Supporting Information

Metalation of Biginelli Compounds. A General Unprecedented Route to C-6 Functionalised 4-Aryl-3, 4-dihydropyrimidinones

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Materials and Methods

LDA was generated by freshly prepared n-butyl lithium 2.3 N solution in hexane and diisopropylamine (distilled from KOH pellets). THF was dried (Na-benzophenone ketyl) under nitrogen and drawn with hypodermic glass syringes. The commercially available aldehydes, ethyl acetoacetate and urea were used without any further purification. All liquid electrophiles were dried using suitable drying agents and/or distilled over 4Å molecular sieves. Reactions were run under a blanket of dry nitrogen gas in a single necked RBF sealed with septum cap. The reagents were added by using hypodermic syringes and/or cannula. The low temperature (-10°C) attained by using liquid nitrogen slush. Pre-coated aluminium TLC plates (60F₂₅₄, 0.2 mm) were used for TLC monitoring of the reaction

Analysis and spectra

The ¹H (200 or 300 MHz) and ¹³C (50 MHz or 75 MHz) spectra were recorded on ppm scale (J values in Hz) using tetramethylsilane as internal standard. Melting points are uncorrected.

General procedure

To a suspension of DHPM **1a** (1.3 g, 5 mmol) in 10 mL dry THF under a blanket of dry N₂, LDA (4 equiv. in 37 ml dry THF) was added drop-wise through a cannula at -10°C. After the addition, reaction mixture was warmed to room temperature and stirred for additional 3 hrs until blood red colored carbanion was generated. To this carbanion, appropriate electrophile

(3.0 equiv.), dissolved in 10 ml dry THF was added drop-wise. Upon addition of the electrophile, the red color was quenched in most of the cases, indicating the consumption of the carbanion. Stirring was continued for additional time (Table 2), to complete the reaction, after which a saturated aqueous solution of NH_4Cl was introduced. The reaction was treated with brine and extracted with ethyl acetate (3 x 25 ml). The extracts were dried over anhydrous Na_2SO_4 and the mixture concentrated under reduced pressure. The products were isolated by flash chromatography using silica gel-G (60-120 mesh) and mixtures of ethyl acetate/hexane as eluent. For preparing samples for micro-analytical analysis, crystallization was done using combinations of dry DCM and hexane or methanol and petroleum ether.

Entry 1, table 1. 5-Ethoxycarbonyl-6-methyl-(d_1)-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (3a)

Crystalline white solid; R_f : 0.6 (30% v/v ethyl acetate/hexane); Yield 63%; M.p. 216°C (Methanol); IR (KBr): ν_{max} 3255, 1715, 1700 cm^{-1} ; ^1H NMR (CDCl_3): δ 1.16 (t, 3H, J 7.2 Hz), 2.34 (s, 2H), 4.07 (q, 2H, J 7.2 Hz), 5.39 (d, 1H, J 3.0 Hz), 5.63 (br, 1H, NH, exchanged with D_2O), 7.29 (m, 5H), 7.82

(br, 1H, NH, exchanged with D₂O); ¹³C NMR (CDCl₃): δ 14.1, 18.7, 30.9, 55.7, 60.0, 101.3, 126.5, 127.9, 128.7, 143.6, 146.1, 153.1, 165.6. Anal. Required for C₁₄H₁₅N₂O₃D: C, 64.35; H, 6.56; N, 10.72. Found: C, 64.29; H, 5.92; N, 10.38; MS: *m/z* 260 (M⁺).

Entries 2-7, table 1. 5-Ethoxycarbonyl-6-propyl-4-phenyl-3,4-dihydro pyrimidin-2(1H)-one (3b)

Cream white solid; *R_f*: 0.5 (30% v/v ethyl acetate/hexane); Yield 50-71%; M.p. 162-165°C (DCM); IR (KBr): *v*_{max} 3245, 1705, 1665 cm⁻¹; ¹H NMR (CDCl₃): δ 0.95 (t, 3H, *J* 7.2 Hz), 1.15 (t, 3H, *J* 6.9 Hz), 1.62 (m, 2H), 2.66 (m, 2H), 4.06 (q, 2H, *J* 7.0 Hz), 5.37 (d, 1H, *J* 3 Hz), 6.43 (br, 1H, NH, exchanged with D₂O), 7.25 (m, 5H), 8.68 (br, 1H, NH, exchanged with D₂O); ¹³C NMR (CDCl₃): δ 13.7, 14.0, 21.6, 26.8, 33.3, 55.3, 59.8, 100.8, 126.4, 127.7, 128.5, 143.8, 150.6, 153.8, 165.3. Anal. Required for C₁₆H₂₀N₂O₃: C, 66.65; H, 6.99; N, 9.72. Found: C, 66.88; H, 6.53; N, 9.65; MS: *m/z* 288 (M⁺).

Entry 1, table 2. 5-Ethoxycarbonyl-1,3,6-trimethyl-4-phenyl-3,4-dihdropyrimidin-2(1H)-one (3c)

White solid; *R_f*: 0.3 (20% ethyl acetate/hexane); Yield 26%; M.p. 97°C (DCM); IR (KBr): ν_{max} 3223, 1725, 1665 cm^{-1} ; ^1H NMR (CDCl_3): δ 1.26 (t, 3H, *J* 7.2 Hz), 2.48 (s, 3H), 2.91 (s, 3H), 3.26 (s, 3H), 4.13 (q, 2H, *J* 7.09 Hz), 5.24 (s, 1H), 7.26 (m, 5H); ^{13}C NMR (CDCl_3): δ 14.1, 16.5, 30.9, 34.3, 60.0, 60.7, 103.5, 126.5, 127.7, 128.5, 140.9, 149.1, 153.7, and 165.8; Anal. Required for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}_3$: C, 66.65; H, 6.99; N, 9.72. Found: C, 66.93; H, 7.06; N, 9.39; MS: *m/z* 288 (M^+).

Entry 1, table 2. 5-Ethoxycarbonyl-6-ethyl-3-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (3d)

White solid; *R_f*: 0.3 (30% ethyl acetate/hexane); Yield 30%; M.p. 141-143°C (DCM); IR (KBr): ν_{max} 3253, 1687, 1666 cm^{-1} ; ^1H NMR (CDCl_3): δ 1.21 (t, 6H, *J* 7.5 Hz), 2.68 (m, 2H), 2.85 (s, 3H), 4.09 (q, 2H, *J* 7.09 Hz), 5.20 (s, 1H), 7.31 (m, 5H), 8.41 (br, 1H, NH, exchanged with D_2O); ^{13}C NMR (CDCl_3): δ 12.4, 14.1, 24.9, 32.6, 59.8, 62.5, 100.1, 127.1, 127.9, 128.5, 141.4, 151.8, 153.1, and 165.2; Anal. Required for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}_3$: C,

66.65; H, 6.99; N, 9.72. Found: C, 66.78; H, 6.80; N, 9.30; MS: m/z 288 (M^+).

Entry 1, table 2.5-Ethoxycarbonyl-6-ethyl-4-phenyl-3,4-dihydro pyrimidin-2(1H)-one (3e)

White solid; R_f : 0.3 (60% ethyl acetate/hexane); Yield: 30%; M.p. 132°C (DCM); IR (KBr): $\nu_{\max}$ 3249, 1701, 1650 cm^{-1} ; ^1H NMR (CDCl_3): δ 1.16 (t, 3H, J 7.1 Hz), 1.24 (t, 3H, J 7.5 Hz), 2.76 (m, 2H), 4.07 (q, 2H, J 7.09 Hz), 5.40 (d, 1H, J 2.74 Hz), 5.51 (br, 1H, NH, exchanged with D_2O), 7.31 (m, 6H, 1H-exchanged with D_2O); ^{13}C NMR (CDCl_3): δ 12.3, 14.0, 25.3, 55.7, 60.0, 73.8, 104.1, 120.6, 126.5, 127.9, 128.7, 137.0, 146.7, and 151.1; Anal. Required for $\text{C}_{15}\text{H}_{18}\text{N}_2\text{O}_3$: C, 65.68; H, 6.61; N, 10.21. Found: C, 65.63; H, 6.18; N, 9.97; MS: m/z 274 (M^+).

Entry 1, table 2. 5-Ethoxycarbonyl-3,6-dimethyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (3f)

Crystalline White solid; R_f : 0.3 (30% ethyl acetate/hexane); Yield: 5%; M.p. 177°C (DCM); IR (KBr): $\nu_{\max}$ 3242, 1699, 1665 cm^{-1} ; ^1H NMR (CDCl_3): δ 1.18 (t, 3H, J 7.4 Hz), 2.32 (s, 3H), 2.83 (s, 3H), 4.08 (q, 2H, J 7.09 Hz), 5.18 (s, 1H), 7.26 (m, 5H),

8.61 (br, 1H, NH, exchanged with D₂O); ¹³C NMR (CDCl₃): δ 14.1, 18.3, 32.6, 59.8, 62.4, 100.8, 126.1, 127.1, 127.9, 128.4, 131.1, 141.4, 146.5, 146.7, 153.1, and 165.6. Anal. Required for C₁₅H₁₈N₂O₃: C, 65.68; H, 6.61; N, 10.21. Found: C, 65.63; H, 6.18; N, 9.97; MS: *m/z* 274 (M⁺).

Entry 2, table 2. 5-Ethoxycarbonyl-6-phenylethyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (3g)

White powder; *R_f*: 0.4 (40% ethyl acetate/hexane); Yield: 50%; M.p. 162°C (DCM); IR (KBr): *v*_{max} 3228, 1705, 1653 cm⁻¹; ¹H NMR (CDCl₃): δ 1.17 (t, 3H, *J* 7.2 Hz), 2.95 (m, 4H), 4.08 (q, 2H, *J* 7.5 Hz), 5.40 (d, 1H, *J* 2.7 Hz), 5.44 (br, 1H, NH, exchanged with D₂O), 7.27 (m, 10H), 7.36 (br, 1H, NH, exchanged with D₂O); ¹³C NMR (CDCl₃): δ 14.1, 34.2, 37.2, 60.1, 126.4, 126.6, 128.0, 128.4, 128.5, 128.7, 140.2, 159.5, 165.8; Anal. Required for C₂₁H₂₂N₂O₃: C, 71.98; H, 6.33; N, 7.99; Found: C, 71.53; H, 6.40; N, 7.62; MS: *m/z* 350 (M⁺).

Entry 3, table 2. 5-Ethoxycarbonyl-6-chloromethyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (3h)

Crystalline cream solid; *R_f*: 0.5 (60% ethyl acetate/hexane); Yield: 55%; M.p. 211-214°C (Methanol); IR (KBr): $\nu_{\max}$ 3355, 3122, 1693, 1647, 781 cm^{-1} ; ^1H NMR (CDCl_3 + $\text{DMSO}-d_6$): δ 1.17 (t, 3H, *J* 7.1 Hz), 4.08 (q, 2H, *J* 7.0 Hz), 4.76 (ABq, 2H, *J* 32.9 Hz, *J* 11.2 Hz), 5.36 (d, 1H, *J* 2.7 Hz), 7.06 (br, 1H, NH, exchanged with D_2O), 7.29 (m, 5H), 9.01 (br, 1H, NH, exchanged with D_2O); ^{13}C NMR (CDCl_3 + $\text{DMSO}-d_6$): 13.3, 54.3, 59.6, 102.0, 126.0, 127.1, 127.8, 143.1, 144.5, 152.1, 163.9; Anal. Required for $\text{C}_{14}\text{H}_{15}\text{N}_2\text{O}_3\text{Cl}$: C, 57.05; H, 5.13; N, 9.50; Found: C, 56.70 H, 5.08; N, 9.37; MS: *m/z* 294 (M^+).

Entry 4, table 2. 5-Ethoxycarbonyl-6-(2-hydroxy-2-methylpropyl)-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (3i)

White solid; *R_f*: 0.4 (65% ethyl acetate/hexane); Yield: 38%; M.p. 160-162°C (Methanol); IR (KBr): $\nu_{\max}$ 3480, 3260, 1695, 1635 cm^{-1} ; ^1H NMR: (CDCl_3) δ 1.14 (t, 3H, *J* 7.2 Hz), 1.33 (s, 3H), 1.35 (s, 3H), 2.72 (s, 1H exchanged with D_2O), 3.08 (ABq, 2H, *J* 79.8 Hz, *J* 14.4 Hz), 4.05 (q, 2H, *J* 7.2 Hz), 5.42 (d, 1H, *J* 2.7 Hz), 5.51 (br, 1H, NH, exchanged with D_2O), 7.32 (m, 5H), 8.06 (br, 1H, NH, exchanged with D_2O); ^{13}C NMR (CDCl_3): δ 14.0, 29.6, 30.1, 41.3, 56.0, 60.1, 71.8, 73.6, 103.0, 126.6, 127.9,

128.7, 143.7, 147.9, 152.4, 165.9, and 175.8; Anal. Required for $C_{17}H_{22}N_2O_4$: C, 64.13; H, 6.97; N, 8.80. Found: C, 64.12; H, 6.58; N, 8.55; MS: m/z 318 (M^+).

Entry 4, table 2. 7,7-Dimethyl-4-phenyl-3,4,7,8-tetrahydro-1H-pyrano[4,3-d]pyrimidine-2,5-dione (4a)

White solid; R_f : 0.6 (70% ethyl acetate/hexane); Yield: 35%; M.p. 240°C (Methanol); IR (KBr): $\nu_{\max}$ 3274, 1710, 1664 cm^{-1} ; ^1H NMR (CDCl_3 + $\text{DMSO}-d_6$): δ 1.22 (s, 3H), 1.37 (s, 3H), 2.47 (ABq, 2H, J 64.2 Hz, J 17.7 Hz), 5.29 (d, 1H J 3.6 Hz) 6.96 (br, 1H, NH, exchanged with D_2O), 7.21 (m, 5H), 9.47 (br, 1H, NH, exchanged with D_2O); ^{13}C NMR (CDCl_3 + $\text{DMSO}-d_6$): δ 25.9, 28.0, 35.6, 53.4, 97.4, 126.0, 127.2, 128.0, 128.1, 143.0, 145.9, 152.0, and 163.5. Anal. Required for $C_{15}H_{16}N_2O_3$: C, 66.16; H, 5.92; N, 10.29; Found: C, 65.82; H, 5.90; N, 9.93; MS: m/z 272 (M^+).

Entry 4, table 2. 7,7-Dimethyl-4-phenyl-2-thioxo-1,2,3,4,7,8-hexahydro-pyrano[4,3-d]pyrimidin-5-one (4b)

Yellow crystalline solid; *R*_f: 0.5 (60% ethyl acetate/hexane); Yield: 62%; M.p. 252°C (Methanol); IR (KBr): ν_{max} 3265, 1666, 1623 cm^{-1} ; ^1H NMR (CDCl_3 + $\text{DMSO}-d_6$) δ 1.29 (s, 3H), 1.45 (s, 3H), 2.59 (ABq, 2H, *J* 36.7 Hz, *J* 15.5 Hz), 5.38 (d, 1H *J* 2.5 Hz), 7.34 (m, 5H), 8.56 (br, 1H, NH, exchanged with D_2O), 10.42 (br, 1H, NH, exchanged with D_2O); ^{13}C NMR (CDCl_3 + $\text{DMSO}-d_6$): δ 26.1, 28.3, 35.3, 54.1, 77.9, 99.0, 126.4, 127.7, 128.4, 142.3, 142.8, 163.6, and 175.0; Anal. Required for $\text{C}_{15}\text{H}_{16}\text{N}_2\text{O}_2\text{S}$: C, 62.48; H, 5.59; N, 9.71; Found: C, 62.06; H, 5.60; N, 9.54; MS: *m/z* 289 (M^+).

Entry 5, table 2. 7-Benzyl-7-methyl-4-phenyl-3,4,7,8-tetrahydro-1H-pyrano[4,3-d]pyrimidine-2,5-dione (4c)

Component-A (Major)

White solid; *R*_f: 0.5 (80% ethyl acetate/hexane); Yield: 60 %; M.p. 232°C (Ethanol); IR (KBr): ν_{max} 3404, 1693, 1674 cm^{-1} ; ^1H NMR (CDCl_3 + $\text{DMSO}-d_6$): δ 1.26 (s, 3H), 2.54 (ABq, 2H, *J* 74.7 Hz, *J* 17.4 Hz), 2.98 (m, 2H), 5.19 (d, 1H, *J* 1.8 Hz), 7.25 (m, 10H), 7.61 (br, 1H, NH, exchanged with D_2O), 9.52 (br, 1H, NH, exchanged with D_2O); ^{13}C NMR (CDCl_3 + $\text{DMSO}-d_6$): 23.4, 29.3, 32.2, 45.2, 52.2, 78.2, 95.7, 125.0, 125.3, 125.9, 126.6,

126.8, 129.1, 134.2, 145.6, 150.2, and 162.0; Anal. Required for $C_{21}H_{20}N_2O_3$: C, 72.40; H, 5.79; N, 8.04; Found: C, 72.84; H, 5.28; N, 7.83. MS: m/z 349 (M^+).

Component-B (Minor)

White solid; R_f : 0.5 (85% ethyl acetate/hexane); Yield: 12 %; High Melting; IR (KBr): ν_{max} 3403, 1685, 1674 cm^{-1} ; 1H NMR ($CDCl_3$ + DMSO- d_6 and D_2O): δ 1.38 (s, 3H), 2.51 (m, 2H), 2.84 (ABq, 2H, J 33.6 Hz, J 13.2 Hz), 5.48 (s, 1H), 6.94 – 7.46 (m, 10H); ^{13}C NMR ($CDCl_3$ + DMSO- d_6 and D_2O): δ 24.6, 32.8, 43.1, 52.7, 78.5, 96.6, 125.2, 125.5, 126.3, 126.9, 127.1, 127.2, 127.3, 129.3, 129.4, 134.4, 142.9, 145.6, 150.9, and 162.4; Anal. Required for $C_{21}H_{20}N_2O_3$: C, 72.40; H, 5.79; N, 8.04; Found: C, 72.26; H, 5.30; N, 8.12; MS: m/z 349 (M^+).

Diastereomer separation: 1H NMR of the crude product mixture was complex. However the ratio of the two diastereomers (7: 3) was determined from the isolated yield. From the 1H NMR spectrum, of the isolated diastereomers, the chemical shift showed considerable difference e.g., Me (δ , 1.26 and 1.38, s, 3H), C-4H (δ , 5.19 and 5.48, d, 1H, J <2), CH_2 (ABq δ 2.54 and 2.84, J 18 Hz, 2H) and benzylic CH_2 (δ 2.9 and 2.51, dd, 2H, J 6.0 and 17.4 Hz). Difference in the chemical shifts of the two can be clearly seen from the 1H NMR spectra given below.

(m, 5H), 7.67 (d, 2H, J 8.51 Hz), 8.17 (d, 2H, J 8.53 Hz), 8.94 (br, 1H, NH, exchanged with D₂O); ¹³C NMR (CDCl₃ + DMSO-*d*₆): δ 13.7, 55.1, 59.8, 72.0, 101.3, 123.1, 126.1, 126.2, 126.4, 127.4, 128.3, 143.8, 146.6, 148.1, 152.0, 152.2, 165.7; Anal. Required for C₂₁H₂₁N₃O₆: C, 61.31; H, 5.14; N, 10.21; Found: C, 62.02; H, 5.51; N, 9.99; MS: m/z 411 (M⁺).

Component-B

Light yellow amorphous solid; R_f : 0.4 (70% ethyl acetate/hexane); Yield: 3%; M.p. 228°C (Ethanol); IR (KBr): $\nu_{\max}$ 3576, 3245, 1681, 1665 cm⁻¹; ¹H NMR (CDCl₃ + DMSO-*d*₆): δ 1.12 (t, 3H, J 6.9 Hz), 3.23 (m, 2H), 4.03 (q, 2H, J 6.9 Hz), 5.15 (m, 2H, OH, exchanged with D₂O), 5.35 (d, 1H, J 2.7 Hz), 6.48 (br, 1H, NH, exchanged with D₂O), 7.23 (m, 5H), 7.65 (d, 2H, J 8.4 Hz), 8.14 (d, 2H, J 8.7 Hz), 8.48 (br, 1H, NH, exchanged with D₂O); Anal. Required for C₂₁H₂₁N₃O₆: C, 61.63; H, 5.14; N, 10.21; Found: C, 62.12; H, 5.35; N, 10.16; MS: m/z 411 (M⁺).

Diastereomer separation: The ¹H NMR of crude product mixture shows the presence of two diastereomers because of new chiral center generation adjacent to C-6 position of DHPM. From the ¹H NMR spectrum of crude product mixture the diastereomeric ratio found is 76:23. However two diastereomer are separated by the careful crystallization of the purified mixture (column chromatography) of isomers in absolute ethyl alcohol, the minor component B is separated first as amorphous solid (light yellow) and is immediately separated by filtration. The second

component A is slightly more soluble in the crystallization solvent and separated as dark yellow crystals, later on. The melting points of the diastereomers were different (*vide experimental*). Also the ^1H NMR spectra of the two components show considerable shift in the ABX system, which helps in distinguishing two diastereomers (see spectra below).

Entry 7, table 2. 5-Ethoxycarbonyl-6-[2-hydroxy-2-(2,4-dimethoxyphenyl)ethyl]-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (3k)

Yellow crystalline solid; R_f : 0.4 (70% ethyl acetate/hexane);
Yield: 60%; M.p. 207-209°C (Methanol); IR (KBr): ν_{max} 3357,

3282, 1697, 1635 cm^{-1} ; ^1H NMR ($\text{CDCl}_3 + \text{DMSO}-d_6$): δ 1.11 (t, 3H, J 7.1 Hz), 3.26 (ABX-System, 2H, J 14.4 Hz, J 8.4 Hz, J 3.3 Hz), 3.79 (s, 3H), 3.86 (s, 3H), 4.02 (q, 2H, J 7.1 Hz), 4.37 (m, 1H, OH, exchanged with D_2O), 5.15 (m, 1H), 5.33 (d, 1H, J 3.02 Hz), 6.42-7.36 (m, 9H, 1H, exchanged with D_2O), 8.09 (br, 1H, NH, exchanged with D_2O); ^{13}C NMR ($\text{CDCl}_3 + \text{DMSO}-d_6$): δ 13.7, 30.6, 37.6, 38.2, 55.0, 55.1, 59.7, 68.1, 98.0, 101.5, 103.9, 123.9, 126.4, 127.0, 127.3, 128.2, 143.8, 148.3, 152.0, 156.8, 159.8, 165.8; Anal. Required for $\text{C}_{23}\text{H}_{26}\text{N}_2\text{O}_6$: C, 64.78; H, 6.15; N, 6.57; Found: C, 65.01; H, 6.35; N, 6.23; MS: m/z 426 (M^+).

Diastereomer separation: The diastereomeric excess of two isomers was determined in analogy with Entry 9 (NH, proton) 74:26. ^1H NMR spectrum of the crude mixture showed the two quartets for the C-5 ester fraction, the major one at 4.01 ppm and minor at 4.09 ppm. However the major component whose quartet (due to ethyl ester) comes at 4.02 ppm has strong tendency to crystallize from methanol, so about 90% of the pure compound get crystallized directly from the crude reaction mixture (spectrum is given at the page S-36).

Entry 8, table 2. 5-Ethoxycarbonyl-6-propylmercaptomethyl-4-phenyl-3, 4-dihydropyrimidin-2(1H)-one (31)

Cream solid; *R_f*: 0.6 (40% ethyl acetate/hexane); Yield: 35%; M.p. 100-103°C (DCM); IR (KBr): ν 3220, 1701, 1639 cm^{-1} ; ^1H NMR (CDCl_3): δ 0.93 (t, 3H, *J* 7.2 Hz), 1.16 (t, 3H, *J* 7.5 Hz), 1.57 (m, 2H), 2.45 (t, 2H, *J* 7.2 Hz), 3.97 (ABq, 2H, *J* 43.4 Hz, *J* 15.4 Hz), 4.07 (q, 2H, *J* 7.0 Hz), 5.42 (d, 1H, *J* 2.4 Hz), 5.72 (br, 1H, NH, exchanged with D_2O), 7.29 (m, 5H), 7.70 (br, 1H, NH, exchanged with D_2O); ^{13}C NMR (CDCl_3): δ 13.3, 14.0, 22.6, 30.7, 33.9, 55.9, 60.3, 103.0, 126.5, 128.0, 128.7, 143.3, 145.5, 152.5, and 165.1; Anal. Required for $\text{C}_{17}\text{H}_{22}\text{N}_2\text{O}_3\text{S}$: C, 61.05; H, 6.63; N, 8.38; Found: C, 59.68; H, 6.17; N, 8.12; MS: *m/z* 334 (M^+).

Entry 8, table 2. 5-Ethoxycarbonyl-6-(bis-propylmercapto-methyl)4-phenyl-3,4-dihydropyrimidin-2(1H)-one (3m)

Light yellow solid; *R_f*: 0.4 (25% ethyl acetate/hexane); Yield: 30%; M.p. 74-76°C (DCM); IR (KBr): ν_{max} 3342, 1710, 1669 cm^{-1} ; ^1H NMR (CDCl_3): δ 0.92 (t, 3H, *J* 6.9 Hz), 1.00 (t, 3H, *J* 7.2 Hz), 1.20 (t, 3H, *J* 7.1 Hz), 1.64 (m, 4H), 2.57 (m, 4H), 4.12 (q, 2H, *J* 7.0 Hz), 5.43 (br, 1H, NH, exchanged with D_2O), 5.46 (d, 1H, *J* 2.6 Hz), 6.41 (s, 1H), 7.35 (m, 6H, 1H, exchanged with D_2O); ^{13}C NMR (CDCl_3): δ 9.3, 13.3, 13.4, 14.0, 22.6, 34.8, 44.1, 60.6, 102.5, 126.5, 128.2, 128.8, 143.1, 147.0, 156.5,

and 164.7; Anal. Required for $C_{20}H_{28}N_2O_3S_2$: C, 58.79; H, 6.91; N, 6.86; Found: C, 59.02; H, 6.53; N, 7.06; MS: m/z 408 (M^+).

Entry 9, table 2. 5-Ethoxycarbonyl-6-(bis-phenyl-mercaptomethyl)-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (3n)

Crystalline white solid; R_f : 0.5 (30% ethyl acetate/hexane); Yield: 35%; M.p. 138°C (DCM); IR (KBr): ν_{max} 3213, 1712, 1681 cm^{-1} ; 1H NMR ($CDCl_3$): δ 1.04 (t, 3H, J 6.9 Hz), 3.93 (q, 2H, J 6.3 Hz), 5.25 (d, 1H, J 2.7 Hz), 5.33 (br, 1H, NH, exchanged with D_2O), 7.11 (s, 1H), 6.85-7.59 (m, 16H, 1H, exchanged with D_2O). ^{13}C NMR ($CDCl_3$): 13.8, 50.8, 55.6, 60.4, 103.4, 126.4, 127.8, 128.3, 128.6, 129.0, 129.1, 129.2, 131.5, 132.2, 132.4, 134.0, 142.3, 144.5, 164.3, and 186.4. Anal. Required for $C_{26}H_{24}N_2O_3S_2$: C, 65.52; H, 5.08; N, 5.88. Found: C, 65.13; H, 4.74; N, 5.59. MS: m/z 476 (M^+).

Entry 10, table 2. 5-Ethoxycarbonyl-6-methyl-3-propionyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (3o)

White powder; R_f : 0.5 (30% ethyl acetate/hexane); Yield: 60%; M.p. 202°C (DCM); IR (KBr): ν_{max} 3228, 1697, 1645 cm^{-1} ; 1H NMR ($CDCl_3$): δ 1.13 (t, 3H, J 7.2 Hz), 1.24 (t, 3H, J 7.0 Hz), 2.39 (s, 3H), 2.80 (m, 1H), 3.07 (m, 1H), 4.16 (q, 2H, J 7.06 Hz-),

6.62 (s, 1H), 7.29 (m, 5H) 8.46 (br, 1H, NH, exchanged with D₂O); ¹³C NMR (CDCl₃): δ 9.1, 14.1, 17.7, 31.8, 53.5, 60.5, 105.5, 126.7, 127.9, 128.5, 139.9, 145.2, 152.1, 165.0, and 175.3; Anal. Required for C₁₇H₂₀N₂O₄: C, 64.54; H, 6.37; N, 8.86; Found: C, 64.61; H, 6.22; N, 8.43; MS: *m/z* 316 (M⁺).

Entry 11, table 2.5-Ethoxycarbonyl-6-methyl-3-formyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (3p)

Pale yellow solid; *R_f*: 0.5 (25% ethyl acetate/hexane); Yield: 40%; M.p. 222°C (DCM); IR (KBr): *v*_{max} 3240, 3140, 1730, 1720, 1700, 1650 cm⁻¹; ¹H NMR (CDCl₃): δ 1.22 (t, 3H, *J* 7.1 Hz), 2.45 (s, 3H), 4.14 (q, 2H, *J* 7.1 Hz), 6.35 (s, 1H), 7.34 (m, 5H), 7.59 (br, 1H, NH, exchanged with D₂O), 9.31 (s, 1H); ¹³C NMR (CDCl₃): δ 14.1, 18.2, 43.5, 52.8, 60.6, 91.3, 104.9, 127.2, 128.3, 128.6, 139.4, 144.0, 160.9, 164.5; Anal. Required for C₁₅H₁₆N₂O₄: C, 62.49; H, 5.59; N, 9.72; Found: C, 62.70; H, 5.51; N, 9.67; MS: *m/z* 288 (M⁺).

Entry 12, table 2. 5-Ethoxycarbonyl-6-trimethylsilanylmethyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (3q)

Pale yellow solid; *R_f*: 0.5 (30% ethyl acetate/hexane); Yield: 75%; M.p. 185°C (DCM); IR (KBr): ν_{max} 3238, 1699, 1635 cm^{-1} ; ^1H NMR (CDCl_3): δ 0.10 (s, 9H), 1.19 (t, 3H, *J* 7.2 Hz), 2.49 (ABq, 2H, *J* 56.09 Hz, *J* 12.5 Hz), 4.08 (q, 2H, *J* 7.0 Hz), 5.43 (br, 1H, NH, exchanged with D_2O), 5.44 (d, 1H, *J* 2.8 Hz), 6.68 (br, 1H, NH, exchanged with D_2O), 7.34 (m, 5H); ^{13}C NMR (CDCl_3): δ -1.1, 14.1, 23.6, 55.4, 59.6, 98.4, 126.5, 126.5, 127.6, 127.8, 128.5, 128.6, 144.2, 150.5, 153.5, and 165.9; Anal. Required for $\text{C}_{17}\text{H}_{24}\text{N}_2\text{O}_3\text{Si}$: C, 61.41; H, 7.28; N, 8.43; Found: C, 61.12; H, 7.35; N, 8.16; MS: *m/z* 333 (M^+).

Entry 1, table 3. 5-Ethoxycarbonyl-6-propyl-4-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1H)-one (3r)

Yellow viscous oil; *R_f*: 0.4 (35% v/v ethyl acetate/hexane); Yield 65%; IR (KBr): ν_{max} 3226, 1696, 1656 cm^{-1} ; ^1H NMR (CDCl_3): δ 0.96 (t, 3H, *J* 7.2 Hz), 1.16 (t, 3H, *J* 6.9 Hz), 1.63 (m, 2H), 2.66 (m, 2H), 3.76 (s, 3H), 4.05 (q, 2H, *J* 7.1 Hz), 5.32 (d, 1H, *J* 2.5 Hz), 6.24 (br, 1H, NH, exchanged with D_2O), 6.80 (d, 2H, *J* 7.2 Hz), 7.21 (d, 2H, *J* 7.2 Hz) 8.53 (br, 1H, NH, exchanged with D_2O); ^{13}C NMR (CDCl_3): δ 13.7, 14.0, 21.6, 26.8, 33.4, 54.9, 55.1, 59.8, 101.2, 113.9, 127.7, 136.2, 150.2, 153.8, 159.1, and 165.4; Anal. Required for

C₁₇H₂₂N₂O₄: C, 64.13; H, 6.97; N, 8.80. Found: C, 63.66; H, 6.15; N, 8.95; MS: *m/z* 318 (M⁺).

Entry 2, table 3. 5-Ethoxycarbonyl-6-propyl-4-(3,4,5-trimethoxy-phenyl)-3,4-dihydropyrimidin-2(1H)-one (3s)

White crystalline solid; *R_f*: 0.45 (60% v/v ethyl acetate/hexane); Yield 78%; M.p. 215-217°C (DCM); IR (KBr): ν_{max} 3230, 3107, 1698, 1643 cm⁻¹; ¹H NMR (CDCl₃): δ 1.01 (t, 3H, *J* 7.2 Hz), 1.18 (t, 3H, *J* 7.2 Hz), 1.68 (m, 2H), 2.57 (m, 1H), 2.85 (m, 1H), 3.81 (s, 9H), 4.09 (q, 2H, *J* 7.0 Hz), 5.35 (d, 1H, *J* 2.7 Hz), 5.81 (br, 1H, NH, exchanged with D₂O), 6.52 (s, 2H), 8.0 (br, 1H, NH, exchanged with D₂O); ¹³C NMR (CDCl₃): δ 13.8, 14.1, 21.6, 33.6, 55.9, 56.0, 60.0, 60.7, 100.9, 103.4, 137.6, 139.3, 150.2, 153.2, 153.3 and 165.3; Anal. Required for C₁₉H₂₆N₂O₃: C, 60.30; H, 6.93; N, 7.40 Found: C, 59.98; H, 7.14; N, 7.26; MS: *m/z* 378 (M⁺).

Entry 3, table 3. 5-Ethoxycarbonyl-6-propyl-1,2,3,4-tetrahydropyrimidin-2(1H)-one (3t)

White crystalline solid; *R_f*: 0.45 (45% v/v ethyl acetate/hexane); Yield 67%; M.p. 162-164°C (DCM); IR (KBr): $\nu_{\max}$ 3253, 3126, 1704, 1654 cm^{-1} ; ^1H NMR (CDCl_3): δ 0.98 (t, 3H, *J* 7.5 Hz), 1.25 (t, 3H, *J* 7.2 Hz), 1.61 (m, 2H), 2.63 (m, 2H), 4.15 (s, 2H), 4.16 (q, 2H, *J* 7.2 Hz), 5.42 (br, 1H, NH, exchanged with D_2O), 7.33 (br, 1H, NH, exchanged with D_2O); ^{13}C NMR (CDCl_3): δ 13.7, 14.2, 21.3, 33.4, 59.9, 96.2, 151.0, 154.2 and 165.4; Anal. Required for $\text{C}_{10}\text{H}_{16}\text{N}_2\text{O}_3$: C, 56.59; H, 7.60; N, 13.20 Found: C, 56.36; H, 8.0; N, 13.60; MS: *m/z* 212 (M^+).

Entry 4, table 3. 5-Ethoxycarbonyl-6-propyl-4-ethyl-3,4-dihydropyrimidin-2(1H)-one (3u)

Cream solid; *R_f*: 0.5 (45% v/v ethyl acetate/hexane); Yield 72%; M.p. 145-147°C (DCM); IR (KBr): $\nu_{\max}$ 3234, 3108, 1693, 1643 cm^{-1} ; ^1H NMR (CDCl_3): δ 0.91 (t, 3H, *J* 7.5 Hz), 0.97 (t, 3H, *J* 7.5 Hz), 1.27 (t, 3H, *J* 7.2 Hz) 1.60 (m, 4H), 2.64 (m, 2H), 4.18 (m, 2H), 4.28 (m, 1H), 6.19 (br, 1H, NH, exchanged with D_2O), 8.13 (br, 1H, NH, exchanged with D_2O); ^{13}C NMR (CDCl_3): δ 8.6, 13.7, 14.2, 21.6, 29.8, 33.6, 52.8, 59.8, 100.9, 150.7, 154.4 and 165.6; Anal. Required for $\text{C}_{12}\text{H}_{20}\text{N}_2\text{O}_3$: C, 59.98; H, 8.39; N, 11.66 Found: C, 60.16; H, 8.53; N, 11.52; MS: *m/z* 240 (M^+).

5-Ethoxycarbonyl-6-methyl(*d*₁)-4-phenyl-3,4-dihydropyrimidin-
2(1H)-one (3a)

(¹H NMR)

(¹³C NMR)

5-Ethoxycarbonyl-6-propyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-
one (3b)

(^1H NMR)

(^{13}C NMR)

5-Ethoxycarbonyl-1,3,6-trimethyl-4-phenyl-3,4-dihydro
pyrimidin-2(1H)-one (3c)

(¹H NMR)

(¹³C NMR)

5-Ethoxycarbonyl-6-ethyl-3-methyl-4-phenyl-3,4-dihydro
pyrimidin-2(1H)-one (3d)

(¹H NMR)

(¹³C NMR)

5-Ethoxycarbonyl-6-ethyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-
one (3e)

(¹H NMR)

(¹³C NMR)

5-Ethoxycarbonyl-3,6-dimethyl-4-phenyl-3,4-dihydro
pyrimidin-2(1H)-one (3f)

(¹H NMR)

(¹³C NMR)

5-Ethoxycarbonyl-6-phenylethyl-4-phenyl-3,4-dihydropyrimidin-
2(1H)-one (3g)

(¹H NMR)

(¹³C NMR)

5-Ethoxycarbonyl-6-chloromethyl-4-phenyl-3,4-dihydro
pyrimidin-2(1H)-one (3h)

(¹H NMR)

(¹³C NMR)

5-Ethoxycarbonyl-6-(2-hydroxy-2-methylpropyl)-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (3i)

(¹H NMR)

(¹³C NMR)

7,7-Dimethyl-4-phenyl-3,4,7,8-tetrahydro-1H-pyrano[4,3-d]pyrimidine-2,5-dione. (4a)

(¹H NMR)

7,7-Dimethyl-4-phenyl-2-thioxo-1,2,3,4,7,8-hexahydropyrano
[4,3-d]pyrimidin-5-one. (4b)

(¹H NMR)

(¹³C NMR)

7-Benzyl-7-methyl-4-phenyl-3,4,7,8-tetrahydro-1H-pyrano[4,3-d]pyrimidine-2,5-dione (4c)

(¹H NMR)

(¹³C NMR)

5-Ethoxycarbonyl-6- [2-hydroxy-2- (4-nitro-phenyl) ethyl] -4-phenyl-3,4-dihydropyrimidin-2(1H)-one (3j)

(¹H NMR)

(¹³C NMR)

5-Ethoxycarbonyl-6-[2-hydroxy-2-[(2,4-dimethoxyphenyl)ethyl]-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (3k)

(¹H NMR)

(¹³C NMR)

5-Ethoxycarbonyl-6-propylsulfanylmethyl-4-phenyl-3,4-dihydro-pyrimidin-2(1H)-one (31)

(¹H NMR)

(¹³C NMR)

(¹H NMR)

5-Ethoxycarbonyl-6-(bis-phenylsulfanylmethyl)-4-phenyl-3, 4-dihydropyrimidin-2(1H)-one (3n)

(¹H NMR)

(¹³C NMR)

5-Ethoxycarbonyl-6-ethyl-3-propionyl-4-phenyl-3,4-dihydro-
pyrimidin-2(1H)-one (3o)

(¹H NMR)

(¹³C NMR)

(¹H NMR)

5-Ethoxycarbonyl-6-trimethylsilanylmethyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (3q)

(¹H NMR)

(¹³C NMR)

pyrimidin-2 (1H) -one (3r)

(¹H NMR)

5-Ethoxycarbonyl-6-propyl-4-(3,4,5-trimethoxy-phenyl)-3,4-dihydropyrimidin-2(1H)-one (3s)

(¹H NMR)

(¹³C NMR)

5-Ethoxycarbonyl-6-propyl-1,2,3,4-tetrahydropyrimidin-2(1H)-
one (3t)

(¹H NMR)

(¹³C NMR)

5-Ethoxycarbonyl-6-propyl-4-ethyl-3,4-dihydropyrimidin-2(1H)-
one (3u)

(¹H NMR)

(¹³C NMR)