Supporting Information:

InCl₃ catalyzed three component reactions for the synthesis of some novel functionalized/annulated barbituric acids

Meenakshi Sharma*, Pallabi Borah and Pulak J. Bhuyan*

Medicinal Chemistry Division, North East Institute of Science & Technology, Jorhat 785006, Assam, India.

Supporting Information

Experimental details, Melting points, IR, ¹H NMR (300 MHz), ¹³C NMR, MS and analytical data of all compounds 4 and 6. Copies of ¹H NMR and ¹³C NMR of all compounds.

General Considerations:

¹H NMR and ¹³C NMR Spectra were recorded on Bruker Avance-DPX 300MHz and 75MHz FT NMR in CDCl₃ using TMS as an internal standard. Chemical shifts were reported in ppm (δ units). [Solvent peak (CDCl₃) at around δ 7.26 peaks are not considered in all the spectra].

Experimental:

Representative procedure for the synthesis of compound 4 and 6:

A mixture of aldehyde (0.105g, 1mmol), 1,3-dimethylbarbituric acid (0.155g, 1mmol) and pyrrolidine (0.07g, 1mmol) in presence of 10 mol% of InCl_3 were taken in a round bottomed flask. To this, ethanol (5 mL) added and stirred the reaction mixture vigorously at room temperature for 2h. After completion of reaction (monitored by TLC), solid compound appeared was filtered off and recrystallized from ethanol. The product **4a** was obtained in 82% (0.25 g) yield. The structure of the compound was ascertained from spectroscopic data and elemental analysis. Similarly compounds **4b-o** and **6a-d** were synthesized and characterized.

Compound 4(a): Yield: 82%; Mp: 175-176°C; IR (CHCl_3) ν_{max} = 1607, 1674, 3460 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 2.09 (br, 4H), 2.78 (br, 1H), 3.06 (br, 2H), 3.31(s, 6H), 3.63 (br, 1H), 5.17 (s, 1H), 7.11-7.90 (m, 5H); ^{13}C NMR (75MHz, CDCl_3) δ , 23.92, 24.37, 27.28, 28.56, 34.17, 45.25, 83.97, 126.50, 127.75, 127.84, 128.06, 128.92, 129.12, 130.08, 151.03, 152.97, 163.16; MS (ESI) 316.41 ($\text{M}+\text{H}$) $^+$; Anal. Calcd for $\text{C}_{17}\text{H}_{21}\text{N}_3\text{O}_3$: C,64.74; H, 6.71; N,13.32 %. Found: C, 64.76; H, 6.72; N, 13.33 %.

Compound 4(b): Yield: 81 %; Mp: 176-177 °C; IR (CHCl_3) ν_{max} = 1605, 1678, 3461 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 2.12 (br, 4H), 2.32 (br, 3H), 2.76 (br, 1H), 3.07 (br, 2H), 3.28 (s, 6H), 3.64 (br, 1H), 5.15 (s, 1H), 7.13 (d, J = 7.91 Hz, 2H), 7.51 (d, J = 8.00 Hz, 2H); ^{13}C NMR (75MHz, CDCl_3) δ 21.02, 24.80, 27.87, 28.31, 45.75, 50.08, 60.97, 127.29, 127.71, 129.48, 129.82, 134.06, 138.30, 138.96, 153.00, 163.15, 169.07, 170.78; MS (ESI) 330.31 ($\text{M}+\text{H}$) $^+$;

Anal. Calcd for $C_{18}H_{23}N_3O_3$: C, 65.63; H, 7.04; N, 12.76 %. Found: C, 65.65; H, 7.05; N, 12.77 %.

Compound 4(c): Yield: 81 %; Mp: 168-169°C; IR ($CHCl_3$) ν_{max} = 1605, 1678, 3461 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ 2.09 (br, 4H), 2.71 (br, 1H), 2.95 (br, 1H), 3.16 (br, 1H), 3.21 (s, 6H), 3.51 (br, 1H), 3.71 (s, 3H), 5.06 (s, 1H), 6.77 (d, J = 8.58 Hz, 2H), 7.47 (d, J = 8.55 Hz, 2H); ^{13}C NMR (75MHz, $CDCl_3$) δ 23.22, 23.88, 24.58, 27.29, 41.97, 54.14, 55.30, 69.26, 114.43, 129.31, 130.23, 134.51, 137.21, 138.01, 153.00, 160.01, 163.17, 170.71; MS (ESI) 346.11 (M+H) $^+$; Anal. Calcd for $C_{18}H_{23}N_3O_4$: C, 62.59; H, 6.71; N, 12.17 %. Found: C, 62.60; H, 6.73; N, 12.18 %.

Compound 4(d): Yield: 80 %; Mp: 175-176 °C; IR ($CHCl_3$) ν_{max} = 1607, 1676, 3465 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ 2.08 (br, 4H), 2.77 (br, 1H), 3.28 (s, 6H), 3.40 (br, 2H), 3.70 (br, 1H), 5.33 (s, 1H), 7.86 (d, J = 8.73 Hz, 2H), 8.21 (d, J = 8.73 Hz, 2H); ^{13}C NMR (75MHz, $CDCl_3$) δ 23.76, 24.81, 27.30, 28.66, 46.07, 68.85, 83.00, 123.42, 124.20, 124.45, 127.51, 128.44, 128.70, 144.71, 147.94, 152.82, 163.11; MS (ESI) 361.10 (M+H) $^+$; Anal. Calcd for $C_{17}H_{20}N_4O_5$: C, 56.66; H, 5.59; N, 15.55 %. Found: C, 56.67; H, 5.60; N, 15.56 %.

Compound 4 (e): Yield: 82 %; Mp: 178-179°C; IR ($CHCl_3$) ν_{max} = 1602, 1679, 3460 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ 2.09 (br, 4H), 2.75 (br, 1H), 3.09 (br, 1H), 3.29 (s, 6H), 3.35 (br, 1H), 3.60 (br, 1H), 5.17 (s, 1H), 7.31 (d, J = 8.34 Hz, 2H), 7.55 (d, J = 8.37 Hz, 2H); ^{13}C NMR (75MHz, $CDCl_3$) δ 23.71, 30.95, 67.89, 113.63, 125.84, 126.08, 129.03, 129.25, 131.31, 131.85, 133.86, 134.23, 134.48, 136.16, 169.68, 180.78, 185.00; MS (ESI) 350.12 (M+H) $^+$; Anal. Calcd for $C_{17}H_{20}ClN_3O_3$: C, 58.37; H, 5.76; N, 12.01 %. Found: C, 58.38; H, 5.77; N, 12.03 %.

Compound 4(f): Yield: 80 %; Mp: 179-180°C; IR (CHCl₃) $\nu_{\max}$ = 1607, 1679, 3462 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.82 (br, 4H), 2.35 (br, 1H), 2.78 (br, 1H), 2.97 (br, 3H), 3.28 (s, 3H), 3.35 (s, 3H), 3.84 (br, 1H), 5.15 (s, 1H), 7.12-7.88 (m, 5H); ¹³C NMR (75MHz, CDCl₃) δ 24.21, 26.22, 26.32, 27.29, 28.19, 52.02, 54.41, 69.15, 83.62, 129.25(2C), 129.31(2C), 135.02, 136.54, 152.96, 163.15, 186.10; MS (ESI) 330.09 (M+H)⁺; Anal. Calcd for C₁₈H₂₃N₃O₃: C, 65.63; H, 7.04; N, 12.76 %. Found: C, 65.65; H, 7.05; N, 12.77 %.

Compound 4(g): Yield: 82 %; Mp: 179-180°C; IR (CHCl₃) $\nu_{\max}$ = 1609, 1677, 3461cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.82 (br, 4H), 2.33 (br, 1H), 2.67 (s, 1H), 2.79 (br, 1H), 2.96 (br, 3H), 3.28 (s, 3H), 3.35 (s, 3H), 3.85 (br, 1H), 5.16 (s, 1H), 7.14- 7.89 (m, 4H); ¹³C NMR (75MHz, CDCl₃) δ 20.01, 24.52, 26.23, 26.33, 27.28, 28.21, 52.03, 54.42, 69.12, 83.60, 129.23(2C), 129.30(2C), 135.05, 136.56, 152.97, 163.16, 170.71 ; MS (ESI) 344.11(M+H)⁺; Anal. Calcd for C₁₉H₂₅N₃O₃: C, 66.45; H, 7.34; N, 12.24 %. Found: C, 66.47; H, 7.35; N, 12.26 %.

Compound 4(h) : Yield: 82 %; Mp: 178-179°C; IR (CHCl₃) $\nu_{\max}$ = 1619, 1670, 3462cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.81 (br, 4H), 2.32 (br, 1H), 2.68 (s, 3H), 2.77 (br, 1H), 2.95 (br, 3H), 3.27 (s, 3H), 3.33 (s, 3H), 3.87 (br, 1H), 5.12 (s, 1H), 7.12- 7.85 (m, 4H); ¹³C NMR (75MHz, CDCl₃) δ 24.35, 26.24, 26.37, 27.24, 28.26, 52.03, 54.43, 59.01, 69.17, 83.65, 116.30, 117.22, 129.25 ,129.39, 135.12, 136.55, 152.94, 163.19, 170.11 ; MS (ESI) 360.15(M+H)⁺; Anal. Calcd for C₁₉H₂₅N₃O₄: C, 63.49; H, 7.01; N, 11.69 %. Found: C, 63.50; H, 7.02; N, 11.70 %.

Compound 4(i) : Yield: 81 %; Mp: 180-181°C; IR (CHCl₃) $\nu_{\max}$ = 1602, 1671, 3459cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.83 (br, 4H), 2.37 (br, 1H), 2.79 (br, 1H), 2.92 (br, 3H), 3.27 (s, 3H), 3.32 (s, 3H), 3.85 (br, 1H), 5.14 (s, 1H), 7.13-7.89 (m, 4H); ¹³C NMR (75MHz, CDCl₃) 24.20, 26.21, 26.33, 27.27, 28.15, 52.04, 54.45, 69.17, 83.61, 129.24(2C), 129.32(2C), 135.05, 136.57, 152.95, 163.17, 186.15 ; MS (ESI) 375.11(M+H)⁺; Anal. Calcd for C₁₈H₂₂N₄O₅: C, 57.75; H, 5.92; N, 14.96 %. Found: C, 57.77; H, 5.93; N, 14.97 %.

Compound 4(j) : Yield: 83 %; Mp: 179-180°C; IR (CHCl₃) $\nu_{\max}$ = 1605, 1667, 3451cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.82 (br, 4H), 2.33 (br, 1H), 2.79 (br, 1H), 2.96 (br, 3H), 3.28 (s, 3H), 3.35 (s, 3H), 3.85 (br, 1H), 5.16 (s, 1H), 7.14- 7.58 (m, 4H); ¹³C NMR (75MHz, CDCl₃) δ 24.32, 26.20, 26.31, 27.29, 28.20, 52.05, 54.41, 69.19, 83.65, 127.21, 127.32, 129.13, 129.31, 135.04, 136.57, 152.94, 163.18, 170.81 ; MS (ESI) 364.21(M+H)⁺; Anal. Calcd for C₁₈H₂₂ClN₃O₃: C, 59.42; H, 6.09; N, 11.55 %. Found: C, 59.43; H, 6.11; N, 11.56 %.

Compound 4(k): Yield: 82 %; Mp: 177-178°C; IR (CHCl₃) $\nu_{\max}$ = 1601, 1670, 3465cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 3.18 (s, 4H), 3.31 (s, 3H), 3.35 (s, 3H), 3.78 (s, 1H), 3.92 (s, 3H), 5.84 (s, 1H), 7.10-7.35 (m, 5H); ¹³C NMR (75MHz, CDCl₃) δ 28.50, 28.78, 43.70 (2C), 64.23(2C), 71.94, 91.94, 125.74, 126.42 (2C), 129.02 (2C), 129.77, 151.57, 164.75, 165.53; MS (ESI) 332.15(M+H)⁺; Anal. Calcd for C₁₇H₂₁N₃O₄: C, 61.62; H, 6.39; N, 12.68 %. Found: C, 61.63; H, 6.40; N, 12.69 %.

Compound 4(l): Yield: 81 %; Mp: 174-175 °C; IR (CHCl₃) $\nu_{\max}$ = 1619, 1686, 3464cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.26 (t, *J* = 7.20 Hz, 6H), 2.99 (q, *J* = 7.22 Hz, 4H), 3.31 (s, 3H), 3.35 (s, 3H), 5.89 (s, 1H), 7.10-8.06 (m, 6H); ¹³C NMR (75MHz, CDCl₃) δ 11.31(2C), 28.62,

28.83, 42.03(2C), 67.01, 91.99, 125.48, 126.45(2C), 128.07(2C), 141.80, 151.76, 164.25, 165.29; MS (ESI) 318.30(M+H)⁺; Anal. Calcd for C₁₇H₂₃N₃O₃: C, 64.33; H, 7.30; N, 13.24 %. Found: C, 64.36; H, 7.33; N, 13.26 %.

Compound 4(m): Yield: 80 %; Mp: 171-172°C; IR (CHCl₃) $\nu_{\max}$ = 1619, 1682, 3051 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.22 (d, *J* = 6.51 Hz, 6H), 3.31 (m, 1H), 3.34 (s, 6H), 3.68 (s, NH), 5.39 (s, 1H), 7.09-7.26 (m, 5H); ¹³C NMR (75MHz, CDCl₃+ 1drop DMSO-d₆) δ 25.65 (2C), 33.30 (2C), 38.91, 48.55, 96.65, 129.96, 131.39 (2C), 132.66 (2C), 136.39, 156.59 (2C), 160.09; MS (ESI) 304.12 (M+H)⁺; Anal. Calcd for C₁₆H₂₁N₃O₃: C, 63.35; H, 6.98; N, 13.85 %. Found: C, 63.37; H, 6.99; N, 13.87 %.

Compound 4(n): Yield: 79 %; Mp: 172-173°C; IR (CHCl₃) $\nu_{\max}$ = 1611, 1680, 3055 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.25 (d, *J* = 6.50 Hz, 6H), 2.31 (s, 3H), 3.30 (m, 1H), 3.34 (s, 6H), 3.67 (s, NH), 5.34 (s, 1H), 7.11-7.29 (m, 4H); ¹³C NMR (75MHz, CDCl₃+1drop DMSO-d₆) δ 21.19, 25.64 (2C), 33.31 (2C), 38.92, 48.54, 96.64, 129.95, 131.38 (2C), 132.67 (2C), 136.35, 156.57 (2C), 160.05; MS (ESI) 318.31 (M+H)⁺; Anal. Calcd for C₁₇H₂₃N₃O₃: C, 64.33; H, 7.30; N, 13.24 %. Found: C, 64.34; H, 7.32; N, 13.25 %.

Compound 4(o): Yield: 75 %; Mp: 174-175°C; IR (CHCl₃) $\nu_{\max}$ = 1610, 1687, 3065 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.24 (d, *J* = 6.49 Hz, 6H), 3.31 (m, 1H), 3.32 (s, 6H), 3.68 (s, NH), 5.95 (s, 1H), **7.07-7.27** (m, 4H); ¹³C NMR (75MHz, CDCl₃+ 1drop DMSO-d₆) δ 25.63 (2C), 33.32 (2C), 38.93, 48.55, 96.67, 129.93, 131.37 (2C), 132.64 (2C), 136.32, 156.55 (2C), 160.04; MS (ESI) 349.02 (M+H)⁺; Anal. Calcd for C₁₆H₂₀N₄O₅: C, 55.17; H, 5.79; N, 16.08 %. Found: C, 55.18; H, 5.80; N, 16.09 %.

Compound 6(a): Yield: 83 %; Mp: 170-171°C; IR (CHCl₃) ν_{max} = 1614, 1681, 3061 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 2.15 (br, 4H), 3.03 (br, 2H), 3.30 (s, 6H), 3.64 (br, 2H), 5.64 (s, 1H), 6.81-7.56 (m, 4H); ¹³C NMR (75MHz, CDCl₃) δ 23.42, 23.96, 24.92, 27.19, 45.55, 52.22, 54.60, 84.41, 117.58, 120.55, 124.51, 127.61, 130.09, 152.59, 154.75, 161.57, 163.90; MS (ESI) 314.22 (M+H)⁺; Anal. Calcd for C₁₇H₁₉N₃O₃: C, 65.16; H, 6.11; N, 13.40 %. Found: C, 65.17; H, 6.12; N, 13.41 %.

Compound 6(b): Yield: 82 %; Mp: 171-172°C; IR (CHCl₃) ν_{max} = 1612, 1684, 3064 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.80 (br, 4H), 2.30 (br, 1H), 2.77 (br, 1H), 2.95 (br, 3H), 3.28 (s, 3H), 3.35 (s, 3H), 3.84 (br, 1H), 5.53 (s, 1H), 7.21-7.89 (m, 4H); ¹³C NMR (75MHz, CDCl₃) δ 24.98, 25.96, 26.42, 27.19 (2C), 45.54, 52.24, 54.61, 84.40, 117.57, 120.56, 124.50, 127.60, 130.08, 152.60, 154.74, 161.55, 163.92; MS (ESI) 328.21 (M+H)⁺; Anal. Calcd for C₁₈H₂₁N₃O₃: C, 66.04; H, 6.41; N, 12.84 %. Found: C, 66.05; H, 6.42; N, 12.85 %.

Compound 6(c): Yield: 81 %; Mp: 172-173°C; IR (CHCl₃) ν_{max} = 1610, 1682, 3067 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 3.15 (s, 4H), 3.30 (s, 3H), 3.35 (s, 3H), 3.76 (s, 1H), 3.90 (s, 3H), 5.80 (s, 1H), 7.19-7.35 (m, 4H); ¹³C NMR (75MHz, CDCl₃) δ 28.19(2C), 45.55 (2C), 54.60 (2C), 71.19, 84.42, 116.55, 121.55, 126.51, 127.66, 131.09, 151.84, 152.93, 154.31, 163.19; MS (ESI) 330.11 (M+H)⁺; Anal. Calcd for C₁₇H₁₉N₃O₄: C, 62.00; H, 5.81; N, 12.76 %. Found: C, 62.01; H, 5.83; N, 12.77 %.