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A novel method for the synthesis of highly functionalized 3,4-dihydropyrimidin-2(1*H*)-ones through the 1,4-addition on pyrimidin-2(1*H*)-ones

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Abstract—A novel method for synthesizing hitherto unreported 3,4-dihydropyrimidin-2(1*H*)-ones (DHPMs) through 1,4-addition of nucleophiles on pyrimidin-2(1*H*)-ones is disclosed herein.

1. Introduction

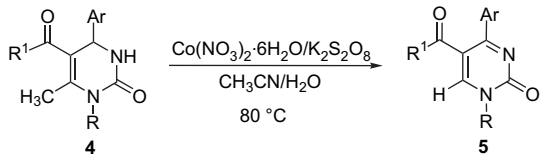
The synthesis of Biginelli compounds has attracted attention for more than a decade.[1] The interest in DHPM synthesis is not only due to its structural similarity with the well-known Hantzsch dihydropyridine (calcium channel modulators) but also to their various medicinal and biological applications.[2,3] DHPM synthesis involves either the one-pot coupling of ethyl acetoacetate, urea and an aldehyde[4] or the reaction of protected urea with enones.[5] Most methods including combinatorial chemistry approaches have exploited commercially available aldehydes or 1,3-dicarbonyl compounds (the most varied components) to synthesize DHPMs.[6,7]

We have shown that the cardiotonic activities of **4a–e** are better than Digoxin[8] which inspired us to synthesize highly functionalized DHPMs to further improve the activity. However, the synthesis of DHPM scaffolds with strictly defined substitution patterns is often difficult due to the lack of starting materials and lower yields of one-pot condensations involving structurally complex building blocks.[1e,9]

2. Results and discussion

2.1. Synthesis of highly functionalized DHPMs

We recently disclosed a novel method for the synthesis of 6-unsubstituted pyrimidin-2(1*H*)-ones **5** by $Co^{2+}/S_2O_8^{2-}$ mediated oxidation of **4** (Scheme 1).[10] α,β-Unsaturated conjugated systems of **5a–e** were expected to act as Michael acceptors. Therefore 1,4-addition of (substituted)indole, pyrrole, phenol, electron-rich imine, azide and hydride can be expected to yield hitherto unreported DHPMs (Scheme 2). Metal ions (Ni^{2+}, Cu^{+}, Fe^{3+}, Ce^{4+} or In^{3+}) were proven to be more effective for inter- and intramolecular Michael addition reactions.[11–13] In our method, $InCl_3$, $FeCl_3$ and ceric ammonium nitrate (CAN) were screened initially for catalytic activity. We found that CAN promoted reactions were clean and afforded higher yields of product.



Scheme 1. Unprecedented oxidation of 6-methyl DHPMs (**4**) by Co^{3+}.

For an illustrative example, **5a** in anhydrous methanol was stirred with indole at ambient temperature under argon atmosphere. To the stirring reaction mixture was added 5 mol % of CAN and the total consumption of **5a** after an hour as monitored by TLC was an indication of completion of the reaction (Scheme 2). However, the reaction when conducted without the addition of CAN did not afford any appreciable amount of **6a**.

The ^{1}H NMR spectrum of **6a** showed a doublet with J=3 Hz at δ 5.54 ppm. This is attributed to the CH group adjoining the NH group, which is commonly observed in DHPM chemistry.[6b,14] The ^{13}C NMR spectrum of **6a** had absorptions around δ 48 and 101 ppm (respectively for CH(4) and C(5)) confirming the formation of 1,4-addition product. The product formation was further ascertained by mass

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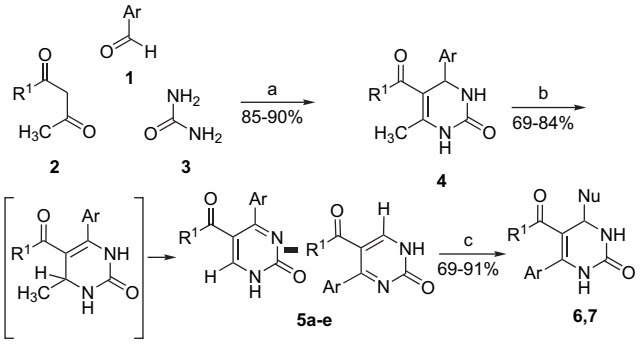


Scheme 2. Synthesis of highly functionalized DHPMs. (a) Na_2SO_4, $In(OTf)_3$ (5 mol %), MW; (b) $Co(NO_3)_2{\cdot}6H_2O/K_2S_2O_8$, CH_3CN/H_2O, 80 °C; (c) Nu (2 equiv), $Ce(NH_4)_2(NO_3)_6$ (5 mol %), rt.

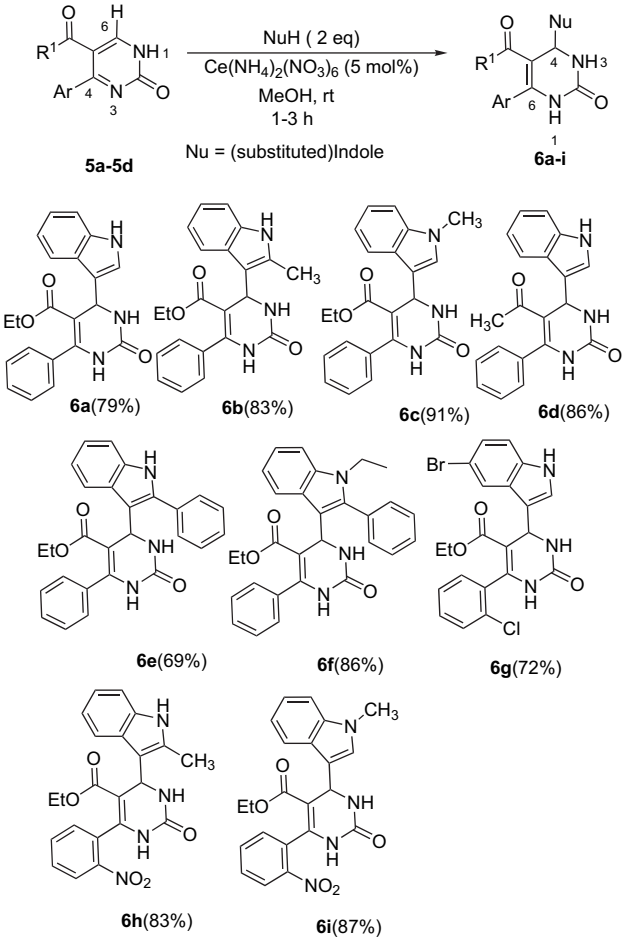
spectrum (m/z=361), IR spectrum (ν=3589, 3370, 3293 cm^{-1} corresponding three NH stretching) and elemental analysis. The crystallographic data finally confirmed the structure of the product ascribed to **6a** (Fig. 1).[15]

2.2. Screening of substituted indole addition on 5a–e

The structural and electronic requirements needed for 1,4-addition on **5a–e** by (substituted)indoles were deduced from the conclusions of the following experiments. (i) Chemoselective addition on **5a–e** by (substituted)indoles yielded exclusively 1,4-addition product. (ii) (Substituted)indoles form C–C bond on **5a–e** regioselectively at C(3) position. (iii) 3-(Substituted)indoles (2-(3-indolyl)ethylamine) or indole bearing strong electron-withdrawing groups (3-formyl indole, 1-methyl-2-formyl indole, ethyl 2-indole-carboxylate, 2-ethoxycarbonyl-3-methylindole and 5-nitroindole) failed to afford isolable yields of product. In contrast electron-donating groups such as a methyl or an ethyl group in indole increased the yields of the reaction. (iv) (Ethyl 6-methyl-4-phenyl-pyrimidin-2(1*H*)-one)-5-carboxylate (C(6)-methyl-substituted **5a**)[16] did not undergo 1,4-addition.

The characteristic peaks of **6b–i** were similar to X-ray determined structure of **6a** confirming their formation. Indole bearing moderate electron-withdrawing group or halogen atom afforded moderate to good yields of DHPMs (Scheme 3, compounds **6e** and **6g**). Phenol, resorcinol, amines (aniline, methylamine and 1-phenylethylamine), azides, ethyl acetoacetate, imines, *N*-ethyl carbazole and *N*-aryl pyrazole failed to afford corresponding 1,4-addition products. But pyrrole and hydride ($NaBH_4$) were added onto **5** under the same conditions to yield novel DHPMs. To the best of our knowledge, pyrrolyl dihydropyrimidin-2(1*H*)-ones and 6-aryl-4-unsubstituted dihydropyrimidin-2(1*H*)-one have not been reported in the literature (Scheme 4).

The application of CAN as a catalyst during the addition of indole on α,β-unsaturated system has also been reported by



Scheme 3. Highly functionalized 4-indolyl-3,4-DHPM.

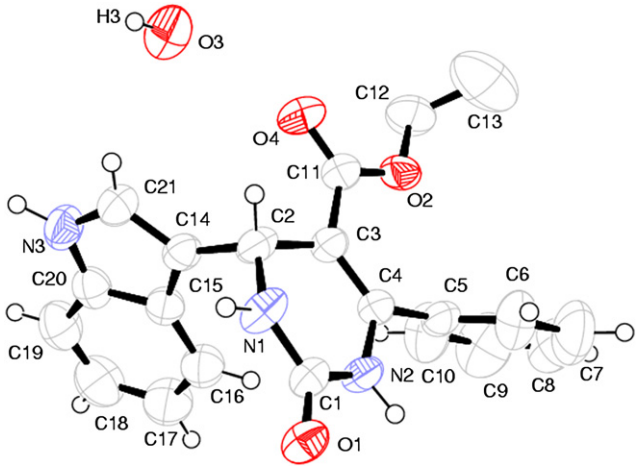
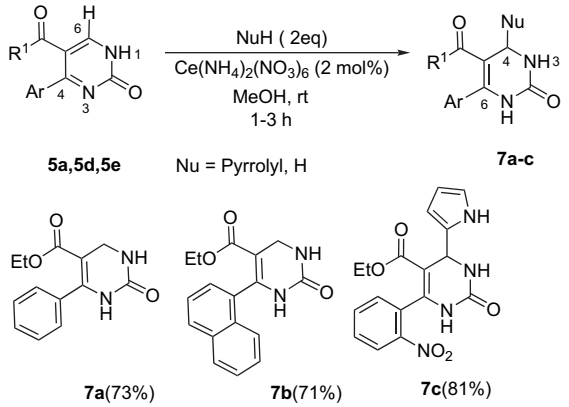


Figure 1. ORTEP diagram of **6a**.



Scheme 4. Synthesis of 4-unsubstituted and 4-pyrrolyl-3,4-DHPMs.

others.[11g] We believe that catalytic amount of CAN would promote the reaction by coordination with carbonyl group thereby rendering C-4 position of **5a**–**e** more electrophilic towards addition. But the mechanistic details of the reaction were not studied. Catalytic amount of CAN used in the reaction merely promoted 1,4-addition and did not oxidize **6** and **7**.

3. Experimental procedure

3.1. General

Melting points were determined using open capillary tubes and are reported uncorrected. IR measurements were carried out using KBr pellets in FTIR spectrometer. The ^{1}H NMR and ^{13}C NMR were recorded in 500 MHz high resolution NMR spectrometer using TMS as an internal standard. All NMR spectra of pyrimidin-2(1*H*)-ones were recorded in $CDCl_3$. Mass spectra were obtained in EI ionization mode at 70 eV. TLC analysis was performed using precoated Poly-Gram sheets. Column chromatography was carried out using 100–200 mesh silica gel or flash-column with 200–400 mesh silica gel. Acetonitrile was freshly distilled from P_2O_5 prior to use. Ceric ammonium nitrate was used as purchased locally. Indole-3-carboxaldehyde, indium trichloride, indium triflate and *N*-methyl indole were purchased from Aldrich Sigma Chemicals.

All the DHPMs needed for oxidation were prepared using reported procedure and purified through column chromatography before subjecting to dehydrogenation.[6b]

3.2. Experimental procedure for the cobalt nitrate and potassium persulfate mediated oxidation of 3,4-dihydropyrimidin-2(1*H*)-ones[10]

A 50 mL round bottom flask containing a magnetic bar was charged with 1 mmol (0.260 g) of **4a** and 10 mL acetonitrile. To this solution was added a mixture of cobalt(II) nitrate hexahydrate (5 mmol, 1.46 g) and potassium persulfate (2.5 mmol, 0.68 g) in 3 mL of water and the solution was stirred at 80 °C (oil bath). The stirring was continued at 80 °C for 3 h. TLC showed the complete disappearance of **4a**. The reaction mixture was diluted with 20 mL of $CHCl_3$ and the supernatant was decanted. The residue was poured into 20 g of crushed ice and extracted with $CHCl_3$ (2×20 mL). The organic extracts were pooled, washed with brine solution (2×20 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuum to afford 0.23 g of crude product. The column purification of residue using 1:1 petroleum ether–ethyl acetate afforded 0.19 g of **5a** as colourless viscous compound, which upon cooling forms a crystalline solid. The same procedure was employed for synthesizing **5b**–**f**.

3.3. Synthesis of ethyl 6-methyl-4-phenyl-pyrimidin-2(1*H*)-one-5-carboxylate (5f)[16]

A 50 mL round bottom flask containing a magnetic bar was charged with **4a** (1 mmol, 0.260 g), $NaHCO_3$ (5 mmol, 0.420 g) and 10 mL of acetone. To this suspension was added CAN (3 mmol, 1.65 g) in water for an hour and stirred at −5 °C under argon atmosphere. The stirring was continued overnight at room temperature and the reaction mixture was diluted with $CHCl_3$ (20 mL) and decanted. The residue was washed with $CHCl_3$ (2×30 mL). The combined $CHCl_3$ layer was neutralized, washed with NaCl solution (2×20 mL), dried over anhydrous Na_2SO_4 and column chromatographed using 1:1 mixture of ethyl acetate–petroleum ether to afford 0.214 g of **5f**.

3.4. Experimental procedure for 1,4-addition of indole on pyrimidin-2(1*H*)-ones (6)

3.4.1. Typical procedure for the synthesis of 6a. A 25 mL round bottom flask containing a magnetic bar was charged with pyrimidin-2(1*H*)-one, **5a**, (0.150 g, 0.6 mmol) in 5 mL of anhydrous methanol. To this solution was added indole (0.143 g, 1.2 mmol) and the solution was stirred at room temperature under argon atmosphere. Upon addition of 5 mol % of CAN, the solution turned to dark brown immediately and stirring was continued for 1–3 h at room temperature. After completion of the reaction (monitored by TLC), the reaction mixture was poured into 50 mL of water and extracted with $CHCl_3$ (3×30 mL). The organic extracts were pooled, dried over anhydrous Na_2SO_4 and purified by passing through a small column of SiO_2 using 2:1 petroleum ether–ethyl acetate to afford **6a**.

A similar reaction conducted using $FeCl_3$ was worked up by adding three to five drops of 6 N HCl (~0.5 mL), extracted with $CHCl_3$ (3×30 mL), dried over anhydrous Na_2SO_4 and column chromatographed using 2:1 petroleum ether–ethyl acetate. The $InCl_3$ catalyzed reaction was worked up similar to the ceric ammonium nitrate procedure.

3.5. General procedure for the reduction of pyrimidin-2(1*H*)-ones

3.5.1. Typical procedure for the synthesis of 7a. A 25 mL round bottom flask containing a magnetic bar was charged with pyrimidin-2(1*H*)-one, **5a**, (0.150 g, 0.6 mmol) in 5 mL of anhydrous methanol. To this solution was added indole (0.045 g, 1.2 mmol) and the resulting solution was stirred at room temperature under an Ar atmosphere. CAN of 2 mol % was added. The reaction was vigorous and completed within half an hour (monitored by TLC). To the reaction mixture, 5 mL of 6 N HCl was added to decompose the excess $NaBH_4$ and the reaction mixture was extracted with $CHCl_3$ (3×30 mL), dried over anhydrous Na_2SO_4 and passed through a small column of SiO_2 (1:1 petroleum ether–ethyl acetate) to yield 4-unsubstituted DHPMs.

3.6. Spectral characterization

3.6.1. Ethyl 6-phenyl-4-(1*H*-indol-3-yl)-3,4-dihydropyrimidin-2(1*H*)-one-5-carboxylate (6a). Colourless solid. Mp 190–191 °C. R_f 0.31 (25% ethyl acetate–petroleum ether). IR (KBr): 1087, 1241, 1371, 1456, 1659, 1710, 2918, 3077, 3195, 3293, 3370, 3589 cm^{-1}. ^{1}H NMR: δ 0.67 (t, J=7.5 Hz, 3H, OCH_2CH_3), 3.65 (q, J=7.5 Hz, 2H, OCH_2CH_3), 5.54 (d, J=3.1 Hz, 1H, CH(4)), 6.97 (t, J=6.9 Hz, 1H), 7.05 (t, J=6.9 Hz, 1H), 7.17 (d, J=2.3 Hz, 1H), 7.24 (dd, J=2.3, 8.4 Hz, 2H), 7.34 (m, 4H), 7.67 (t,

J=2.3, 3.1 Hz, 1H, NH(3)), 7.71 (d, J=8.4 Hz, 1H), 9.24 (d, J=1.5 Hz, 1H, NH(1)), 10.92 (d, J=1.6 Hz, 1H, indole-NH). ^{13}C NMR: δ 13.9, 48.3, 59.5, 101.1, 112.2, 118.5, 119.2, 119.7, 121.7, 123.5, 125.6, 128.3, 128.9, 129.3, 135.9, 137.2, 148.4, 152.9, 165.7. MS (EI, *m/z*): 361 (M^+). Anal. Calcd for $C_{21}H_{19}N_3O_3$: C, 69.79; H, 5.30; N, 11.63. Found: C, 69.70; H, 5.22; N, 11.42.

3.6.2. Ethyl 6-phenyl-4-(2-methyl-1*H*-indol-3-yl)-3,4-dihydropyrimidin-2(1*H*)-one-5-carboxylate (6b). Colourless solid. Mp 195–197 °C. R_f 0.35 (25% ethyl acetate–petroleum ether). IR (KBr): 1083, 1458, 1649, 1707, 3078, 3220, 3294, 3381, 3589 cm^{-1}. ^{1}H NMR: δ 0.68 (t, J=7.7 Hz, 3H, OCH_2CH_3), 2.42 (s, 3H), 3.66 (q, J=7.7 Hz, 2H, OCH_2CH_3), 5.57 (d, J=3.8 Hz, 1H, CH(4)), 7.01 (t, J=6.9 Hz, 1H), 7.19 (t, J=6.9 Hz, 1H), 7.34 (m, 2H), 7.36 (m, 5H), 7.78 (d, J=8.5 Hz, 1H), 9.28 (d, J=1.5 Hz, 1H), 10.54 (d, J=1.6 Hz, 1H). ^{13}C NMR: δ 13.9, 18.4, 48.1, 59.5, 100.9, 110.4, 117.6, 119.3, 119.9, 121.8, 126.0, 127.7, 128.2, 129.0, 129.3, 130.2, 137.6, 148.6, 152.9, 165.7. MS (EI, *m/z*): 375 (M^+). Anal. Calcd for $C_{22}H_{21}N_3O_3$: C, 70.38; H, 5.64; N, 11.19. Found: C, 70.21; H, 5.48; N, 11.07.

3.6.3. Ethyl 6-phenyl-4-(1-methyl-1*H*-indol-3-yl)-3,4-dihydropyrimidin-2(1*H*)-one-5-carboxylate (6c). Colourless solid. Mp 188–190 °C. R_f 0.40 (25% ethyl acetate–petroleum ether). IR: 752, 1181, 1230, 1456, 1544, 1636, 1695, 2985, 3110, 3228, 3381 cm^{-1}. ^{1}H NMR: δ 0.66 (t, J=7.7 Hz, 3H, OCH_2CH_3), 3.73 (s, 3H, N-Me), 3.65 (q, J=7.7 Hz, 2H, OCH_2CH_3), 5.53 (d, J=3.8 Hz, 1H, CH(4)), 7.02 (t, J=6.9 Hz, 1H), 7.13 (t, J=4 Hz, 2H), 7.36 (tt, J=1.55, 6.9 Hz, 4H), 7.71 (q, J=1.6 Hz, 1H), 7.74 (d, J=8.45 Hz, 1H), 9.24 (d, J=1.5 Hz, 1H, NH(1)). ^{13}C NMR: δ 13.9, 32.9, 48.0, 59.5, 101.0, 110.4, 117.6, 119.3, 119.9, 121.8, 126.0, 127.7, 128.2, 129.0, 129.3, 135.9, 137.6, 148.6, 152.9, 165.7. MS (EI, *m/z*): 375 (M^+). Anal. Calcd for $C_{22}H_{21}N_3O_3$: C, 70.38; H, 5.64; N, 11.19. Found: C, 70.27; H, 5.63; N, 11.05.

3.6.4. 5-Acetyl-6-phenyl-4-(1*H*-indol-3-yl)-3,4-dihydropyrimidin-2(1*H*)-one (6d). Colourless solid. Mp 225–227 °C. R_f 0.30 (25% ethyl acetate–petroleum ether). IR: 1690, 2928, 3249, 3380 cm^{-1}. ^{1}H NMR: δ 2.26 (s, 3H), 5.59 (d, J=3.8 Hz, 1H), 6.98 (t, J=7.5 Hz, 1H), 7.00–7.12 (m, 1H), 7.44 (d, J=3.8 Hz, 1H), 7.47 (d, J=6.9 Hz, 1H), 7.51 (t, J=7.7 Hz, 2H), 7.58 (d, J=3.8 Hz, 1H, NH(3)), 7.65 (t, J=7.7 Hz, 2H), 7.74 (d, J=6.9 Hz, 1H), 7.79 (d, J=7.7 Hz, 1H), 9.31 (s, 1H, NH(1)), 10.87 (s, 1H, indole-NH). ^{13}C NMR: δ 16.4, 49.5, 104.1, 119.1, 121.6, 124.6, 128.8, 129.1, 129.4, 130.1, 131.6, 132.6, 136.5, 138.1, 140.1, 142.5, 149.5, 163.3. MS (EI, *m/z*): 331 (M^+). Anal. Calcd for $C_{20}H_{17}N_3O_2$: C, 72.49; H, 5.17; N, 12.68. Found: C, 72.38; H, 5.18; N, 12.67.

3.6.5. Ethyl 6-(phenyl)-4-(2-phenyl-1*H*-indol-3-yl)-3,4-dihydropyrimidin-2(1*H*)-one-5-carboxylate (6e). Pale yellow solid. Mp 237–239 °C. R_f 0.40 (25% ethyl acetate–petroleum ether). IR: 2929, 3250, 3400 cm^{-1}. ^{1}H NMR: δ 0.64 (t, J=7.5 Hz, 3H), 3.55 (dq, J=1.6, 7.5 Hz, 2H), 5.75 (d, J=2.3 Hz, 1H), 7.02 (t, J=6.9 Hz, 1H), 7.20 (q, J=7.7 Hz, 2H), 7.32 (q, J=5.4 Hz, 3H), 7.36 (d, J=7.7 Hz, 1H, NH), 7.41 (t, J=7.7 Hz, 3H), 7.47 (t, J=7.7 Hz, 3H), 7.67 (m, 1H), 7.75 (d, J=6.9 Hz, 1H), 9.32 (s, 1H, NH(1)), 11.26 (s, 1H, indole-NH). ^{13}C NMR: δ 13.6, 49.6, 59.8, 101.0, 110.3, 115.2, 117.6, 119.8, 119.7, 121.7, 125.9, 127.5, 127.8, 127.6, 127.9, 128.1, 128.3, 128.7, 128.8, 128.9, 129.1, 131.4, 135.6, 138.8, 145.4, 152.7, 165.7. MS (EI, *m/z*): 437 (M^+). Anal. Calcd for $C_{27}H_{23}N_3O_3$: C, 74.13; H, 5.30; N, 9.60. Found: C, 74.15; H, 5.22; N, 9.48.

3.6.6. Ethyl 6-phenyl-4-(1-ethyl-2-phenyl-1*H*-indol-3-yl)-3,4-dihydropyrimidin-2(1*H*)-one-5-carboxylate (6f). Colourless solid. Mp 228–230 °C. R_f 0.60 (25% ethyl acetate–petroleum ether). IR: 1705, 2955, 3244, 3380 cm^{-1}. ^{1}H NMR: δ 0.62 (t, J=7.7 Hz, 3H, OCH_2CH_3), 1.21 (t, J=7.7 Hz, 3H, NCH_2CH_3), 3.67 (q, J=7.7 Hz, 2H, OCH_2CH_3), 3.96 (q, J=7.7 Hz, 2H, NCH_2CH_3), 5.40 (s, 1H, CH(4)), 5.71 (d, J=2.3 Hz, 1H), 6.86 (s, 1H), 7.15 (t, J=7.7 Hz, 1H), 7.26 (t, J=7.7 Hz, 2H), 7.32 (m, 2H), 7.34 (m, 5H), 7.50 (m, 3H), 7.75 (d, J=8.5 Hz, 1H). ^{13}C NMR: δ 13.6, 15.5, 31.0, 49.5, 59.7, 101.7, 110.4, 115.2, 117.6, 119.3, 119.9, 121.8, 126.0, 127.4, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.6, 128.6, 131.5, 135.7, 139.0, 145.4, 152.7, 165.4. MS (EI, *m/z*): 465 (M^+). Anal. Calcd for $C_{29}H_{27}N_3O_3$: C, 74.82; H, 5.85; N, 9.03. Found: C, 74.62; H, 5.73; N, 9.15.

3.6.7. Ethyl 6-(2-chlorophenyl)-4-(5-bromo-1*H*-indol-3-yl)-3,4-dihydropyrimidin-2(1*H*)-one-5-carboxylate (6g). Yellow solid. Mp 212–214 °C. R_f 0.30 (25% ethyl acetate–petroleum ether). IR: 1097, 1237, 1347, 1457, 1527, 1651, 1692, 2927, 3100, 3263, 3321, 3413 cm^{-1}. ^{1}H NMR: δ 1.07 (t, J=7.5 Hz, 3H), 4.03 (q, J=7.5 Hz, 2H), 5.16 (d, J=2.8 Hz, 1H), 7.19 (s, 1H), 7.21 (d, J=7.2 Hz, 1H), 7.28 (d, J=7.0 Hz, 1H), 7.33 (t, J=7.2 Hz, 4H), 7.53 (m, 1H), 7.94 (s, 1H), 7.99 (s, 1H), 9.80 (s, 1H). ^{13}C NMR: δ 12.5, 47.8, 59.6, 101.2, 111.3, 114.8, 118.4, 119.4, 121.6, 124.1, 125.9, 127.2, 130.2, 131.1, 133.4, 134.9, 136.9, 145.8, 152.6, 164.2. MS (EI, *m/z*): 475 (M^+). Anal. Calcd for $C_{21}H_{17}BrClN_3O_3$: C, 53.13; H, 3.61; N, 8.85. Found: C, 53.08; H, 3.58; N, 8.93.

3.6.8. Ethyl 6-(2-nitrophenyl)-4-(2-methyl-1*H*-indol-3-yl)-3,4-dihydropyrimidin-2(1*H*)-one-5-carboxylate (6h). Pale yellow solid. Mp 233–235 °C. R_f 0.30 (25% ethyl acetate–petroleum ether). IR (KBr): 1240, 1530, 1612, 1645, 1698, 3100, 3250, 3400 cm^{-1}. ^{1}H NMR: δ 0.62 (t, J=7.5 Hz, 3H), 2.24 (s, 3H), 3.55 (dq, J=1.6, 7.5 Hz, 2H), 5.55 (d, J=3.1 Hz, 1H), 6.9 (t, J=3.9 Hz, 2H), 7.25 (t, J=9.2 Hz, 1H), 7.29 (d, J=6.9 Hz, 1H), 7.48 (d, J=3.1 Hz, 1H, NH), 7.59 (m, 2H), 7.72 (m, 1H), 8.17 (d, J=8.4 Hz, 1H), 9.64 (s, 1H, NH(1)), 10.86 (s, 1H, indole-NH). ^{13}C NMR: δ 12.0, 13.9, 47.9, 59.6, 100.0, 111.4, 114.8, 118.5, 119.3, 120.6, 124.3, 124.8, 126.5, 130.4, 131.7, 133.6, 134.6, 135.8, 140.2, 147.0, 152.1, 165.0. MS (EI, *m/z*): 420 (M^+). Anal. Calcd for $C_{22}H_{20}N_4O_5$: C, 62.85; H, 4.79; N, 13.33. Found: C, 62.71; H, 4.66; N, 13.10.

3.6.9. Ethyl 6-(2-nitrophenyl)-4-(1-methyl-1*H*-indol-3-yl)-3,4-dihydropyrimidin-2(1*H*)-one-5-carboxylate (6i). Pale yellow solid. Mp 208–210 °C. R_f 0.35 (25% ethyl acetate–petroleum ether). IR (KBr): 1097, 1237, 1347, 1457, 1527, 1651, 1692, 2927, 3100, 3263, 3321, 3413 cm^{-1}. ^{1}H NMR: δ 0.64 (t, J=7.7 Hz, 3H, OCH_2CH_3), 3.60 (q,

J=7.7 Hz, 2H, OCH_2CH$_3$), 3.75 (s, 3H, NCH_3), 5.51 (d, J=3.5 Hz, 1H), 7.01 (m, 1H), 7.12 (q, J=6.9 Hz, 1H), 7.26 (s, 1H), 7.36 (t, J=7.7 Hz, 1H), 7.65 (d, J=7.7 Hz, 1H), 7.76 (d, J=7.7 Hz, 4H), 8.20 (d, J=8.5 Hz, 1H), 9.52 (s, 1H, NH(1)). ^{13}C NMR: δ 12.3, 33.0, 48.2, 59.9, 101.0, 112.4, 115.2, 119.1, 120.3, 121.1, 124.5, 125.7, 126.8, 130.6, 131.2, 131.8, 133.9, 134.3, 135.8, 147.0, 152.1, 165.1. MS (EI, *m*/*z*): 420 (M$^+$). Anal. Calcd for $C_{22}H_{20}N_4O_5$: C, 62.85; H, 4.79; N, 13.33. Found: C, 62.74; H, 4.69; N, 13.20.

3.6.10. Ethyl 4-phenyl-5,6-dihydropyrimidin-2(1*H*)-one-5-carboxylate (7a). Colourless solid. Mp 238–240 °C. R_f 0.21 (25% ethyl acetate–petroleum ether). IR (KBr): 1612, 1650, 1703, 3100, 3250 cm^{-1}. ^{1}H NMR: δ 0.86 (q, J=7.5 Hz, 3H), 3.90 (q, J=7.5 Hz, 2H), 4.25 (dd, J=13.8, 11.5 Hz, 2H), 5.90 (s, 1H), 7.05–7.39 (m, 5H). ^{13}C NMR: δ 13.7, 41.5, 60.2, 99.8, 126.9, 129.6, 130.4, 134.3, 144.5, 154.5, 164.9. MS (EI, *m*/*z*): 246 (M$^+$). Anal. Calcd for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.28; H, 5.71; N, 11.28.

3.6.11. Ethyl 4-(1-naphthyl)-5,6-dihydropyrimidin-2(1*H*)-one-5-carboxylate (7b). Colourless solid. Mp 244–246 °C. R_f 0.23 (25% ethyl acetate–petroleum ether). IR (KBr): 1614, 1651, 1706, 3248 cm^{-1}. ^{1}H NMR: δ 0.36 (q, J=7.5 Hz, 3H), 3.65 (q, J=7.5 Hz, 2H), 4.08 (dd, J=14.5, 11.5 Hz, 2H), 7.20 (s, 1H), 7.30–7.60 (m, 5H), 7.80–7.91 (m, 2H), 9.10 (s, 1H). ^{13}C NMR: δ 13.0, 40.6, 59.4, 100.1, 123.7, 125.2, 126.3, 126.4, 128.4, 128.9, 131.1, 130.2, 130.5, 132.8, 145.9, 154.1, 164.2. MS (EI, *m*/*z*): 296 (M$^+$). Anal. Calcd for $C_{17}H_{16}N_2O_3$: C, 68.91; H, 5.40; N, 9.45. Found: C, 68.87; H, 5.38; N, 9.58.

3.6.12. Ethyl 6-(2-nitrophenyl)-4-(2-pyrrolyl)-3,4-dihydropyrimidin-2(1*H*)-ones-5-carboxylate (7c). Brown colour solid. Mp 241–242 °C. R_f 0.30 (25% ethyl acetate–petroleum ether). IR (KBr): 1013, 1091, 1296, 1392, 1494, 1583, 1620, 1718, 3199, 3282, 3401 cm^{-1}. ^{1}H NMR: δ 0.66 (t, J=7.7 Hz, 3H, OCH$_2$CH_3), 3.65 (q, J=7.7 Hz, 2H, OCH_2CH$_3$), 5.19 (d, J=3.0 Hz, 1H), 6.61 (d, J=3.0 Hz, 2H), 7.42 (d, J=6.9 Hz, 1H), 7.43 (m, 1H), 7.36 (t, J=7.7 Hz, 1H), 7.61 (m, 2H), 8.13 (d, J=8.5 Hz, 1H), 9.30 (s, NH(1)), 10.50 (s, 1H, pyrrole-NH). ^{13}C NMR: δ 13.9, 48.7, 59.6, 102.2, 106.8, 111.8, 115.3, 118.1, 124.6, 126.6, 131.5, 134.5, 137.8, 147.5, 153.6, 165.0, 165.3. MS (EI, *m*/*z*): 356 (M$^+$). Anal. Calcd for $C_{17}H_{16}N_4O_5$: C, 57.30; H, 4.53; N, 15.72. Found: C, 57.22; H, 4.47; N, 15.45.

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