H_{29}N_3O_4$: C, 72.03; H, 6.04; N, 8.69; O, 13.24.Found C, 72.01; H, 6.05; N, 8.70; O, 13.23.

5-(6,6-dimethyl-4-oxo-2-phenyl-1-(p-tolyl)-4,5,6,7-tetrahydro-1H-indol-3-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (7d): white solid (yield 75%); mp: 324.6-325.4 ^oC (>300.0 ^oC)[6g]; IR (KBr, υ/ cm^{-1}): 3414, 3220, 3103, 2957, 2871, 1759, 1720, 1694, 1645, 1515, 1493, 1405, 1367, 1287, 1257, 1204, 1111, 1049, 1033, 974, 930, 835,803, 773, 725, 703, 653, 633; ^1H NMR (300 MHz, DMSO-d_6): δ (ppm), 11.14 (s, 2H), 7.35 – 7.00 (m, 9H), 4.68 (s, 1H), 2.54 (s, 2H), 2.30 (s, 3H), 2.22 (s, 2H), 0.99 (s, 6H); ^{13}C NMR (75 MHz, DMSO-d_6): 193.83, 169.70, 151.68, 143.88, 138.12, 136.90, 134.56, 130.37, 130.27, 130.09, 128.85, 128.21, 127.83, 116.20, 112.09, 51.56, 49.07, 47.55, 36.46, 35.73, 28.49, 21.05; MS (GCMS, m/z) 455.9 [M]+ ; Anal. Calcd. For $C_{27}H_{25}N_3O_4$: C, 71.19; H, 5.53; N, 9.22; O, 14.06. Found C, 71.18; H, 5.53; N, 9.21; O, 14.08.

5-(6,6-dimethyl-4-oxo-1,2-diphenyl-4,5,6,7-tetrahydro-1H-indol-3-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (7e): white solid (yield 79%); mp: 315.0-315.8 ^oC; IR (KBr, υ/ cm^{-1}): 3435, 3230, 3103, 2960, 2833, 1739, 1730, 1710, 1631, 1597, 1497, 1472, 1420, 1386, 1346, 1258,1232, 1198, 1157, 1112, 1064, 1048, 798, 771, 711, 691, 653; ^1H NMR (300 MHz, DMSO-d_6): δ (ppm), 7.65 – 6.95 (m, 10H), 4.85 (s, 1H), 3.16 (s, 6H), 2.55 (s, 2H), 2.22 (s, 2H), 0.99 (s, 6H); ^{13}C NMR (126 MHz, DMSO-d_6): 194.07, 168.02, 152.34, 143.91, 136.89, 136.60, 130.26, 129.85, 129.71, 128.78, 128.62, 128.22, 128.01, 115.94, 112.39, 51.27, 47.71, 36.29, 35.65, 28.70, 28.38; MS (GCMS, m/z) 469.9 [M]+ ; Anal. Calcd. For $C_{28}H_{27}N_3O_4$: C, 71.62; H, 5.80; N, 8.95; O, 13.63. Found C, 71.60; H, 5.81; N, 8.94; O, 13.65.

5-(6,6-dimethyl-4-oxo-1,2-diphenyl-4,5,6,7-tetrahydro-1H-indol-3-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (7f): white solid (yield 71%); mp: 344.2-345.0 ^oC; IR (KBr, υ/ cm^{-1}): 3451, 3223, 3082, 2967, 2954, 2935, 2838, 2869, 1738, 1729, 1629, 1537, 1496, 1470, 1439, 1409, 1362, 1341, 1257, 1231, 1197, 1157, 1112, 1064, 1049, 1028, 1003, 945, 889, 819, 798, 772, 749, 711, 691, 653; ^1H NMR (300 MHz, DMSO-d_6): δ (ppm), 11.14 (s, 2H), 7.55 – 7.02 (m, 10H), 4.69 (s, 1H), 2.56 (s, 2H), 2.23 (s, 2H), 1.00 (s, 6H); ^{13}C NMR (75 MHz, DMSO-d_6): 193.88, 169.70, 152.60, 151.71, 143.79, 137.08, 136.87, 130.36, 130.02, 129.81, 128.85, 128.12, 116.28, 112.21, 51.55, 47.57, 36.40, 35.76, 28.50; MS (GCMS, m/z) 441.9 [M]+; Anal. Calcd. For $C_{26}H_{23}N_3O_4$: C, 70.73; H, 5.25; N, 9.52; O, 14.50. Found C, 70.71; H, 5.26; N, 9.51; O, 14.52.

5-(1-(4-bromophenyl)-6,6-dimethyl-4-oxo-2-phenyl-4,5,6,7-tetrahydro-1H-indol-3-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (7g): light pink solid (yield 84%); mp: 325.4-326.2 ^oC; IR (KBr, υ/ cm^{-1}): 3432, 3083, 2959, 2871, 1684, 1659, 1556, 1494, 1471, 1412, 1392, 1374, 1287, 1255, 1159, 1092, 1064, 1015, 987, 882, 855, 810, 756, 738, 724, 710, 651; ^1H NMR (300 MHz, DMSO-d_6): δ (ppm), 7.62 (d, *J* = 8.6 Hz, 2H), 7.32 (d, *J* = 6.8 Hz, 3H), 7.18 (t, *J* = 8.2 Hz, 4H), 4.86 (s, 1H), 3.15 (s, 6H), 2.58 (s, 2H), 2.22 (s, 2H), 0.99 (s, 6H); ^{13}C NMR (126 MHz, DMSO-d_6): 194.13, 167.96, 152.31, 143.96, 136.44, 136.20, 132.67, 130.29, 130.11, 129.58, 128.95, 128.40, 121.67, 116.14, 112.65, 51.24, 47.68, 36.16, 35.67, 28.71, 28.35; MS (GCMS, m/z) 548.8 [M]+ ; Anal. Calcd. For $C_{28}H_{26}BrN_3O_4$: C, 61.32; H, 4.78; Br, 14.57; N, 7.66; O, 11.67. Found C, 61.29; H, 4.78; Br, 14.56; N, 7.67; O, 11.70.

5-(1-(4-bromophenyl)-6,6-dimethyl-4-oxo-2-phenyl-4,5,6,7-tetrahydro-1H-indol-3-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (7h): white solid (yield 82%); mp: 321.6-322.4 ^oC; IR (KBr, υ/ cm^{-1}): 3397, 3223, 3098, 2958, 2867, 1761, 1719, 1691, 1645, 1587, 1537, 1493, 1467, 1406, 1372, 1353, 1296, 1259, 1205, 1153, 1114, 1070, 1049, 1012, 970, 931, 888, 839, 810, 795, 773, 759, 725, 704, 685, 651; ^1H NMR (300 MHz, DMSO-d_6): δ (ppm), 11.16 (s, 2H), 7.61 (d, *J* = 8.5 Hz, 2H), 7.38 – 7.25 (m, 3H), 7.16 (t, *J* = 7.6 Hz, 4H), 4.70 (s, 1H), 2.58 (s, 2H), 2.23 (s, 2H), 1.00 (s, 6H); ^{13}C NMR (75 MHz, DMSO-d_6): 193.93, 169.62, 151.68, 143.85, 136.75, 136.40, 132.76, 130.42, 130.22, 129.74, 129.00, 128.43, 121.72, 116.51, 112.47, 51.54, 49.07, 47.52, 35.78, 28.46; MS (GCMS, m/z) 520.8 [M]+ ; Anal. Calcd. For $C_{26}H_{22}BrN_3O_4$: C, 60.01; H, 4.26; Br, 15.36; N, 8.07; O, 12.30. Found C, 59.99; H, 4.25; Br, 15.37; N, 8.06; O, 12.33.

5-(1-(4-chlorophenyl)-6,6-dimethyl-4-oxo-2-phenyl-4,5,6,7-tetrahydro-1H-indol-3-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (7i): white solid (yield 68%); mp: 315.6-316.4 ^oC (>300.0 ^oC)[6g]; IR (KBr, υ/ cm^{-1}): 3435, 3098, 2956, 2874, 1698, 1682, 1649, 1579, 1542, 1496, 1473, 1415, 1375, 1283, 1258, 1090, 1046, 1014, 984, 845, 810, 774, 758, 726, 704, 650; ^1H NMR (300 MHz, DMSO-d_6): δ (ppm), 11.14 (s, 2H), 7.48 (d, *J* = 8.6 Hz, 2H), 7.38 – 7.19 (m, 5H), 7.18 – 7.09 (m, 2H), 4.70 (s, 1H), 2.58 (s, 2H), 2.23 (s, 2H), 1.00 (s, 6H); ^{13}C NMR (75 MHz, DMSO-d_6): 193.91, 169.62, 151.67, 143.89, 136.80, 135.98, 133.20, 130.42, 129.94, 129.82, 129.75, 128.99, 116.48, 112.43, 51.53, 47.51, 36.31, 35.77, 28.46; MS (GCMS, m/z) 476.8 [M]+ ; Anal. Calcd. For $C_{26}H_{22}ClN_3O_4$: C, 65.62; H, 4.66; Cl, 7.45; N, 8.83; O, 13.44. Found C, 65.61; H, 4.65; Cl, 7.44; N, 8.84; O, 13.46.

5-(2-(4-chlorophenyl)-6,6-dimethyl-4-oxo-1-phenyl-4,5,6,7-tetrahydro-1H-indol-3-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (7j): white solid (yield 83%); mp: 321.2-322.0 ^oC; IR (KBr, υ/ cm^{-1}): 3432, 3097, 2957, 2869, 1693, 1688, 1646, 1580, 1539, 1493, 1468, 1412, 1375, 1354, 1288, 1259, 1092, 1048, 1013, 984, 839, 812, 776, 759, 726, 704, 685, 650; ^1H NMR (300 MHz, DMSO-d_6): δ (ppm), 11.17 (s, 2H), 7.42 (t, *J* = 7.0 Hz, 3H), 7.35 (d, *J* = 7.7 Hz, 2H), 7.22 (d, *J* = 7.6 Hz, 2H), 7.13 (d, *J* = 7.1 Hz, 2H), 4.73 (s, 1H), 2.56 (s, 2H), 2.23 (s, 2H), 1.00 (s, 6H); ^{13}C NMR (75 MHz, DMSO-d_6): 193.88, 169.58, 151.67, 144.06, 136.83, 135.64, 133.16, 132.11, 129.93, 128.95, 128.12, 116.36, 112.69, 51.54, 47.50, 36.39, 35.76, 28.46; MS (GCMS, m/z) 476.7 [M]+ ; Anal. Calcd. For

$C_{26}H_{22}ClN_3O_4$: C, 65.62; H, 4.66; Cl, 7.45; N, 8.83; O, 13.44. Found C, 65.61; H, 4.64; Cl, 7.45; N, 8.85; O, 13.45.

5-(1-(4-chlorophenyl)-6,6-dimethyl-4-oxo-2-phenyl-4,5,6,7-tetrahydro-1H-indol-3-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (7k): white solid (yield 78%); mp: 310.4-311.2 °C (>300.0 °C)[6g]; IR (KBr, υ/ cm^{-1}): 3422, 3099, 3080, 2956, 2931, 2869, 1698, 1682, 1648, 1567, 1544, 1496, 1473, 1415, 1375, 1283, 1258, 1171, 1157, 1113, 1090, 1075, 1026, 984, 927, 884, 844, 810, 773, 758, 726, 704, 650; ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm), 7.49 (d, *J* = 8.5 Hz, 2H), 7.29 (dd, *J* = 15.8, 7.4 Hz, 5H), 7.16 (d, *J* = 5.2 Hz, 2H), 4.86 (s, 1H), 3.16 (s, 6H), 2.58 (s, 2H), 2.22 (s, 2H), 0.99 (s, 6H); ^{13}C NMR (126 MHz, DMSO-d_6): 194.12, 167.96, 152.32, 144.01, 136.49, 135.77, 133.15, 130.29, 129.83, 129.73, 129.59, 128.94, 128.39, 116.12, 112.61, 51.24, 47.69, 36.15, 35.67, 28.71, 28.36; MS (GCMS, m/z) 504.8 [M]+ ; Anal. Calcd. For $C_{28}H_{26}ClN_3O_4$: C, 66.73; H, 5.20; Cl, 7.03; N, 8.34; O, 12.70. Found C, 66.71; H, 5.21; Cl, 7.02; N, 8.33; O, 12.73.

5-(1-(4-chlorophenyl)-6,6-dimethyl-4-oxo-2-(thiophen-2-yl)-4,5,6,7-tetrahydro-1H-indol-3-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (7l): light pink solid (yield 69%); mp: 301.3-302.1 °C; IR (KBr, υ/ cm^{-1}): 3435, 3081, 2958, 2870, 1682, 1651, 1548, 1496, 1472, 1416, 1374, 1284, 1255, 1156, 1091, 1061, 1016, 984, 881, 854, 806, 757, 739, 725, 709, 652; ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm), 7.56 (dd, *J* = 18.3, 6.8 Hz, 3H), 7.35 (d, *J* = 8.6 Hz, 2H), 7.10 – 6.94 (m, 2H), 4.97 (s, 1H), 3.16 (s, 6H), 2.55 (s, 2H), 2.22 (s, 2H), 0.99 (s, 6H); MS (GCMS, m/z) 510.8 [M]+ ; Anal. Calcd. For $C_{26}H_{24}ClN_3O_4S$: C, 61.23; H, 4.74; Cl, 6.95; N, 8.24; O, 12.55; S, 6.29. Found C, 61.21; H, 4.75; Cl, 6.94; N, 8.23; O, 12.56; S, 6.31.

5-(1-(4-chlorophenyl)-4,9-dioxo-2-phenyl-4,9-dihydro-1H-benzo[f]indol-3-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (9a): red solid (yield 61%); mp: 221.8-222.6 °C; IR (KBr, υ/ cm^{-1}): 3400, 3197, 3082, 2955, 2596, 1685, 1624, 1618, 1596, 1572, 1520, 1494, 1452, 1380, 1358, 1333, 1288, 1241, 1186, 1125, 1089, 1032, 1015, 993, 948, 923, 871, 862, 824, 816, 793, 775, 757, 722, 692, 670, 662, 657; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm), 8.22 (d, *J* = 7.5 Hz, 1H), 8.03 (d, *J* = 7.4 Hz, 1H), 7.75 (dt, *J* = 15.0, 5.5 Hz, 5H), 7.61 – 7.12 (m, 6H), 4.98 (s, 1H), 3.42 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) 182.01, 173.07, 165.90, 160.61, 151.61, 151.37, 134.36, 133.72, 132.73, 132.58, 130.90, 129.26, 128.41, 128.09, 127.47, 127.13, 126.77, 112.15, 46.67, 29.21; MS (GCMS, m/z) 537.1 [M]+ ; Anal. Calcd. For $C_{30}H_{20}ClN_3O_5$: C, 66.98; H, 3.75; Cl, 6.59; N, 7.81; O, 14.87. Found C, 66.96; H, 3.76; Cl, 6.57; N, 7.80; O, 14.91.

5-(1-(4-methoxyphenyl)-4,9-dioxo-2-(p-tolyl)-4,9-dihydro-1H-benzo[f]indol-3-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (9b): red solid (yield 57%); mp: 235.6-236.4 °C; IR (KBr, υ/ cm^{-1}): 3401, 3198, 2955, 2599, 2298, 1685, 1621, 1608, 1596, 1569, 1520, 1492, 1452, 1380, 1359, 1333, 1241, 1125, 1090, 1032, 1015, 948, 923, 871, 862, 824, 816, 775, 757, 722, 692, 670, 662; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm), 8.62 (d, *J* = 6.5 Hz, 1H), 8.09 (d, *J* = 7.6 Hz, 1H), 7.73 – 7.64 (m, 2H), 7.23 – 7.08 (m, 6H), 6.98 (d, *J* = 8.6 Hz, 2H), 4.94 (s, 1H), 3.88 (s, 3H), 3.42 (s, 6H), 2.36 (s, 3H); MS (GCMS, m/z) 547.1 [M]+ ; Anal. Calcd. For $C_{32}H_{25}N_3O_6$: C, 70.19; H, 4.60; N, 7.67; O, 17.54. Found C, 70.17; H, 4.60; N, 7.68; O, 17.55.

Typical procedure for the synthesis of pyrrolo[2,3-d]pyrimidin derivatives (11a-11j): Amino uracil **10** (1 mmol), barbituric acid **3** (1 mmol), phenylglyoxal hydrate **4** (1 mmol) and ethanol (8 mL) were taken in a 50 mL round bottom flask. The mixture was stirred at refluxing temperature for 30 min. After completion of the reaction, the reaction mixture was cooled, formed solids were filtered and washed with cold ethanol to obtain the products **11a-j**.

5-(1,3-dimethyl-2,4-dioxo-6-phenyl-2,3,4,7-tetrahydro-1H-pyrrolo[2,3-d]pyrimidin-5-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (11a): white solid (yield 88%); mp: >350.0 °C; IR (KBr, υ/ cm^{-1}): 3435, 3260, 3198, 3080, 3059, 3009, 2950, 1683, 1653, 1603, 1569, 1433, 1376, 1300, 1119, 1067, 1035, 978, 861, 793, 762, 754, 745, 708, 693, 680; ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm), 11.94 (s, 1H), 7.77 – 7.23 (m, 5H), 5.17 (s, 1H), 3.51 (s, 3H), 3.17 (s, 6H), 3.13 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6): 168.16, 159.27, 152.38, 151.06, 142.88, 139.75, 131.66, 130.84, 129.29, 128.55, 128.45, 109.17, 97.27, 47.30, 31.12, 28.91, 27.87; MS (GCMS, m/z) 409.1 [M]+ ; Anal. Calcd. For $C_{20}H_{19}N_5O_5$: C, 58.68; H, 4.68; N, 17.11; O, 19.53. Found C, 58.66; H, 4.69; N, 17.10; O, 19.55.

5-(1,3-dimethyl-2,4-dioxo-6-phenyl-2,3,4,7-tetrahydro-1H-pyrrolo[2,3-d]pyrimidin-5-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (11b): white solid (yield 86%); mp: >350.0 °C; IR (KBr, υ/ cm^{-1}): 3395, 3223, 3088, 2948, 2885, 1708, 1689, 1652, 1603, 1567, 1509, 1497, 1448, 1410, 1365, 1322, 1276, 1256, 1231, 1190, 1125, 1068, 1048, 979, 922, 855, 818, 790, 768, 775, 743, 705, 675, 623, 605; ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm), 11.88 (s, 1H), 11.21 (s, 2H), 7.65 – 7.31 (m, 5H), 5.02 (s, 1H), 3.50 (s, 3H), 3.16 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6): 169.60, 159.02, 151.53, 150.98, 139.56, 131.77, 130.77, 129.12, 128.59, 128.43, 128.22, 126.90, 108.79, 97.36, 46.89, 30.99, 27.66; MS (GCMS, m/z) 381.1 [M]+ ; Anal. Calcd. For $C_{18}H_{15}N_5O_5$: C, 56.69; H, 3.96; N, 18.37; O, 20.98. Found C, 56.66; H, 3.97; N, 18.36; O, 21.01.

5-(6-(4-methoxyphenyl)-1,3-dimethyl-2,4-dioxo-2,3,4,7-tetrahydro-1H-pyrrolo[2,3-d]pyrimidin-5-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (11c): white solid (yield 79%); mp: >350.0 °C; IR (KBr, υ/ cm^{-1}): 3420, 3368, 3268, 3079, 3056, 3002, 2952, 2870, 1683, 1645, 1516, 1441, 1413, 1376, 1302, 1285, 1170, 1105, 1057, 1028, 983, 926, 847, 795, 772, 754, 745, 708, 693, 651; ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm), 11.86 (s, 1H), 7.50 (d, *J* = 8.5 Hz, 2H), 7.08 (d, *J* = 8.6 Hz, 2H), 5.10 (s, 1H), 3.80 (s, 3H), 3.49 (s, 3H), 3.17 (s, 6H), 3.13 (s, 3H); MS (GCMS, m/z) 439.1 [M]+ ; Anal. Calcd. For C21H21N5O6: C, 57.40; H, 4.82; N, 15.94; O, 21.84. Found C, 57.38; H, 4.81; N, 15.93; O, 21.88.

5-(6-(4-methoxyphenyl)-1,3-dimethyl-2,4-dioxo-2,3,4,7-tetrahydro-1H-pyrrolo[2,3-d]pyrimidin-5-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (11d): white solid (yield 84%); mp: >350.0 °C; IR (KBr, υ/ cm^{-1}): 3391, 3226, 3108, 2956, 2872, 2845, 1718, 1707, 1691, 1651, 1604, 1569, 1514, 1492, 1451, 1409, 1366, 1302, 1254, 1208, 1191, 1169, 1114, 1037, 982, 932, 889, 843, 807, 780, 706, 673; ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm), 11.80 (s, 1H), 11.20 (s, 2H), 7.49 (d, *J* = 7.9 Hz, 2H), 7.07 (d, *J* = 7.9 Hz, 2H), 4.95 (s, 1H), 3.80 (3, 3H), 3.49 (s, 3H), 3.16 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6): 169.79, 159.60, 159.12, 151.64, 151.10, 139.37, 131.87, 129.95, 123.29, 114.69, 108.03, 97.31, 55.74, 46.98, 31.08, 27.77; MS (GCMS, m/z) 411.1 [M]+ ; Anal. Calcd. For $C_{19}H_{17}N_5O_6$: C, 55.47; H, 4.17; N, 17.02; O, 23.34. Found C, 55.43; H, 4.18; N, 17.03; O, 23.36.

1,3-dimethyl-5-(4-oxo-6-phenyl-2-thioxo-2,3,4,7-tetrahydro-1H-pyrrolo[2,3-d]pyrimidin-5-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (11e): white solid (yield 76%); mp: >350.0 °C; IR (KBr, υ/ cm^{-1}): 3529, 3426, 3258, 3109, 3057, 2903, 1672, 1632, 1606, 1507, 1447, 1383, 1288, 1260, 1163, 1119, 1028, 990, 918, 803, 765, 699, 650; ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm), 13.46 (s, 1H), 12.02 (s, 1H), 12.00 (s, 1H), 7.57 (d, *J* = 7.2 Hz, 2H), 7.53 – 7.39 (m, 3H), 5.15 (s, 1H), 3.16 (s, 6H); ^{13}C NMR (75 MHz, DMSO-d_6): 172.96, 168.18, 158.35, 152.30, 139.32, 132.81, 130.42, 129.20, 128.74, 108.91, 101.33, 47.06, 28.89; MS (GCMS, m/z) 397.1 [M]+ ; Anal. Calcd. For $C_{18}H_{15}N_5O_4S$: C, 54.40; H, 3.80; N, 17.62; O, 16.11; S, 8.07. Found C, 54.39; H, 3.80; N, 17.61; O, 16.13; S, 8.07.

5-(6-(4-bromophenyl)-4-oxo-2-thioxo-2,3,4,7-tetrahydro-1H-pyrrolo[2,3-d]pyrimidin-5-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (11f): light tan solid (yield 82%); mp: >350.0 °C; IR (KBr, υ/ cm^{-1}): 3384, 3243, 3105, 3034, 2886, 2343, 1671, 1602, 1505, 1451, 1428, 1382, 1290, 1262, 1184, 1163, 1119, 1006, 989, 832, 811, 758, 717, 604; ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm), 13.49 (s, 1H), 12.07 (s, 1H), 12.02 (s, 1H), 7.69 (d, *J* = 8.1 Hz, 2H), 7.50 (d, *J* = 8.1 Hz, 2H), 5.14 (s, 1H), 3.16 (s, 6H); ^{13}C NMR (126 MHz, DMSO-d_6): 172.97, 167.92, 158.16, 152.13, 139.32, 131.98, 131.48, 130.60, 129.45, 121.89, 109.31, 101.24, 84.25, 46.86, 28.77; MS (GCMS, m/z) 474.9 [M]+ ; Anal. Calcd. For $C_{18}H_{14}BrN_5O_4S$: C, 45.39; H, 2.96; Br, 16.78; N, 14.70; O, 13.44; S, 6.73. Found C, 45.37; H, 2.95; Br, 16.76; N, 14.71; O, 13.47; S, 6.74.

5-(6-(4-bromophenyl)-4-oxo-2-thioxo-2,3,4,7-tetrahydro-1H-pyrrolo[2,3-d]pyrimidin-5-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (11g): light tan solid (yield 74%); mp: >350.0 °C; IR (KBr, υ/ cm^{-1}): 3385, 3181, 2369, 1674, 1615, 1428, 1250, 1147, 1123, 1077, 1007, 824, 780, 728, 605; ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm), 12.03 (s, 1H), 12.00 (s, 1H), 11.81 (s, 1H), 11.27 (s, 2H), 7.68 – 7.65 (m, 2H), 7.48 – 7.45 (m, 2H), 5.01 (s, 1H); MS (GCMS, m/z) 448.9 [M]+ ; Anal. Calcd. For $C_{16}H_{10}BrN_5O_4S$: C, 42.87; H, 2.25; Br, 17.83; N, 15.62; O, 14.28; S, 7.15. Found C, 42.84; H, 2.26; Br, 17.82; N, 15.63; O, 14.29; S, 7.16.

5-(2-amino-4-oxo-6-phenyl-4,7-dihydro-1H-pyrrolo[2,3-d]pyrimidin-5-yl)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (11h): light olie green solid (yield 68%); mp: >350.0 °C; IR (KBr, υ/ cm^{-1}): 3474, 3382, 3109, 3043, 2914, 2870, 2788, 1679, 1633, 1556, 1432, 1380, 1327, 1317, 1288, 1267, 1250, 1179, 1157, 1124, 1108, 1076, 1041, 1022, 985, 928, 900, 874, 824, 796, 781, 753, 706, 693, 661; ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm), 11.44 (s, 1H), 10.14 (s, 1H), 7.57 (d, *J* = 7.6 Hz, 2H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 1H), 6.28 (s, 2H), 5.10 (s, 1H), 3.16 (s, 6H); MS (GCMS, m/z) 380.1 [M]+ ; Anal. Calcd. For $C_{18}H_{16}N_6O_4$: C, 56.84; H, 4.24; N, 22.10; O, 16.82. Found C, 56.82; H, 4.24; N, 22.10; O, 16.84.

5-(2-amino-6-(4-bromophenyl)-4-oxo-4,7-dihydro-1H-pyrrolo[2,3-d]pyrimidin-5-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (11i): black solid (yield 75%); mp: >350.0 °C; IR (KBr, υ/ cm^{-1}): 3427, 3382, 3181, 3042, 2916, 2871, 2369, 1678, 1617, 1514, 1429, 1326, 1311, 1290, 1255, 1179, 1147, 1123, 1098, 1078, 1002, 983, 926, 869, 825, 782, 729, 691, 657; ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm), 11.45 (s, 1H), 11.18 (s, 2H), 10.25 (s, 1H), 7.63 (d, *J* = 8.3 Hz, 2H), 7.45 (d, *J* = 8.3 Hz, 2H), 6.27 (s, 2H), 4.97 (s, 1H); MS (GCMS, m/z) 431.9 [M]+ ; Anal. Calcd. For $C_{16}H_{11}BrN_6O_4$: C, 44.57; H, 2.57; Br, 18.53; N, 19.49; O, 14.84. Found C, 44.55; H, 2.57; Br, 18.52; N, 19.48; O, 14.88.

5-(2-amino-4-oxo-6-phenyl-4,7-dihydro-1H-pyrrolo[2,3-d]pyrimidin-5-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (11j): light olive green solid (yield 86%); mp: >350.0 °C; IR (KBr, υ/ cm^{-1}): 3467, 3381, 3224, 3081, 2943, 2883, 2791, 1703, 1681, 1653, 1605, 1562, 1498, 1449, 1376, 1325, 1278, 1257, 1232, 1185, 1159, 1126, 1098, 1074, 1047, 983, 924, 886, 856, 824, 792, 776, 743, 705, 683, 651; ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm), 12.18 (s, 2H), 11.52 (s, 1H), 10.44 (s, 1H), 7.45 (d, *J* = 7.7 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.17 (t, *J* = 7.2 Hz, 1H), 6.17 (s, 2H), 5.15 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): 170.13, 159.33, 153.27, 151.69, 151.59, 131.92, 131.24, 129.17, 127.92, 127.65, 106.90, 99.51, 47.18, 40.71, 40.44, 40.16, 39.88, 39.61, 39.33, 39.05; MS (GCMS, m/z) 352.1 [M]+ ; Anal. Calcd. For $C_{16}H_{12}N_6O_4$: C, 54.55; H, 3.43; N, 23.85; O, 18.17. Found C, 54.53; H, 3.44; N, 23.84; O, 18.19.

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Notes and references

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