

Supplementary Information

Structure-Activity Relationship of *N,N'*-Disubstituted Pyrimidinetrienes as Ca_v1.3 Channel Selective Antagonists for the Parkinson's Disease

Soosung Kang^a, *Garry Cooper*^{a,b}, *Sara Fernandez Dunne*^c, *Chi-Hao Luan*^c, *D. James Surmeier*^b,
and *Richard B. Silverman*^{a,*}

^aDepartment of Chemistry, Department of Molecular Biosciences, Chemistry of Life Processes Institute, and Center for Molecular Innovation and Drug Discovery, Northwestern University, Evanston, IL 60208, ^bDepartment of Physiology, Feinberg School of Medicine, Northwestern University, Chicago, IL 60611, ^cHigh-Throughput Analysis Laboratory, Northwestern University, Evanston, IL 60208

*Address correspondence to the Department of Chemistry; telephone: 847-491-5653; email: Agman@chem.northwestern.edu

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1-(3-Chlorophenethyl)-3-((1*S*,2*R*)-2-methylcyclopentyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (19), and **1-(3-chlorophenethyl)-3-((1*R*,2*S*)-2-methylcyclopentyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (24)**: White powder; mp 75-77 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.26 – 7.13 (m, 4H), 5.19 (td, *J* = 9.6, 6.8 Hz, 1H), 4.08 (m, 2H), 3.62 (ss, 2H), 2.87 (t, *J* = 7.7 Hz, 2H), 2.21 (m, 2H), 2.01 – 1.65 (m, 4H), 1.48 (m, 1H), 0.81 (d, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 165.42, 164.53, 151.77, 139.82, 134.25, 129.84, 129.10, 127.19, 126.93, 57.35, 42.64, 40.11, 37.49, 34.36, 33.60, 28.65, 25.10, 14.60; MS (ESI): calculated for C₁₈H₂₁ClN₂O₃ [M - H]⁻, 347.12; found, 347.34; HPLC purity: 95.2% (19), 94.9% (24)

1-(4-Chlorophenethyl)-3-((1*S*,2*R*)-2-methylcyclopentyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (20) and **1-(4-chlorophenethyl)-3-((1*R*,2*S*)-2-methylcyclopentyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (25)**: White powder; mp 87-90 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.25 (d, *J* = 8.4 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 5.18 (td, *J* = 9.6, 6.8 Hz, 1H), 4.06 (m, 2H), 3.61 (ss, 2H), 2.86 (t, *J* = 7.7 Hz, 2H), 2.22 (m, 2H), 1.94 (m, 2H), 1.83 – 1.64 (m, 2H), 1.48 (m, 1H), 0.80 (d, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 165.42, 164.54, 151.79, 136.25, 132.53, 130.36, 128.66, 57.35, 42.74, 40.11, 37.47, 34.34, 33.30, 28.63, 25.09, 14.56; MS (ESI): calculated for C₁₈H₂₁ClN₂O₃ [M - H]⁻, 347.12; found, 347.33; HPLC purity: 98.3% (20), 95.1% (25)

(*S*)-1-(3-Chlorophenethyl)-3-(2,2-dimethylcyclopentyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (21) and **(*R*)-1-(3-chlorophenethyl)-3-(2,2-dimethylcyclopentyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (26)**: White powder; mp 101-103 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.35 – 7.01 (m, 4H), 4.82 (dd, *J* = 9.7, 6.1 Hz, 1H), 4.20 – 4.02 (m, 2H), 3.62 (d, *J* = 2.2 Hz, 2H), 2.87 (t, *J* = 7.8 Hz, 2H), 2.27 (m, 1H), 2.08 – 1.82 (m, 3H), 1.74 – 1.63 (m, 1H), 1.44 (m, 1H), 1.06 (s, 3H), 0.85 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 165.28, 164.47, 151.73, 139.79, 134.29, 129.84, 129.13, 127.21, 126.96, 63.92, 43.02, 42.71, 40.99, 40.21, 33.63, 30.08, 28.13, 23.90, 23.45; MS (ESI): calculated for C₁₉H₂₃ClN₂O₃ [M - H]⁻, 361.13; found, 361.42; HPLC purity: 95.2% (21), 94.9% (26).

(*S*)-1-(4-Chlorophenethyl)-3-(2,2-dimethylcyclopentyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (22) and **(*R*)-1-(4-chlorophenethyl)-3-(2,2-dimethylcyclopentyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (27)**: White powder; mp 92-95 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.32 – 7.09 (m, 4H), 4.81 (dd, *J* = 9.6, 6.2 Hz, 1H), 4.17 – 3.95 (m, 2H), 3.62 (d, *J* = 2.4 Hz, 2H), 2.87 (t, *J* = 7.7 Hz, 2H), 2.26 (m, 1H), 2.07 – 1.79 (m, 3H), 1.74 – 1.59 (m, 1H), 1.44 (m, 1H), 1.06 (s, 3H), 0.83 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 165.28, 164.48, 151.74, 136.22, 132.58, 130.37, 128.69, 63.92, 43.01, 42.82, 40.99, 40.22, 33.33, 30.07, 28.13, 23.86, 23.44; HRMS (ESI): calculated for C₁₉H₂₃ClN₂O₃ [M - H]⁻, 393.1432; found, 393.1448; HPLC purity: 98.5% (22), 96.5% (27).

1-(3-Chlorophenethyl)-3-(3-methylcyclopentyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (30): White powder; mp 110-114 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.26 – 7.09 (m, 4H), 5.30 – 5.12 (m, 1H), 4.06 (m, 2H), 3.61 (s, 2H), 2.87 (dd, *J* = 9.2, 6.5 Hz, 2H), 2.08 – 1.93 (m, 1H), 1.91 – 1.81 (m, 2H), 1.80 – 1.68 (m, 2H), 1.69 – 1.56 (m, 1H), 1.46 (m, 1H), 1.04 (d, *J* = 6.6 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 164.78, 164.53, 150.81, 139.88, 134.25, 129.84, 129.08, 127.16, 126.91, 54.11, 42.56, 40.08, 37.24, 34.55, 33.66, 33.31, 28.28, 19.70; HRMS (ESI): calculated for C₁₈H₂₁ClN₂O₃ [M - H]⁻, 347.1168; found, 347.1171; HPLC purity: 99%

1-(4-Chlorophenethyl)-3-(3-methylcyclopentyl)pyrimidine-2,4,6(1H,3H,5H)-trione (31): White powder; mp 97-106 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.28 – 7.16 (m, 4H), 5.29 – 5.08 (m, 1H), 4.06 (m, 2H), 3.62 (s, 2H), 2.90 (m, 2H), 2.06 – 1.81 (m, 4H), 1.80 – 1.55 (m, 2H), 1.30 (m, 1H), 1.04 (m, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 164.75, 164.72, 164.51, 150.87, 150.83, 136.28, 132.59, 130.35, 128.71, 54.17, 53.68, 42.76, 42.72, 40.11, 37.26, 36.80, 34.71, 34.56, 33.72, 33.39, 33.31, 29.50, 28.28, 20.28, 19.69; MS (ESI): calculated for C₁₈H₂₁ClN₂O₃ [M - H]⁻, 347.12; found, 347.25; HPLC purity: 99%

1-(3-Chlorophenethyl)-3-(3,3-dimethylcyclopentyl)pyrimidine-2,4,6(1H,3H,5H)-trione (32): White powder; mp 109-111 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.27 – 7.10 (m, 4H), 5.46 – 5.20 (m, 1H), 4.22 – 4.05 (m, 2H), 3.65 (s, 2H), 2.95 – 2.80 (m, 2H), 2.07 – 1.98 (m, 2H), 1.98 – 1.84 (m, 2H), 1.71 – 1.52 (m, 1H), 1.48 – 1.38 (m, 1H), 1.17 (s, 3H), 1.02 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 164.74, 164.49, 150.85, 139.84, 134.32, 129.85, 129.12, 127.17, 126.97, 53.85, 42.63, 42.39, 40.13, 39.48, 39.41, 33.69, 29.41, 28.04, 27.98; MS (ESI): calculated for C₂₄H₂₆N₂O₄ [M - H]⁻, 405.18; found, 405.16.

1-(4-Chlorophenethyl)-3-(3,3-dimethylcyclopentyl)pyrimidine-2,4,6(1H,3H,5H)-trione (33): White powder; mp 121-124 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.31 – 7.27 (m, 2H), 7.22 – 7.18 (m, 2H), 5.32 – 5.26 (m, 1H), 4.15 – 4.02 (m, 2H), 3.64 (s, 2H), 2.94 – 2.80 (m, 2H), 2.07 – 1.96 (m, 2H), 1.89 (ddt, *J* = 11.9, 9.5, 4.0 Hz, 2H), 1.57 (ddd, *J* = 11.8, 8.5, 1.3 Hz, 1H), 1.52 – 1.39 (m, 1H), 1.17 (s, 3H), 1.01 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 164.74, 164.50, 150.86, 136.27, 132.60, 130.36, 128.71, 53.83, 42.73, 42.39, 40.13, 39.46, 39.40, 33.39, 29.40, 28.03, 27.97; MS (ESI): calculated for C₂₄H₂₆N₂O₄ [M - H]⁻, 405.18; found, 405.16.

1-(3-Chlorophenethyl)-3-(3-ethylcyclopentyl)pyrimidine-2,4,6(1H,3H,5H)-trione (34): White powder; mp 89-91 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.26 – 7.10 (m, 4H), 5.16 (m, 1H), 4.06 (m, 2H), 3.60 (s, 1H), 2.87 (m, 2H), 2.31 – 1.92 (m, 2H), 1.90 – 1.78 (m, 2H), 1.76 – 1.56 (m, 1H), 1.55 – 1.33 (m, 2H), 1.33 – 1.09 (m, 1H), 0.90 (td, *J* = 7.4, 2.5 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 164.80, 164.54, 150.82, 139.89, 134.25, 129.84, 129.08, 127.16, 126.91, 53.94, 53.52, 42.57, 42.54, 41.64, 40.92, 40.08, 35.11, 34.76, 33.66, 32.41, 30.91, 29.28, 28.55, 28.18, 27.83, 12.93, 12.83; MS (ESI): calculated for C₁₉H₂₃ClN₂O₃ [M - H]⁻, 361.13; found, 361.20; HPLC purity: 96.2%

1-(4-Chlorophenethyl)-3-(3-ethylcyclopentyl)pyrimidine-2,4,6(1H,3H,5H)-trione (35): White powder; mp 105-111 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.26 (d, *J* = 8.2 Hz, 2H), 7.17 (d, *J* = 8.3, 2H), 5.15 (m, 1H), 4.05 (m, 2H), 3.60 (s, 2H), 2.85 (m, 2H), 1.99 (m, 2H), 1.90 – 1.56 (m, 4H), 1.55 – 1.38 (m, 2H), 1.34 (m, 1H), 0.91 (td, *J* = 7.5, 2.6 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 164.79, 164.76, 164.54, 150.86, 150.84, 136.31, 132.52, 130.34, 128.67, 53.95, 53.52, 42.69, 42.67, 41.64, 40.92, 40.09, 35.13, 34.75, 33.36, 32.40, 30.89, 29.28, 28.54, 28.17, 27.82, 12.92, 12.83; MS (ESI): calculated for C₁₉H₂₃ClN₂O₃ [M - H]⁻, 361.13; found, 361.21; HPLC purity: 97.4%

1-(3-Chlorophenethyl)-3-(2,3-dimethylcyclopentyl)pyrimidine-2,4,6(1H,3H,5H)-trione (36): White powder; mp 75-79 °C; major diastereomer; ¹H NMR (500 MHz, CDCl₃) δ 7.26 – 7.08 (m, 4H), 5.42 – 5.15 (m, 1H), 4.17 – 4.01 (m, 2H), 3.72 – 3.54 (m, 2H), 2.88 (q, *J* = 7.8, 6.9 Hz, 2H), 2.23 – 2.11 (m, 1H), 2.07 – 1.98 (m, 2H), 1.69 – 1.58 (m, 1H), 1.15 – 1.05 (m, 1H), 0.97 (d, *J* =

6.1 Hz, 3H), 0.76 (d, $J = 7.1$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 165.38, 164.50, 151.73, 139.78, 134.29, 129.84, 129.12, 127.19, 126.95, 59.18, 44.68, 42.67, 40.85, 40.08, 34.50, 33.62, 27.62, 18.68, 12.65; MS (ESI): calculated for $\text{C}_{19}\text{H}_{23}\text{ClN}_2\text{O}_3$ $[\text{M} - \text{H}]^-$, 361.13; found, 361.40.

1-(3-Chlorophenethyl)-3-((±)-trans-2-methylcyclopentyl)pyrimidine-2,4,6(1H,3H,5H)-trione (37): White powder; mp 119-122 °C; Trans/cis mixture (88%-trans); ^1H NMR (500 MHz, CDCl_3) δ 7.25 – 7.13 (m, 4H), 4.66 (td, $J = 9.4, 7.9$ Hz, 1H), 4.07 (m, 2H), 3.63 (s, 2H), 2.87 (m, 2H), 2.47 (m, 1H), 2.21 (m, 2H), 2.09 – 1.60 (m, 2H), 1.21 (m, 2H), 0.94 (d, $J = 6.7$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 165.01, 164.55, 151.08, 139.82, 134.26, 129.83, 129.09, 127.18, 126.93, 61.59, 42.57, 40.09, 36.20, 33.78, 33.62, 28.08, 23.27, 18.29; MS (ESI): calculated for $\text{C}_{18}\text{H}_{21}\text{ClN}_2\text{O}_3$ $[\text{M} - \text{H}]^-$, 347.12; found, 347.25; HPLC purity: 98.0%

1-(4-Chlorophenethyl)-3-((±)-trans-2-methylcyclopentyl)pyrimidine-2,4,6(1H,3H,5H)-trione (38): White powder; mp 110-117 °C; Trans/cis mixture (88%-trans); ^1H NMR (500 MHz, CDCl_3) δ 7.26 (d, $J = 8.3$ Hz, 2H), 7.17 (d, $J = 8.3$ Hz, 2H), 4.64 (td, $J = 9.3, 7.9$ Hz, 1H), 4.07 (m, 2H), 3.62 (s, 2H), 2.87 (m, 2H), 2.45 (m, 1H), 2.06 – 1.75 (m, 4H), 1.74 – 1.62 (m, 1H), 1.22 (m, 1H), 0.93 (d, $J = 6.7$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 165.01, 164.56, 151.08, 136.26, 132.54, 130.35, 128.67, 61.57, 42.67, 40.09, 36.18, 33.76, 33.31, 28.05, 23.25, 18.25; MS (ESI): calculated for $\text{C}_{18}\text{H}_{21}\text{ClN}_2\text{O}_3$ $[\text{M} - \text{H}]^-$, 347.12; found, 347.25; HPLC purity: 100%

1-(3-Chlorophenethyl)-3-(4-methylcyclohexyl)pyrimidine-2,4,6(1H,3H,5H)-trione (39): White powder; mp 130-132 °C; cis/trans = 2:3 mixtures; ^1H NMR (500 MHz, CDCl_3) δ 7.26 – 7.11 (m, 4H), 4.58 (m, 1H), 4.06 (m, 2H), 3.60 (ss, 2H), 2.87 (m, 2H), 2.46 (m, 1H), 2.28 (m, 1H), 1.95 (m, 1H), 1.83 – 1.70 (m, 1H), 1.65 – 1.51 (m, 3H), 1.36 (m, 1H), 1.10 – 0.86 (m, 4H); ^{13}C NMR (126 MHz, CDCl_3) δ 164.80, 164.77, 164.60, 164.58, 151.04, 139.87, 134.28, 129.87, 129.85, 129.10, 129.08, 127.17, 127.15, 126.93, 126.92, 55.46, 42.64, 42.59, 40.21, 40.19, 34.72, 33.65, 31.51, 28.62, 26.15, 23.05, 22.22, 17.21; MS (ESI): calculated for $\text{C}_{19}\text{H}_{23}\text{ClN}_2\text{O}_3$ $[\text{M} - \text{H}]^-$, 361.13; found, 361.25; HPLC purity: 97.3%

1-(4-Chlorophenethyl)-3-(4-methylcyclohexyl)pyrimidine-2,4,6(1H,3H,5H)-trione (40): White powder; mp 129-132 °C; cis/trans = 2:3 mixtures; ^1H NMR (500 MHz, CDCl_3) δ 7.28 – 7.13 (m, 4H), 4.56 (m, 1H), 4.03 (m, 2H), 3.59 (ss, 2H), 2.85 (m, 2H), 2.45 (m, 1H), 2.27 (m, 1H), 1.94 (m, 1H), 1.78 (m, 1H), 1.64 – 1.51 (m, 3H), 1.49 – 1.30 (m, 1H), 1.11 – 0.87 (m, 4H); ^{13}C NMR (126 MHz, CDCl_3) δ 164.82, 164.79, 164.62, 164.60, 151.05, 136.34, 132.49, 130.34, 130.32, 128.66, 55.38, 42.69, 42.67, 40.18, 34.71, 33.33, 31.49, 28.61, 26.14, 23.04, 22.21, 17.19; MS (ESI): calculated for $\text{C}_{19}\text{H}_{23}\text{ClN}_2\text{O}_3$ $[\text{M} - \text{H}]^-$, 361.13; found, 361.19; HPLC purity: 94.8%

1-(3-Chlorophenethyl)-3-(2-methylcyclohexyl)pyrimidine-2,4,6(1H,3H,5H)-trione (41): White powder; mp 86-88 °C; cis/trans mixtures; ^1H NMR (500 MHz, CDCl_3) δ 7.24 – 7.10 (m, 4H), 4.33 (m, 1H), 4.13 – 4.02 (m, 2H), 3.61 (s, 2H), 2.87 (m, 2H), 2.37 (m, 1H), 2.16 (m, 1H), 1.81 (m, 2H), 1.70 – 1.63 (m, 1H), 1.59 (m, 1H), 1.33 (m, 2H), 1.13 – 0.95 (m, 1H), 0.74 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 165.27, 164.59, 151.81, 139.79, 134.28, 129.85, 129.11, 127.18, 126.95, 62.75, 60.34, 53.50, 42.74, 42.29, 35.20, 33.61, 26.36, 25.71, 18.60; MS (ESI): calculated for $\text{C}_{19}\text{H}_{23}\text{ClN}_2\text{O}_3$ $[\text{M} - \text{H}]^-$, 361.13; found, 361.24; HPLC purity: 99%

1-(4-Chlorophenethyl)-3-(2-methylcyclohexyl)pyrimidine-2,4,6(1H,3H,5H)-trione (42):

White powder; mp 118-120 °C; cis/trans mixtures; ¹H NMR (500 MHz, CDCl₃) δ 7.24 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 4.34 – 4.14 (m, 1H), 4.11 – 3.98 (m, 2H), 3.59 (s, 2H), 2.86 (m, 2H), 2.37 (m, 1H), 2.14 (m, 1H), 1.80 (m, 2H), 1.71 – 1.62 (m, 1H), 1.56 (m, 1H), 1.39 – 1.23 (m, 2H), 1.04 (m, 2H), 0.73 (d, *J* = 6.6 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 165.29, 164.63, 151.80, 136.24, 132.49, 130.34, 128.65, 60.38, 53.54, 42.77, 40.50, 35.17, 33.26, 29.22, 26.34, 25.69, 18.54; MS (ESI): calculated for C₁₉H₂₃ClN₂O₃ [M - H]⁻, 361.13; found, 361.25; HPLC purity: 100%

(*R*)-1-(3-Chlorophenethyl)-3-((tetrahydrofuran-2-yl)methyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (47): White powder; mp 90-92 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.33 – 7.08 (m, 4H), 4.27 – 4.16 (m, 1H), 4.10 – 4.01 (m, 3H), 3.90 – 3.82 (m, 1H), 3.78 – 3.69 (m, 2H), 3.67 (d, *J* = 4.5 Hz, 2H), 2.90 – 2.81 (m, 2H), 2.07 – 1.95 (m, 2H), 1.93 – 1.84 (m, 1H), 1.66 – 1.56 (m, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 164.65, 164.52, 151.42, 139.87, 134.26, 129.86, 129.06, 127.14, 126.91, 75.47, 67.77, 45.09, 42.81, 39.63, 33.64, 29.11, 25.25; MS (ESI): calculated for C₁₇H₁₉ClN₂O₄ [M - H]⁻, 349.1; found, 349.25 ; HPLC purity: 92.3%.

(*R*)-1-(4-Chlorophenethyl)-3-((tetrahydrofuran-2-yl)methyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (48): White powder; mp 94-95 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.28 – 7.25 (m, 2H), 7.20 – 7.17 (m, 2H), 4.26 – 4.15 (m, 1H), 4.13 – 4.00 (m, 3H), 3.85 (dt, *J* = 8.3, 6.9 Hz, 1H), 3.78 – 3.69 (m, 2H), 3.66 (d, *J* = 5.0 Hz, 2H), 2.93 – 2.80 (m, 2H), 2.08 – 1.94 (m, 2H), 1.94 – 1.83 (m, 1H), 1.60 (m, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 164.62, 164.52, 151.42, 136.30, 132.51, 130.33, 128.70, 75.45, 67.79, 45.11, 42.92, 39.62, 33.33, 29.11, 25.26; MS (ESI): calculated for C₁₇H₁₉ClN₂O₄ [M - H]⁻, 349.1; found, 349.19; HPLC purity: 96.7%.

1-(3-Chlorophenethyl)-3-((1*R*,2*S*,4*R*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (53): White powder; mp 119-121 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.31 – 7.07 (m, 4H), 5.19 – 5.08 (m, 1H), 4.19 – 4.01 (m, 2H), 3.66 (d, *J* = 2.1 Hz, 2H), 2.89 (t, *J* = 7.8 Hz, 2H), 2.47 (dd, *J* = 12.6, 5.4 Hz, 1H), 1.88 (m, 1H), 1.78 (m, 2H), 1.71 (m, 1H), 1.48 (m, 1H), 1.32 (m, 1H), 1.03 (s, 3H), 0.91 (s, 3H), 0.76 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 166.24, 164.41, 152.62, 139.87, 134.29, 129.85, 129.11, 127.19, 126.95, 61.22, 51.88, 47.38, 45.69, 43.00, 40.87, 33.66, 30.66, 26.93, 26.63, 19.85, 18.81, 14.43; MS (ESI): calculated for C₂₂H₂₇ClN₂O₃ [M - H]⁻, 401.16; found, 401.32.

1-(4-Chlorophenethyl)-3-((1*R*,2*S*,4*R*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (54): White powder; mp 118-120 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.27 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 5.18 – 5.04 (m, 1H), 4.14 – 3.96 (m, 2H), 3.65 (d, *J* = 2.5 Hz, 2H), 2.87 (t, *J* = 7.8 Hz, 2H), 2.45 (dd, *J* = 12.5, 5.5 Hz, 1H), 1.92 – 1.83 (m, 1H), 1.82 – 1.75 (m, 2H), 1.73 – 1.65 (m, 1H), 1.51 – 1.43 (m, 1H), 1.35 – 1.26 (m, 1H), 1.02 (s, 3H), 0.91 (s, 3H), 0.75 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 166.25, 164.43, 152.64, 136.33, 132.54, 130.36, 128.69, 61.19, 51.86, 47.38, 45.68, 43.10, 40.87, 33.36, 30.63, 26.93, 26.62, 19.85, 18.81, 14.40; MS (ESI): calculated for C₂₂H₂₇ClN₂O₃ [M - H]⁻, 401.16; found, 401.39.

1-(3-Chlorophenethyl)-3-(((1*R*,2*S*,5*R*)-6,6-dimethylbicyclo[3.1.1]heptan-2-yl)methyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (55): White powder; mp 96-99 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.32 – 7.07 (m, 4H), 4.21 – 4.02 (m, 2H), 3.95 (dd, *J* = 13.0, 8.6 Hz, 1H), 3.85 (dd, *J* = 13.1, 6.9 Hz, 1H), 3.64 (s, 2H), 2.89 (t, *J* = 7.8 Hz, 2H), 2.43 – 2.29 (m, 2H), 2.02 – 1.81 (m, 4H), 1.76 (m,

1H), 1.58 – 1.48 (m, 1H), 1.18 (ss, 6H), 0.87 (d, $J = 9.7$ Hz, 1H); ^{13}C NMR (126 MHz, CDCl_3) δ 164.66, 164.52, 151.52, 139.76, 134.29, 129.85, 129.11, 127.17, 126.97, 46.88, 43.47, 42.69, 41.13, 39.60, 39.44, 38.74, 33.62, 33.15, 27.82, 25.97, 22.70, 19.00; MS (ESI): calculated for $\text{C}_{22}\text{H}_{27}\text{ClN}_2\text{O}_3$ $[\text{M} - \text{H}]^-$, 401.16; found, 401.28.

1-(4-Chlorophenethyl)-3-(((1*R*,2*S*,5*R*)-6,6-dimethylbicyclo[3.1.1]heptan-2-yl)methyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (56): White powder; mp 128-131 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.27 (d, $J = 8.4$ Hz, 2H), 7.17 (d, $J = 8.4$ Hz, 2H), 4.10 – 4.04 (m, 2H), 3.94 (dd, $J = 13.1, 8.5$ Hz, 1H), 3.84 (dd, $J = 13.0, 6.8$ Hz, 1H), 3.62 (s, 2H), 2.90 – 2.84 (m, 2H), 2.45 – 2.26 (m, 2H), 2.00 – 1.79 (m, 4H), 1.78 – 1.68 (m, 1H), 1.59 – 1.44 (m, 1H), 1.17 (ss, 6H), 0.86 (d, $J = 9.7$ Hz, 1H); ^{13}C NMR (126 MHz, CDCl_3) δ 164.66, 164.54, 151.52, 136.22, 132.55, 130.33, 128.69, 46.86, 43.46, 42.77, 41.13, 39.60, 39.43, 38.72, 33.31, 33.12, 27.80, 25.95, 22.69, 19.00; MS (ESI): calculated for $\text{C}_{22}\text{H}_{27}\text{ClN}_2\text{O}_3$ $[\text{M} - \text{H}]^-$, 401.16; found, 401.26.

1-(3-Chlorophenethyl)-3-(((1*R*,2*R*,3*R*,5*S*)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (57) and 1-(3-chlorophenethyl)-3-(((1*S*,2*S*,3*S*,5*R*)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (59): White powder; mp 102-104 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.28 – 7.07 (m, 4H), 5.32 (m, 1H), 4.11 (m, 2H), 3.65 (s, 2H), 2.96 – 2.83 (m, 2H), 2.52 (m, 1H), 2.29 (dt, $J = 9.7, 6.2$ Hz, 1H), 2.24 – 2.12 (m, 2H), 2.05 (h, $J = 3.0$ Hz, 1H), 1.93 – 1.83 (m, 2H), 1.28 (s, 3H), 1.15 (s, 3H), 0.97 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 165.48, 164.49, 157.85, 139.82, 134.28, 129.83, 129.13, 127.21, 126.93, 54.26, 52.13, 48.78, 42.46, 39.82, 39.37, 38.70, 33.64, 31.69, 30.62, 28.45, 23.68, 20.36; MS (ESI): calculated for $\text{C}_{22}\text{H}_{27}\text{ClN}_2\text{O}_3$ $[\text{M} - \text{H}]^-$, 401.16; found, 401.44.

1-(4-Chlorophenethyl)-3-(((1*R*,2*R*,3*R*,5*S*)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (58) and 1-(4-chlorophenethyl)-3-(((1*S*,2*S*,3*S*,5*R*)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (60): Colorless oil; ^1H NMR (500 MHz, CDCl_3) δ 7.26 (d, $J = 8.3$ Hz, 2H), 7.18 (d, $J = 8.3$ Hz, 2H), 5.41 – 5.20 (m, 1H), 4.17 – 3.99 (m, 2H), 3.65 (s, 2H), 2.92 – 2.86 (m, 2H), 2.56 – 2.37 (m, 1H), 2.28 (dt, $J = 9.7, 6.2$ Hz, 1H), 2.21 – 2.07 (m, 2H), 2.07 – 2.00 (m, 1H), 1.93 – 1.79 (m, 2H), 1.28 (s, 3H), 1.14 (s, 3H), 0.96 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 165.51, 164.52, 157.90, 136.27, 132.54, 130.38, 128.66, 60.41, 54.22, 39.37, 48.76, 42.46, 39.37, 38.68, 33.33, 31.69, 30.61, 28.44, 23.67, 20.31; MS (ESI): calculated for $\text{C}_{22}\text{H}_{27}\text{ClN}_2\text{O}_3$ $[\text{M} - \text{H}]^-$, 401.16; found, 401.57.

methyl 1-(3-(3-Chlorophenethyl)-2,4,6-trioxotetrahydropyrimidin-1(2*H*)-yl)cyclopentane-carboxylate (61): White powder; mp 83-88 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.39 – 6.96 (m, 4H), 4.18 – 3.97 (m, 1H), 3.71 (s, 3H), 3.64 (s, 2H), 2.94 – 2.77 (m, 2H), 2.55 – 2.36 (m, 2H), 2.21 – 2.02 (m, 2H), 1.94 – 1.64 (m, 4H); ^{13}C NMR (126 MHz, CDCl_3) δ 173.27, 165.21, 164.24, 151.62, 139.75, 134.27, 129.87, 129.09, 127.21, 126.94, 73.02, 52.71, 42.88, 41.36, 37.33, 33.58, 25.55; MS (ESI): calculated for $\text{C}_{19}\text{H}_{21}\text{ClN}_2\text{O}_5$ $[\text{M} - \text{H}]^-$, 391.11; found, 391.13; HPLC purity: 98.4%.

(1-(3-(3-Chlorophenethyl)-2,4,6-trioxotetrahydropyrimidin-1(2*H*)-yl)cyclopentyl)methyl acetate (62): White powder; mp 107-109 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.28 – 7.08 (m, 4H), 4.38 (s, 2H), 4.05 (dd, $J = 8.7, 6.8$ Hz, 2H), 3.57 (s, 2H), 2.87 (dd, $J = 8.8, 6.7$ Hz, 2H), 2.74 – 2.59 (m, 2H), 2.02 (d, $J = 1.4$ Hz, 3H), 1.76 – 1.57 (m, 6H); ^{13}C NMR (126 MHz, CDCl_3) δ

171.53, 166.00, 164.53, 151.87, 140.04, 134.21, 129.84, 129.10, 127.25, 126.84, 72.49, 64.31, 42.83, 41.78, 36.38, 33.67, 22.69, 20.92; MS (ESI): calculated for C₂₀H₂₃ClN₂O₅ [M - H]⁻, 405.12; found, 404.86; HPLC purity: 99.0%.

(1-(3-(3-Chlorophenethyl)-2,4,6-trioxotetrahydropyrimidin-1(2H)-yl)cyclopentyl)methyl isobutyrate (63): White powder; mp 91-93 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.26 – 7.03 (m, 4H), 4.38 (s, 2H), 4.10 – 3.95 (m, 2H), 3.57 (s, 2H), 2.87 (t, *J* = 7.8 Hz, 2H), 2.74 – 2.58 (m, 2H), 2.58 – 2.35 (m, *J* = 6.7 Hz, 1H), 1.83 – 1.49 (m, 6H), 1.15 (d, *J* = 6.9 Hz, 6H); ¹³C NMR (126 MHz, CDCl₃) δ 177.50, 165.87, 164.56, 151.84, 140.02, 134.27, 129.84, 129.13, 127.24, 126.88, 72.59, 64.55, 42.89, 41.73, 36.46, 34.03, 33.71, 22.74, 18.90; MS (ESI): calculated for C₂₂H₂₇ClN₂O₅ [M - H]⁻, 433.15; found, 433.06; HPLC purity: 95.0%.

(S)-benzyl 3-(3-(3-Chlorophenethyl)-2,4,6-trioxotetrahydropyrimidin-1(2H)-yl)pyrrolidine-1-carboxylate (64): Colorless oil; ¹H NMR (500 MHz, CDCl₃) δ 7.51 – 7.02 (m, 9H), 5.43 (m, 1H), 5.24 – 5.06 (m, 2H), 4.10 – 3.99 (m, 2H), 3.85 – 3.49 (m, 6H), 2.87 (m, 2H), 2.42 (m, 1H), 2.13 (m, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 171.20, 164.55, 163.93, 154.59, 154.56, 150.68, 139.58, 139.54, 136.79, 136.71, 134.33, 129.90, 129.06, 128.48, 128.00, 127.90, 127.13, 127.05, 66.94, 66.90, 60.41, 53.45, 51.74, 51.03, 47.08, 46.34, 45.04, 44.85, 42.80, 39.99, 33.57, 28.10, 27.02; MS (ESI): calculated for C₂₄H₂₄ClN₃O₅ [M - H]⁻, 468.13; found, 468.29; HPLC purity: 98.2%.

(S)-1-(3-Chlorophenethyl)-3-(pyrrolidin-3-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (65) : Tautomers; ¹H NMR (500 MHz, DMSO) δ 8.72 (ss, 2H), 7.42 – 7.01 (m, 4H), 5.65 (m, 1H), 3.96 – 3.78 (m, 2H), 3.55 (m, 1H), 3.32 (m, 1H), 3.26 – 3.12 (m, 1H), 3.02 (m, 1H), 2.82 – 2.68 (m, 2H), 2.30 – 2.12 (m, 1H), 2.04-1.89 (m, 1H); ¹³C NMR (126 MHz, DMSO) δ 162.42, 162.33, 162.28, 152.96, 142.10, 139.50, 132.80, 130.12, 128.51, 128.39, 128.31, 127.32, 125.99, 75.86, 75.83, 54.91, 48.58, 48.53, 47.53, 45.81, 40.77, 40.33, 34.26, 33.79, 28.54; MS (ESI): calculated for C₁₆H₁₈ClN₃O₃ [M - H]⁻, 334.10; found, 334.37; HPLC purity: 98.3%

(±)-cis-Isopropyl 3-(3-(3-Chlorophenethyl)-2,4,6-trioxotetrahydropyrimidin-1(2H)-yl)cyclopentane-carboxylate (66): Colorless oil; ¹H NMR (500 MHz, CDCl₃) δ 7.28 – 7.07 (m, 4H), 5.18 (tt, *J* = 9.8, 7.8 Hz, 1H), 5.04 (hept, *J* = 6.2 Hz, 1H), 4.16 – 4.00 (m, 2H), 3.64 (s, 2H), 2.89 – 2.80 (m, 2H), 2.79 – 2.70 (m, 1H), 2.38 (dt, *J* = 12.3, 10.4 Hz, 1H), 2.31 – 2.19 (m, 1H), 2.18 – 2.04 (m, 2H), 1.98 – 1.83 (m, 2H), 1.25 (d, *J* = 6.3 Hz, 6H); ¹³C NMR (126 MHz, CDCl₃) δ 174.11, 164.67, 164.35, 150.69, 139.78, 134.31, 129.88, 129.08, 127.15, 127.14, 126.97, 67.75, 53.44, 43.60, 42.68, 40.06, 33.64, 31.83, 27.93, 27.63, 21.86; HPLC purity: 95.3% .

(±)-cis-3-(3-(3-Chlorophenethyl)-2,4,6-trioxotetrahydropyrimidin-1(2H)-yl)cyclopentanecarboxylic acid (67): ¹H NMR (500 MHz, DMSO) δ 12.13 (s, 1H), 7.42 – 7.11 (m, 4H), 5.07 (tt, *J* = 9.4, 6.9 Hz, 1H), 3.92 (dd, *J* = 8.7, 6.6 Hz, 2H), 3.73 (s, 2H), 2.85 – 2.75 (m, 2H), 2.75 – 2.57 (m, 1H), 2.24 (q, *J* = 11.2 Hz, 1H), 2.09 – 1.88 (m, 3H), 1.86 – 1.70 (m, 2H); ¹³C NMR (126 MHz, DMSO) δ 175.81, 165.88, 165.52, 151.24, 141.10, 132.98, 130.27, 128.49, 127.43, 126.37, 52.16, 42.83, 41.71, 40.57, 32.95, 31.50, 27.71, 27.16 ; HPLC purity: 94.5%.

(±)-cis-3-Fluorophenethyl 3-(3-(3-chlorophenethyl)-2,4,6-trioxotetrahydropyrimidin-1(2H)-yl) cyclopentanecarboxylate (68): Colorless oil; ¹H NMR (500 MHz, CDCl₃) δ 7.33 – 7.07 (m, 5H), 7.03 – 6.86 (m, 3H), 5.17 (tt, *J* = 9.8, 7.9 Hz, 1H), 4.33 (td, *J* = 6.8, 1.3 Hz, 2H), 4.10 – 3.98 (m, 2H), 3.63 (s, 2H), 2.96 (t, *J* = 6.8 Hz, 2H), 2.92 – 2.80 (m, 2H), 2.76 (tt, *J* = 10.1, 7.5 Hz, 1H), 2.37 (dt, *J* = 12.4, 10.1 Hz, 1H), 2.29 – 2.16 (m, 1H), 2.14 – 2.01 (m, 2H), 1.95 – 1.81 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 174.45, 164.65, 164.33, 163.80, 161.85, 150.72, 140.55, 140.49, 139.77, 134.32, 129.96, 129.92, 129.88, 129.09, 127.15, 127.04, 126.99, 124.62, 124.59, 115.99, 115.82, 113.54, 113.37, 64.63, 53.32, 43.44, 42.69, 40.04, 34.83, 33.64, 31.86, 28.02, 27.72; HPLC purity: 94.5%

1-(3-Chlorophenethyl)-3-((1S,2S)-2-hydroxycyclopentyl)pyrimidine-2,4,6(1H,3H,5H)-trione (69): White powder; mp 119-121 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.36 – 7.02 (m, 4H), 4.90 (td, *J* = 9.2, 6.7 Hz, 1H), 4.58 (q, *J* = 6.7 Hz, 1H), 4.10 – 3.97 (m, 2H), 3.65 (dd, *J* = 7.0, 5.2 Hz, 2H), 2.96 – 2.73 (m, 2H), 2.39 – 2.22 (m, 1H), 2.20 – 2.08 (m, 1H), 1.97 – 1.84 (m, 3H), 1.83 – 1.72 (m, 1H), 1.64 – 1.50 (m, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 165.33, 164.59, 151.19, 137.82, 136.26, 128.99, 128.72, 128.59, 126.73, 74.75, 62.31, 42.86, 40.06, 34.16, 33.33, 26.90, 21.67; MS (ESI): calculated for C₁₇H₁₉ClN₂O₄ [M - H]⁻, 349.1; found, 349.23; HPLC purity: 97.1%

1-(3-Chlorophenethyl)-3-((1S,2S)-2-methoxycyclopentyl)pyrimidine-2,4,6(1H,3H,5H)-trione (70): White powder; mp 155-158 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.26 – 7.09 (m, 4H), 5.01 (td, *J* = 8.8, 5.0 Hz, 1H), 4.13 – 4.05 (m, 3H), 3.66 (s, 2H), 3.24 (s, 3H), 2.94 – 2.87 (m, 2H), 2.22 – 2.08 (m, 1H), 1.99 – 1.82 (m, 3H), 1.80 – 1.61 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 164.63, 164.39, 151.01, 139.76, 134.31, 129.87, 129.12, 127.18, 126.98, 84.09, 60.67, 56.78, 42.74, 40.01, 33.65, 33.62, 30.84, 28.02, 22.87, MS (ESI): calculated for C₁₈H₂₁ClN₂O₄ [M - H]⁻, 363.11; found, 363.33; HPLC purity: 95.5%.

(1S,2S)-2-(3-(3-Chlorophenethyl)-2,4,6-trioxotetrahydropyrimidin-1(2H)-yl)cyclopentyl acetate (71): Colorless oil; ¹H NMR (500 MHz, CDCl₃) δ 7.34 – 7.04 (m, 4H), 5.47 – 5.36 (m, 1H), 5.01 (td, *J* = 8.9, 4.9 Hz, 1H), 4.15 – 3.94 (m, 2H), 3.65 (s, 2H), 2.88 (t, *J* = 7.9 Hz, 2H), 2.26 (dddd, *J* = 12.8, 8.3, 7.0, 4.0 Hz, 1H), 2.01 (s, 3H), 2.00 – 1.90 (m, 3H), 1.85 – 1.71 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 171.52, 164.83, 164.36, 151.06, 139.88, 134.27, 129.83, 129.09, 127.16, 126.90, 77.96, 60.81, 42.73, 39.90, 33.65, 31.37, 28.60, 23.26, 21.08; MS (ESI): calculated for C₁₉H₂₁ClN₂O₅ [M - H]⁻, 391.11; found, 391.59; HPLC purity: 95.4% .

(1R,2S)-2-(3-(3-Chlorophenethyl)-2,4,6-trioxotetrahydropyrimidin-1(2H)-yl)cyclopentyl acetate (72): Colorless oil; ¹H NMR (500 MHz, CDCl₃) δ 7.31 – 7.03 (m, 4H), 5.26 – 5.16 (m, 1H), 5.10 (td, *J* = 9.1, 7.1 Hz, 1H), 4.12 – 4.00 (m, 2H), 3.62 (d, *J* = 14.2 Hz, 2H), 2.95 – 2.81 (m, 2H), 2.71 – 2.55 (m, 1H), 2.17 – 2.02 (m, 2H), 2.02 – 1.97 (m, 1H), 1.96 (s, 3H), 1.92 – 1.84 (m, 1H), 1.55 (dtt, *J* = 12.2, 7.8, 1.9 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 170.80, 165.04, 164.29, 151.43, 139.80, 134.31, 129.86, 129.06, 127.12, 126.96, 74.21, 55.61, 42.91, 40.12, 33.69, 30.77, 25.91, 21.37, 21.07; MS (ESI): calculated for C₁₉H₂₁ClN₂O₅ [M - H]⁻, 391.11; found, 391.24; HPLC purity: 94.5%.

(1R,2S)-Ethyl 2-(3-(3-chlorophenethyl)-2,4,6-trioxotetrahydropyrimidin-1(2H)-yl)cyclopentanecarboxylate (73): White powder; mp 102-105 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.29 – 7.10 (m, 4H), 5.42 (dt, *J* = 11.0, 8.6 Hz, 1H), 4.15 – 3.91 (m, 4H), 3.68 – 3.49 (m, 2H), 2.98 (td,

$J = 10.7, 7.1$ Hz, 1H), 2.91 – 2.75 (m, 2H), 2.38 (tdd, $J = 12.1, 10.3, 6.4$ Hz, 1H), 2.22 – 2.04 (m, 1H), 2.04 – 1.88 (m, 3H), 1.55 – 1.39 (m, 1H), 1.19 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 172.37, 165.27, 164.43, 151.59, 139.93, 134.24, 129.85, 129.06, 127.16, 126.89, 60.49, 53.22, 45.32, 42.68, 39.93, 33.65, 29.14, 28.92, 24.43, 14.17; MS (ESI): calculated for $\text{C}_{20}\text{H}_{23}\text{ClN}_2\text{O}_5$ $[\text{M} - \text{H}]^-$, 405.12; found, 405.37; HPLC purity: 99.4% .

(1*S*,2*S*)-2-(3-(3-Chlorophenethyl)-2,4,6-trioxotetrahydropyrimidin-1(2*H*)-yl)cyclopentyl isobutyrate (74): White powder; mp 85-86 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.36 – 7.08 (m, 4H), 5.53 – 5.38 (m, 1H), 4.99 (td, $J = 9.0, 5.0$ Hz, 1H), 4.17 – 3.95 (m, 2H), 3.64 (s, 2H), 2.94 – 2.76 (m, 2H), 2.49 (hept, $J = 7.0$ Hz, 1H), 2.36 – 2.17 (m, 1H), 2.05 – 1.90 (m, 3H), 1.86 – 1.69 (m, 2H), 1.12 (dd, $J = 7.0, 4.5$ Hz, 6H); ^{13}C NMR (126 MHz, CDCl_3) δ 177.70, 164.82, 164.39, 151.10, 139.93, 134.27, 129.82, 129.08, 127.17, 126.89, 60.89, 42.73, 39.90, 33.83, 33.66, 31.28, 28.53, 23.22, 18.93, 18.81; MS (ESI): calculated for $\text{C}_{21}\text{H}_{25}\text{ClN}_2\text{O}_5$ $[\text{M} - \text{H}]^-$, 419.14; found, 419.04; ; HPLC purity: 96.3%.

1-(Pentan-3-yl)-3-(3-(trifluoromethyl)phenethyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (75): White powder; mp 41-43 °C ^1H NMR (500 MHz, CDCl_3) δ 7.40 – 6.87 (m, 4H), 4.60 (p, $J = 7.8$ Hz, 1H), 4.25 – 3.95 (m, 3H), 3.63 (s, 2H), 2.97 – 2.76 (m, 2H), 2.03 – 1.87 (m, 2H), 1.83 – 1.66 (m, 2H), 0.83 (td, $J = 7.5, 1.3$ Hz, 6H); ^{13}C NMR (126 MHz, CDCl_3) δ 165.18, 164.63, 139.76, 134.26, 129.82, 129.12, 127.20, 126.95, 59.00, 42.45, 39.87, 33.58, 24.79, 11.16; MS (ESI): calculated for $\text{C}_{17}\text{H}_{21}\text{ClN}_2\text{O}_3$ $[\text{M} - \text{H}]^-$, 335.12; found, 335.09; HPLC purity: 95.8%.

(*R*)-1-(3-Chlorophenethyl)-3-(1-(naphthalen-1-yl)ethyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (76): White powder; mp 113-115 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.98 – 7.78 (m, 4H), 7.62 – 7.38 (m, 3H), 7.21 – 7.03 (m, 3H), 6.94 (dt, $J = 7.4, 1.4$ Hz, 1H), 6.70 (q, $J = 7.0$ Hz, 1H), 4.07 – 3.90 (m, 2H), 3.55 (d, $J = 2.5$ Hz, 2H), 2.84 – 2.68 (m, 2H), 1.95 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 164.54, 164.14, 150.55, 139.59, 134.20, 133.66, 133.58, 131.39, 129.69, 129.28, 129.01, 128.80, 127.72, 127.03, 126.88, 126.76, 125.42, 124.90, 122.33, 49.48, 42.50, 40.09, 33.43, 16.93; MS (ESI): calculated for $\text{C}_{24}\text{H}_{21}\text{ClN}_2\text{O}_3$ $[\text{M} - \text{H}]^-$, 419.12; found, 419.13; ; HPLC purity: 95.8%.

1-Cyclopentyl-3-(1,2,3,4-tetrahydronaphthalen-1-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (77): White powder; mp 162-164 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.17 – 6.75 (m, 4H), 6.03 (m, 1H), 5.10 (q, $J = 8.8$ Hz, 1H), 3.67 (d, $J = 5.6$ Hz, 2H), 2.96 (m, 1H), 2.76 (m, 1H), 2.32 (m, 1H), 2.10 – 1.78 (m, 9H), 1.53 (h, $J = 8.8, 6.7$ Hz, 2H); ^{13}C NMR (126 MHz, CDCl_3) δ 164.91, 158.19, 137.75, 135.29, 129.27, 126.50, 126.12, 124.29, 54.46, 53.04, 40.80, 29.45, 28.75, 28.56, 27.17, 25.45, 25.42, 22.90; MS (ESI): calculated for $\text{C}_{19}\text{H}_{22}\text{N}_2\text{O}_3$ $[\text{M} - \text{H}]^-$, 325.16; found, 325.33; HPLC purity: 95.7%.

1-Cyclopentyl-3-(2,3-dihydro-1*H*-inden-1-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (78): Colorless oil; ^1H NMR (500 MHz, CDCl_3) δ 7.36 – 6.90 (m, 4H), 6.37 (dd, $J = 9.7, 6.0$ Hz, 1H), 5.08 (p, $J = 8.5$ Hz, 1H), 3.63 (d, $J = 4.4$ Hz, 2H), 3.37 – 3.23 (m, 1H), 3.07 – 2.86 (m, 1H), 2.60 – 2.42 (m, 1H), 2.33 – 2.22 (m, 1H), 2.02 – 1.75 (m, 6H), 1.54 (m, 2H); ^{13}C NMR (126 MHz, CDCl_3) δ 164.90, 164.79, 150.86, 143.86, 140.63, 127.85, 126.39, 124.90, 122.55, 58.36, 54.48, 40.80, 31.25, 28.81, 28.68, 28.59, 25.44; MS (ESI): calculated for $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}_3$ $[\text{M} - \text{H}]^-$, 311.14; found, 311.49; HPLC purity: 96.2%.

1-Cyclopentyl-3-(2,3-dihydro-1H-inden-2-yl)pyrimidine-2,4,6(1H,3H,5H)-trione (79):

White powder; mp 130-131 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.17 (p, *J* = 4.7 Hz, 4H), 5.76 – 5.57 (m, 1H), 5.14 (p, *J* = 8.6 Hz, 1H), 3.66 (s, 2H), 3.48 (dd, *J* = 15.3, 8.5 Hz, 2H), 3.15 (dd, *J* = 15.2, 9.5 Hz, 2H), 2.08 – 1.95 (m, 2H), 1.95 – 1.75 (m, 4H), 1.56 (q, *J* = 8.5, 3.2 Hz, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 165.00, 164.83, 150.89, 140.74, 126.59, 124.42, 54.40, 52.23, 40.68, 35.77, 28.65, 25.46; MS (ESI): calculated for C₁₆H₁₇ClN₂O₃ [M - H]⁻, 319.08; found, 319.24; HPLC purity: 99.8%.

(R)-1-Cyclopentyl-3-(1-(naphthalen-1-yl)ethyl)pyrimidine-2,4,6(1H,3H,5H)-trione (80):

Colorless oil; ¹H NMR (500 MHz, CDCl₃) δ 8.03 – 7.75 (m, 5H), 7.61 – 7.41 (m, 3H), 6.69 (q, *J* = 7.0 Hz, 1H), 5.12 – 4.98 (m, 1H), 3.54 (s, 2H), 1.98 (d, *J* = 7.0 Hz, 3H), 1.96 – 1.71 (m, 6H), 1.57 – 1.49 (m, 2H); ¹H NMR (500 MHz, CDCl₃) δ 8.03 – 7.75 (m, 5H), 7.61 – 7.41 (m, 3H), 6.69 (q, *J* = 7.0 Hz, 1H), 5.12 – 4.98 (m, 1H), 3.54 (s, 2H), 1.98 (d, *J* = 7.0 Hz, 3H), 1.96 – 1.71 (m, 6H), 1.57 – 1.49 (m, 2H); MS (ESI): calculated for C₂₁H₂₂N₂O₃ [M - H]⁻, 349.16; found, 349.18; HPLC purity: 99.7%.

1-Cyclopentyl-3-(3-(trifluoromethyl)phenyl)pyrimidine-2,4,6(1H,3H,5H)-trione (81):

White powder; mp 154-157 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.72 (d, *J* = 8.0 Hz, 1H), 7.64 (t, *J* = 8.0 Hz, 1H), 7.50 (s, 1H), 7.41 (d, *J* = 8.0, 1H), 5.21 (tt, *J* = 11.6, 8.1 Hz, 1H), 3.87 (s, 3H), 2.16 – 1.96 (m, 1H), 1.96 – 1.85 (m, 3H), 1.71 – 1.47 (m, 4H); ¹³C NMR (126 MHz, CDCl₃) δ 164.50, 164.34, 150.77, 134.63, 132.15, 132.05 (q, *J* = 33 Hz), 130.08, 126.28 (q, *J* = 4.2 Hz), 125.83 (q, *J* = 4.2 Hz), 123.42 (q, *J* = 272 Hz), 54.73, 40.48, 28.81, 25.58; MS (ESI): calculated for C₁₆H₁₅F₃N₂O₃ [M - H]⁻, 339.1; found, 339.12; HPLC purity: 92%.

1-(3-Chlorobenzyl)-3-cyclopentylpyrimidine-2,4,6(1H,3H,5H)-trione (82):

White powder; mp 84-86 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.45 – 7.04 (m, 4H), 5.13 (tt, *J* = 9.4, 7.7 Hz, 1H), 4.98 (s, 2H), 3.66 (s, 2H), 2.01 – 1.86 (m, 4H), 1.86 – 1.74 (m, 2H), 1.61 – 1.50 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 164.69, 151.11, 138.03, 134.36, 129.87, 129.17, 128.24, 127.37, 54.54, 44.34, 40.19, 28.70, 25.52; MS (ESI): calculated for C₁₆H₁₇ClN₂O₃ [M - H]⁻, 319.08; found, 319.24; HPLC purity: 99.8%.

1-(4-Chlorobenzyl)-3-cyclopentylpyrimidine-2,4,6(1H,3H,5H)-trione (83):

White powder; mp 96-98 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.46 – 7.35 (m, 2H), 7.33 – 7.23 (m, 2H), 5.16 – 5.09 (m, 1H), 4.98 (s, 2H), 3.65 (s, 2H), 2.01 – 1.87 (m, 4H), 1.87 – 1.76 (m, 2H), 1.62 – 1.49 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 164.68, 164.67, 151.10, 134.61, 133.95, 130.77, 128.75, 54.49, 44.21, 40.19, 28.71, 25.53; MS (ESI): calculated for C₁₆H₁₇ClN₂O₃ [M - H]⁻, 319.08; found, 319.26; HPLC purity: 99.9%.

1-Cyclopentyl-3-(3-phenylpropyl)pyrimidine-2,4,6(1H,3H,5H)-trione (84):

Colorless oil; ¹H NMR (500 MHz, CDCl₃) δ 7.33 – 7.05 (m, 5H), 5.20 – 5.05 (m, 1H), 4.01 – 3.85 (m, 2H), 3.43 (s, 2H), 2.68 (t, *J* = 7.6 Hz, 2H), 2.08 – 1.88 (m, 6H), 1.87 – 1.74 (m, 2H), 1.63 – 1.49 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 164.92, 164.77, 151.07, 141.13, 128.45, 128.17, 126.04, 54.19, 41.83, 40.02, 33.13, 28.70, 28.54, 25.59; MS (ESI): calculated for C₁₈H₂₂N₂O₃ [M - H]⁻, 313.16; found, 313.44; ; HPLC purity: 94.5%.

1-Cyclopentyl-3-(4-isopropylphenethyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (88): White powder; mp 144-145 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.23 – 7.11 (m, 4H), 5.22 – 5.05 (m, 1H), 4.18 – 4.04 (m, 2H), 3.78 (s, 1H), 3.64 (s, 2H), 2.97 – 2.82 (m, 3H), 2.03 – 1.90 (m, 4H), 1.90 – 1.80 (m, 2H), 1.65 – 1.35 (m, 2H), 1.26 (d, *J* = 6.9 Hz, 6H); ¹³C NMR (126 MHz, CDCl₃) δ 164.93, 164.52, 150.89, 147.33, 135.15, 128.94, 126.61, 54.27, 43.07, 40.14, 33.76, 33.61, 28.69, 25.53, 24.05; MS (ESI): calculated for C₂₀H₂₆N₂O₃ [M - H]⁻, 341.19; found, 341.22.

1-Cyclopentyl-3-(2,2-diphenylethyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (89): White powder; mp 93-95 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.32 – 7.13 (m, 10H), 5.13 – 4.92 (m, 1H), 4.58 (dd, *J* = 9.3, 7.4 Hz, 1H), 4.53 – 4.49 (m, 2H), 3.37 (s, 2H), 1.93 – 1.85 (m, 2H), 1.85 – 1.77 (m, 2H), 1.77 – 1.68 (m, 2H), 1.58 – 1.47 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 164.81, 164.65, 150.95, 140.97, 128.55, 128.39, 127.02, 54.14, 48.53, 45.40, 39.98, 28.67, 25.58; MS (ESI): calculated for C₂₃H₂₄N₂O₃ [M - H]⁻, 375.17; found, 375.24; ; HPLC purity: 99.0 %.

1-Cyclopentyl-3-(2,2-diphenylethyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (90): Colorless oil; ¹H NMR (500 MHz, CDCl₃) δ 7.20 (m, 10H), 5.13 – 4.96 (m, 1H), 4.03 (t, *J* = 7.6 Hz, 1H), 3.97 (t, *J* = 7.0 Hz, 2H), 3.22 (s, 2H), 2.44 (q, *J* = 7.3 Hz, 2H), 1.94 (pd, *J* = 7.1, 3.6 Hz, 4H), 1.87 – 1.74 (m, 2H), 1.61 – 1.50 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 164.85, 151.04, 144.32, 128.65, 127.50, 126.44, 54.21, 49.75, 41.37, 39.80, 32.66, 28.68, 25.58; MS (ESI): calculated for C₂₄H₂₆N₂O₃ [M - H]⁻, 389.19; found, 389.24; HPLC purity: 95.8%.

1-(2-([1,1'-Biphenyl]-4-yl)ethyl)-3-cyclopentylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (91): White powder; mp 152-154 °C ¹H NMR (500 MHz, CDCl₃) δ 7.60 – 7.29 (m, 9H), 5.21 – 5.03 (m, 1H), 4.27 – 4.01 (m, 2H), 3.63 (s, 2H), 3.05 – 2.81 (m, 2H), 1.99 – 1.87 (m, 4H), 1.87 – 1.77 (m, 2H), 1.63 – 1.51 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 164.86, 164.51, 150.90, 140.79, 139.67, 136.88, 129.40, 128.75, 127.27, 127.21, 127.01, 54.27, 42.94, 40.13, 33.66, 28.68, 25.53; MS (ESI): calculated for C₂₃H₂₄N₂O₃ [M - H]⁻, 375.17; found, 375.15; HPLC purity: 99.6%.

1-(4-(Benzyloxy)phenethyl)-3-cyclopentylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (92): White powder; mp 182-184 °C ¹H NMR (500 MHz, CDCl₃) δ 7.46 – 7.29 (m, 5H), 7.20 – 7.12 (m, 2H), 6.95 – 6.88 (m, 2H), 5.13 (m, 1H), 5.04 (s, 2H), 4.14 – 3.98 (m, 2H), 3.60 (s, 2H), 2.94 – 2.77 (m, 2H), 2.03 – 1.88 (m, 4H), 1.88 – 1.74 (m, 2H), 1.59 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 164.91, 164.51, 157.63, 150.93, 137.01, 130.16, 130.00, 128.61, 127.99, 127.50, 114.90, 70.02, 54.29, 43.13, 40.14, 33.15, 28.71, 25.56; MS (ESI): calculated for C₂₄H₂₆N₂O₄ [M - H]⁻, 405.18; found, 405.16.

(S)-Methyl 2-(3-cyclopentyl-2,4,6-trioxotetrahydropyrimidin-1(2*H*)-yl)-3-phenylpropanoate (93) and (R)-methyl 2-(3-cyclopentyl-2,4,6-trioxotetrahydropyrimidin-1(2*H*)-yl)-3-phenylpropanoate (94): White powder; mp 124-127 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.31 – 7.00 (m, 5H), 5.62 (dd, *J* = 10.7, 5.8 Hz, 1H), 5.01 (p, *J* = 8.5 Hz, 1H), 3.74 (s, 3H), 3.56 – 3.42 (m, 2H), 3.40 – 3.19 (m, 2H), 1.97 – 1.80 (m, 3H), 1.80 – 1.61 (m, 3H), 1.59 – 1.42 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 169.28, 164.52, 164.23, 150.44, 136.57, 129.10, 128.52, 127.00, 54.99, 54.17, 52.68, 39.71, 34.56, 28.63, 28.45, 25.46, 25.44; MS (ESI): calculated for C₁₉H₂₂N₂O₅ [M - H]⁻, 357.14; found, 357.28; HPLC purity: 99.0% (93), 94.6% (94).

Methyl 3-(4-chlorophenyl)-2-(3-cyclopentyl-2,4,6-trioxotetrahydropyrimidin-1(2H)-yl)propanoate (95): Colorless oil; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.23 – 7.18 (m, 2H), 7.07 – 7.03 (m, 2H), 5.59 (dd, $J = 10.4, 5.9$ Hz, 1H), 5.03 (p, $J = 8.8$ Hz, 1H), 3.75 (s, 2H), 3.58 – 3.39 (m, 3H), 3.34 – 3.25 (m, 1H), 1.96 – 1.83 (m, 3H), 1.80 – 1.65 (m, 3H), 1.62 – 1.45 (m, 2H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 169.06, 164.38, 164.24, 150.44, 135.07, 132.89, 130.47, 128.69, 54.81, 54.30, 52.80, 39.80, 34.09, 28.66, 28.46, 25.45; MS (ESI): calculated for $\text{C}_{19}\text{H}_{21}\text{ClN}_2\text{O}_5$ $[\text{M} - \text{H}]^-$, 391.11; found, 391.33; HPLC purity: 94.5%.

1-(2-(3-Chlorophenyl)propyl)-3-cyclopentylpyrimidine-2,4,6(1H,3H,5H)-trione (97): Colorless oil; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.34 – 7.00 (m, 4H), 5.18 – 5.02 (m, 1H), 4.09 (dd, $J = 13.2, 8.4$ Hz, 1H), 3.97 (dd, $J = 13.2, 7.6$ Hz, 1H), 3.58 (dd, 2H), 3.27 (h, $J = 7.3$ Hz, 1H), 2.05 – 1.88 (m, 3H), 1.88 – 1.76 (m, 3H), 1.65 – 1.55 (m, 2H), 1.30 (d, $J = 7.0$ Hz, 3H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 164.76, 164.63, 150.97, 145.07, 134.22, 129.72, 127.77, 127.08, 125.68, 54.22, 47.58, 40.00, 37.81, 28.75, 28.62, 25.58, 25.55, 18.46; MS (ESI): calculated for $\text{C}_{18}\text{H}_{21}\text{ClN}_2\text{O}_3$ $[\text{M} - \text{H}]^-$, 347.12; found, 347.22; HPLC purity: 95.3%.

1-(2-(4-Chlorophenyl)propyl)-3-((±)-endo-norbornyl)pyrimidine-2,4,6-(1H,3H,5H)-trione (100): Colorless oil; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.26 – 7.22 (m, 2H), 7.17 – 7.12 (m, 2H), 4.60 – 4.46 (m, 1H), 4.07 (dt, $J = 13.2, 9.1$ Hz, 1H), 3.92 (m, 1H), 3.55 (p, $J = 21.2$, 2H), 3.32 – 3.17 (m, 1H), 2.50 (d, $J = 90.8$ Hz, 1H), 2.36 – 2.27 (m, 1H), 2.15 – 2.05 (m, 1H), 1.75 – 1.57 (m, 2H), 1.49 (m, 1H), 1.46 – 1.32 (m, 2H), 1.29 – 1.10 (m, 5H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 166.95, 165.91, 165.84, 164.71, 164.68, 152.32, 152.27, 141.49, 141.40, 132.56, 128.91, 128.89, 128.55, 128.52, 59.54, 52.58, 47.94, 47.82, 42.00, 41.91, 40.95, 40.79, 37.71, 37.65, 37.57, 37.50, 37.47, 37.44, 29.67, 29.13, 28.71, 23.74, 23.60, 18.64, 18.57; MS (ESI): calculated for $\text{C}_{20}\text{H}_{23}\text{ClN}_2\text{O}_3$ $[\text{M} - \text{H}]^-$, 373.13; found, 373.53; HPLC purity: 99.6%.

1-(1-(4-Chlorophenyl)propan-2-yl)-3-((±)-endo-norbornyl)pyrimidine-2,4,6-(1H,3H,5H)-trione (101): Colorless oil; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.24 – 7.19 (m, 2H), 7.10 – 7.05 (m, 2H), 5.26 – 5.03 (m, 1H), 4.62 – 4.44 (m, 1H), 3.62 – 3.34 (m, 2H), 3.32 – 3.19 (m, 1H), 2.98 (dd, $J = 13.7, 6.6$ Hz, 1H), 2.67 – 2.40 (m, 1H), 2.32 (q, $J = 4.8$ Hz, 1H), 2.20 – 2.04 (m, 1H), 1.81 – 1.56 (m, 2H), 1.55 – 1.45 (m, 4H), 1.45 – 1.31 (m, 2H), 1.31 – 1.15 (m, 2H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 165.82, 165.79, 165.06, 165.04, 152.28, 136.85, 136.79, 132.44, 130.26, 130.24, 128.60, 59.46, 42.03, 41.88, 38.98, 38.69, 37.69, 37.62, 37.48, 28.78, 28.71, 23.69, 23.65, 17.93, 17.64; MS (ESI): calculated for $\text{C}_{20}\text{H}_{23}\text{ClN}_2\text{O}_3$ $[\text{M} - \text{H}]^-$, 373.13; found, 373.28; HPLC purity: 98.8%.

(R)-1-(2,2-Dimethylcyclopentyl)-3-(3-(trifluoromethyl)phenethyl)pyrimidine-2,4,6(1H,3H,5H)-trione (109): Colorless oil; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.60 – 7.34 (m, 4H), 4.83 (dd, $J = 9.6, 6.1$ Hz, 1H), 4.18 – 4.05 (m, 2H), 3.63 (d, $J = 1.9$ Hz, 2H), 2.98 (t, $J = 7.7$ Hz, 2H), 2.35 – 2.20 (m, 1H), 2.07 – 1.83 (m, 3H), 1.79 – 1.61 (m, 1H), 1.52 – 1.39 (m, 1H), 1.07 (s, 3H), 0.84 (s, 3H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 165.22, 164.49, 151.72, 138.71, 132.49, 130.81 (q, $J = 32.3$ Hz), 129.04, 125.70 (q, $J = 3.9$ Hz), 124.06 (q, $J = 272.2$ Hz), 123.65 (q, $J = 3.9$ Hz), 63.91, 42.99, 42.62, 40.95, 40.15, 33.72, 30.03, 28.09, 23.83, 23.41; MS (ESI): calculated for $\text{C}_{20}\text{H}_{23}\text{F}_3\text{N}_2\text{O}_3$ $[\text{M} - \text{H}]^-$, 395.16; found, 395.36; HPLC purity: 94.7%.