SUPPORTING INFORMATION

Dihydro-alkylthio-benzyl-oxopyrimidines as inhibitors of Reverse Transcriptase: synthesis and rationalization of the biological data on both wild type enzyme and relevant clinical mutants

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Details of synthesis.

Elemental analysis data.

1-(2-Bromoethoxymethyl)-4-methoxybenzene.

A mixture of 2-bromoethanol (12.8 mmol) and K_2CO_3 (12.8 mmol) in dry DMF (2 mL) was stirred at room temperature for 10'. 4-methoxybenzyl chloride (12.8 mmol) was added and the reaction mixture was stirred at 60°C for 2h and then diluted with water (2 mL) and extracted with ethyl acetate (3 × 10 mL). Finally, the organic phases were dried over anhydrous Na_2SO_4 and evaporated to dryness. The residue was purified by flash cromatografy to give the product as colourless oil.

Yield 54%. ^{1}H NMR($CDCl_3$): δ 3.45 (t, 2H, *J* = 5.8 Hz), 3.73 (t, 2H, *J* = 5.8 Hz), 3.85 (s, 3H), 4.55 (s, 2H), 6.85 (d, 2H, *J* = 8.2 Hz), 7.25 (d, 2H, *J* = 8.2 Hz). Anal. ($C_{10}H_{13}BrO_2$) C,H

6-(2,6-Dichlorobenzyl)-2-(4-methoxybenzylthio)-5-ethylpirimidin-4(3*H*)-one (2). Yield 75%. Mp 233-234 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1514, 1657, 2975. ^{1}H NMR ($CDCl_3$): δ 1.17 (t, 3H, *J* = 7.6 Hz), 2.65 (q, 2H, *J* = 7.6 Hz), 3.96 (s, 2H), 4.28 (s, 2H), 6.69 (d, 2H, *J* = 8.7 Hz), 6.86 (d, 2H, *J* = 8.7 Hz), 7.05 (t, 1H, *J* = 7.9 Hz), 7.26 (d, 1H, *J* = 7.9 Hz). MS (ESI) *m/z*: 435 [M + H]$^+$, 457 [M + Na]$^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 6.23 min. Anal. ($C_{21}H_{20}Cl_2N_2O_2S$) C, H, S; N.

6-(2,6-Dichlorobenzyl)-2-(4-cyanobenzylthio)-5-ethylpyrimidin-4(3*H*)-one (3). Yield 83%. Mp 231-232 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1669, 2362, 2975. ^{1}H NMR ($CDCl_3$): δ 1.18 (t, 3H, *J* = 7.7 Hz), 2.67 (q, 2H, *J* = 7.7 Hz), 4.06 (s, 2H), 4.26 (s, 2H), 7.20-7.40 (m, 7H). MS (ESI) *m/z*: 430 [M + H]$^+$, 452 [M + Na]$^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 4.35 min. Anal. ($C_{21}H_{17}Cl_2N_3OS$) C, H, S; N.

6-(2,6-Dichlorobenzyl)-2-(4-nitrobenzylthio)-5-ethylpyrimidin-4(3*H*)-one (4). Yield 70%. Mp 216-218 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1242, 1663, 2976. ^{1}H NMR ($CDCl_3$): δ 1.17 (t, 3H, *J* = 7.4 Hz), 2.60 (q, 2H, *J* = 7.4 Hz), 4.16 (s, 2H), 4.32 (s, 2H), 7.04-7.29 (m, 5H), 7.97-8.01 (m, 2H). MS (ESI) *m/z*: 450 [M + H]$^+$, 472 [M + Na]$^+$. HPLC (C_8 column; CH_3OH/H_2O, 75/25) t_R 3.69 min. Anal. ($C_{20}H_{17}Cl_2N_3O_3S$) C, H, S; N.

6-(1-(2,6-Dichlorophenyl)-ethyl)-2-(4-nitrobenzylthio)-5-methylpirimidin-4(3*H*)-one (6). Yield 50%. Mp 198-200 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1367, 1613, 2987. ^{1}H NMR (DMSO-d_6): δ 1.43 (s, 3H), 1.48 (d, 3H, *J* = 7.0 Hz), 4.49 (d, 1H, *J* = 14.8 Hz), 4.64 (d, 1H, *J* = 14.8 Hz), 4.75 (q, 1H, *J* =

7.0 Hz), 7.18-7.23 (m, 1H), 7.26-7.41 (m, 2H), 7.64 (d, 2H, J = 8.7 Hz), 8.13 (d, 2H, J = 8.7 Hz), 12.66 (br s, 1H). MS (ESI) m/z: 450 $[M + H]^+$, 472 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 5.93 min. Anal. ($C_{20}H_{17}Cl_2N_3O_3S$) C, H, S; N.

6-(1-(2,6-Dichlorophenyl)-ethyl)-2-(4-cyanobenzylthio)-5-methylpirimidin-4(3*H*)-one (7). Yield 56%. Mp 253-255 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1536, 1643, 2232, 3017. ^1H NMR ($CDCl_3$): δ 1.57 (d, 3H, J = 7.3 Hz), 1.62 (s, 3H), 4.39 (d, 1H, J = 14.9 Hz), 4.63 (d, 1H, J = 14.9 Hz), 4.88 (q, 1H, J = 7.3 Hz), 7.07-7.59 (m, 7H). MS (ESI) m/z: 430 $[M + H]^+$, 452 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 4.38 min. Anal. ($C_{21}H_{17}Cl_2N_3OS$) C, H, S; N.

6-(2,6-Dichlorobenzyl)-2-(2-(4-methoxyphenyl)ethylthio]-5-ethylpyrimidin-4(3H)-one (8). Yield 40%. Mp 204-206. °C. ^1H NMR (DMSO-d_6): δ 1.06 (t, 3H, J = 7.1 Hz), 2.38-2.56 (m, 4H), 2.86 (t, 2H, J = 7.0 Hz), 3.69 (s, 3H), 4.19 (s, 2H), 6.75-6.92 (m, 4H), 7.19-7.35 (m, 3H). MS (ESI) m/z: 449 $[M+H]^+$, 471 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 4.56 min. Anal. ($C_{22}H_{22}Cl_2N_2O_2S$) C, H, S; N.

6-(1-(2,6-Dichlorophenyl)-ethyl)-2-(2-(4-methoxyphenyl)ethylthio]-5-methylpyrimidin-4(3H)-one (9). Yield 64%. Mp 167-169 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1523, 1666, 2975. ^1H NMR ($CDCl_3$): 1.25 (s, 3H), 1.68 (d, 3H, J = 7.0 Hz), 2.94-3.01 (m, 2H), 3.23-3.56 (m, 2H), 3.77 (s, 3H), 4.91 (q, 1H, J = 7.0 Hz), 6.80-7.28 (m, 7H). MS (ESI) m/z: 449 $[M+H]^+$, 471 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 7.98 min. Anal. ($C_{22}H_{22}Cl_2N_2O_2S$) C, H, S; N.

6-(2,6-Difluorobenzyl)-2-(4-ethoxybenzylthio)-5-methylpyrimidin-4(3*H*)-one (11). Yield 44%. Mp 175-177 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1471, 1539, 1661, 3019. ^1H NMR (DMSO-d_6): δ 1.25 (t, 3H, J = 6.9 Hz), 2.00 (s, 3H), 3.88-4.05 (m, 6H), 6.64-6.90 (m, 4H), 7.01-7.36 (m, 3H), 12.48 (br s, 1H). MS (ESI) m/z: 403 $[M+H]^+$, 425 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 60/40) t_R 4.01 min. Anal. ($C_{21}H_{20}F_2N_2O_2S$) C, H, S; N.

6-(2,6-Difluorobenzyl)-2-(3,4-dimethoxybenzylthio)-5-methylpyrimidin-4(3*H*)-one (12). Yield 35%. Mp 166-169 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1471, 1515, 1661, 3014.. ^1H NMR (DMSO-d_6): δ 2.00 (s, 3H), 3.69 (s, 3H), 3.71 (s, 3H), 3.92 (s, 2H), 4.00 (s, 2H), 6.49-7.49 (m, 6H), 12.48 (br s, 1H).

MS (ESI) *m/z*: 419 $[M+H]^+$, 441 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 70/30) t_R 5.84 min. Anal. ($C_{21}H_{20}F_2N_2O_3S$) C, H, S; N.

6-(2,6-Difluorobenzyl)-2-(1,3-benzodioxol-5-ylmethylthio)-5-methylpyrimidin-4(3H)-one (13). Yield 56%. Mp 205-208 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1539, 1663, 2928.. ^1H NMR (DMSO-d_6): δ 2.01 (s, 3H), 3.92 (s, 2H), 3.98 (s, 2H), 5.92 (s, 2H), 6.41-6.67 (m, 3H), 7.00-7.35 (m, 3H), 12.51 (bs, 1H). MS (ESI) *m/z*: 403 $[M+H]^+$, 425 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 70/30) t_R 4.86 min. Anal. ($C_{20}H_{16}F_2N_2O_3S$) C, H, S; N.

Acetic acid 4-(4-(2,6-Difluorobenzyl)-5-methyl-6-oxo-1,6-dihydro-pyrimidin-2-ylmethylthio)-phenyl ester (14). Yield 73%. Mp 229-233 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1541, 1664, 1760, 2928. ^1H NMR (DMSO-d_6): δ 2.00 (s, 3H), 2.22 (s, 3H), 3.92 (s, 2H), 4.06 (s, 2H), 6.86-7.34 (m, 7H). MS (ESI) *m/z*: 417 $[M+H]^+$, 439 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 70/30) t_R 6.12 min. Anal. ($C_{21}H_{18}F_2N_2O_3S$) C, H, S; N.

4-(4-(2,6-Difluorobenzyl)-5-methyl-6-oxo-1,6-dihydro-pyrimidin-2-ylmethylthio)-benzoic acid methyl ester (15). Yield 68%. Mp 212-216 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1459, 1629, 1722, 2921. ^1H NMR (DMSO-d_6): δ 2.01 (s, 3H), 3.81 (s, 3H), 3.93 (s, 2H), 4.14 (s, 2H), 7.01-7.75 (m, 7H). MS (ESI) *m/z*: 417 $[M+H]^+$, 439 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 75/25) t_R 4.89 min. Anal. ($C_{21}H_{18}F_2N_2O_3S$) C, H, S; N.

6-(2,6-Difluorobenzyl)-2-(4-methoxybenzylthio)-5-ethylpirimidin-4(3*H*)-one (16) Yield 98%. Mp 185-186 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1535, 1662, 2964. ^1H NMR ($CDCl_3$): δ 1.14 (t, 3H, *J* = 7.5 Hz), 2.63 (q, 2H, *J* = 7.5 Hz), 3.76 (s, 3H), 3.98 (s, 2H), 4.08 (s, 2H), 6.69-7.20 (m, 7H). MS (ESI) *m/z*: 403 $[M + H]^+$, 425 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 4.20 min. Anal. ($C_{21}H_{20}F_2N_2O_2S$) C, H, S; N.

6-(2,6-Difluorobenzyl)-2-(4-cyanobenzylthio)-5-ethylpyrimidin-4(3*H*)-one (17). Yield 75%. Mp 220-222 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1662, 2984. ^1H NMR ($CDCl_3$): δ 1.14 (t, 3H, *J* = 7.3 Hz), 2.63 (q, 2H, *J* = 7.3 Hz), 3.96 (s, 2H), 4.16 (s, 2H), 6.77-7.45 (m, 7H). MS (ESI) *m/z*: 398 $[M + H]^+$, 420 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 3.36 min. Anal. ($C_{21}H_{17}F_2N_3OS$) C, H, S; N.

6-(2,6-Difluorobenzyl)-2-(4-nitrobenzylthio)-5-ethylpyrimidin-4(3*H*)-one (18). Yield 86%. Mp 201-204 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1534, 1665, 2964. ^1H NMR ($CDCl_3$): δ 1.14 (t, 3H, *J* = 7.3 Hz), 2.64 (q, 2H, *J* = 7.3 Hz), 3.97 (s, 2H), 4.20 (s, 2H), 6.78-8.02 (m, 7H). MS (ESI) *m/z*: 418 $[M + H]^+$, 440 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 4.13 min. Anal. ($C_{20}H_{17}F_2N_3O_3S$) C, H, S; N.

6-(1-(2,6-Difluorophenyl)-ethyl)-2-(4-methoxybenzylthio)-5-methylpirimidin-4(3*H*)-one (19) Yield 70%. Mp 161-163 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1513, 1644, 2962. ^1H NMR (DMSO-d_6): δ 1.59 (d, 3H, *J* = 7.0 Hz), 1.84 (s, 3H), 3.68 (s, 3H), 4.25 (s, 2H), 4.58 (q, 1H, *J* = 7.0 Hz), 6.74-7.13 (m, 7H). MS (ESI) *m/z*: 403 $[M + H]^+$, 425 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 4.93 min. Anal. ($C_{21}H_{20}F_2N_2O_2S$) C, H, S; N.

6-(1-(2,6-Difluorophenyl)-ethyl)-2-(4-cyanobenzylthio)-5-methylpirimidin-4(3*H*)-one (20) Yield 58%. Mp 224-227 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1519, 1664, 2934. ^1H NMR (DMSO-d_6): δ 1.53 (d, 3H, *J* = 7.0 Hz), 1.83 (s, 3H), 4.37-4.55 (m, 3H), 6.96 (t, 1H, *J* = 8.3 Hz), 7.22-7.37 (m, 4H), 7.66 (d, 2H, *J* = 8.3 Hz).. MS (ESI) *m/z*: 398 $[M + H]^+$, 420 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 3.43 min. Anal. ($C_{21}H_{17}F_2N_3OS$) C, H, S; N.

6-(1-(2,6-Difluorophenyl)-ethyl)-2-(4-nitrobenzylthio)-5-methylpirimidin-4(3*H*)-one (21) Yield 67%. Mp 221-223 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1518, 1644, 2942. ^1H NMR (DMSO-d_6): δ 1.53 (d, 3H, *J* = 7.0 Hz), 1.83 (s, 3H), 4.37-4.55 (m, 3H), 6.96-7.46 (m, 5H), 8.04-8.08 (m, 2H), 12.62 (br s, 1H). MS (ESI) *m/z*: 418 $[M + H]^+$, 440 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 70/30) t_R 11.47 min. Anal. ($C_{20}H_{17}F_2N_3O_3S$) C, H, S; N.

6-(1-(2,6-Difluorophenyl)-propyl)-2-(4-methoxybenzylthio)-5-methylpirimidin-4(3*H*)-one (22). Yield 75%. IR ($CHCl_3$) (ν, cm^{-1}): 1540, 1666, 2928. ^1H NMR ($CDCl_3$): δ 0.79-0.97 (m, 3H), 1.98-2.24 (m, 5H), 2.87-2.94 (m, 1H), 3.79 (s, 3H), 4.61 (s, 2H), 6.76-7.30 (m, 7H). MS (ESI) *m/z*: 417 $[M + H]^+$, 439 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 5.53 min. Anal. ($C_{22}H_{22}F_2N_2O_2S$) C, H, S; N.

6-(2,6-Difluorobenzyl)-2-(2-(4-methossyphenyl)ethylthio)-5-methylpirimidin-4(3H)-one (23).

Yield 40%. Mp 168-170 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1542, 1648, 3008. ^1H NMR (CD_3OD): 2.09 (s, 3H), 2.63 (t, 2H, *J* = 7.0 Hz), 3.07 (t, 2H, *J* = 7.0 Hz), 3.46 (s, 3H), 3.98 (s, 2H), 6.76-7.49 (m, 7H). MS (ESI) *m/z*: 403 $[M+H]^+$, 425 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 3.94 min. Anal. ($C_{21}H_{20}F_2N_2O_2S$) C, H, S; N.

6-(4-Cyanobenzyl)-2-(4-methoxybenzylthio)-5-methylpirimidin-4(3*H*)-one (25).

Yield 45%. Mp 180-182 °C. ^1H NMR [$(CD_3)_2SO$)]: δ 1.93 (s, 3H), 3.68 (s, 3H), 3.97 (s, 2H), 4.12 (s, 2H), 6.72 (d, 2H, *J* = 8.6 Hz), 7.03 (d, 2H, *J* = 8.5 Hz), 7.39 (d, 2H, *J* =8.1 Hz), 7.71 (d, 2H, *J* = 8.0 Hz), 12.50 (bs, 1H). MS (ESI) *m/z*: 377 [M+1], 400 [M+Na]. Anal ($C_{21}H_{19}N_3O_2S$) C, H, S, N.

6-(4-Cyanobenzyl)-2-(propylthio)-5-methylpirimidin-4(3*H*)-one (26).

Yield 60%. Mp 179-180 °C. ^1H NMR [$(CD_3)_2SO$)]: δ 0.76 (t, 3H, J = 7.0 Hz), 1.09-1.27 (m, 2H), 1.30-1.44 (m, 2H), 1.92 (s, 3H), 2.89 (t, 2H, *J* = 7.0 Hz), 3.92 (s, 2H), 7.40 (d, 2H, *J* =8.0), 7.71 (d, 2H, *J* = 8.0 Hz), 12.47 (bs, 1H). MS (ESI) *m/z*: 314 [M+1], 336 [M+Na]. Anal ($C_{17}H_{19}N_3OS$) C, H, S, N.

6-(4-Cyanobenzyl)-2-(4-nitrobenzylthio)-5-methylpirimidin-4(3*H*)-one (27).

Yield 80%. Mp 225-226 °C. ^1H NMR [$(CD_3)_2SO$)]: δ 1.91 (s, 3H), 3.95 (s, 2H), 4.33 (s, 2H), 7.35 (d, 2H, *J* = 8.0 Hz), 7.42 (d, 2H, *J* =8.7 Hz), 7.67 (d, 2H, *J* = 8.0 Hz), 8.00 (d, 2H, *J* =8.5 Hz), 12.62 (bs, 1H). MS (ESI) *m/z*: 393 [M+1], 415 [M+Na]. Anal ($C_{20}H_{16}N_4O_3S$) C, H, S, N.

6-(4-Cyanobenzyl)-2-(4-cyanobenzylthio)-5-methylpirimidin-4(3*H*)-one (28).

Yield 74%. Mp 224-225 °C. ^1H NMR [$(CD_3)_2SO$)]: δ 1.91 (s, 3H), 3.94 (s, 2H), 3.94 (s, 2H), 4.30 (s, 2H), 7.31-7.37 (m, 4H), 7.60-7.71 (m, 4H), 12.58 (bs, 1H). MS (ESI) *m/z*: 395 [M+Na]. Anal ($C_{21}H_{16}N_4OS$), C, H, S, N.

6-(2,6-Difluorobenzyl)-2-(4-nitrophenacylthio)-5-methylpirimidin-4(3*H*)-one (30).

Yield 60%. Mp 215 °C. IR (nujol) (ν, cm^{-1}): 2946, 1694, 1664, 1518, 1377, 1350. ^1H NMR ($CDCl_3$): δ 2.05 (s, 3H), 3.29 (d, 1H, *J* = 11.7 Hz), 3.87 (d, 1H, *J* = 11.7 Hz), 3.96 (s, 2H), 6.93-6.85

(m, 2H), 7.24-7.15 (m, 1H), 7.53 (d, 2H, J = 8.7 Hz), 8.23 (d, 2H, J = 8.7 Hz). MS (ESI) m/z: 430 [M–1]. Anal. ($C_{19}H_{13}F_2N_3O_4S$)

6-(2,6-Difluorobenzyl)-2-(4-chlorophenacylthio)-5-methylpirimidin-4(3*H*)-one (31).

Yield 80%. Mp 216-217 °C. IR (nujol) (ν, cm^{-1}): 2925, 1687, 1667. ^{1}H NMR [$(CD_3)_2SO$)]: δ 1.97 (s, 3H), 3.76 (s, 2H), 4.47 (s, 2H), 6.66-6.99 (m, 2H), 7.03-7.11 (m, 1H), 7.61 (d, 2H, J = 8.6 Hz), 7.79 (d, 2H, J = 8.6 Hz), 12.65 (bs, 1H). MS (ESI) m/z: 421 [M+1], 443 [M+Na], 459 [M+K]. Anal. ($C_{19}H_{13}ClF_2N_2O_2S$)

6-(4-Cyanobenzyl)-2-(phenacylthio)-5-methylpirimidin-4(3*H*)-one (32).

Yield 64%. Mp 201-202 °C. ^{1}H NMR [$(CD_3)_2SO$)]: δ 1.87 (s, 3H), 3.69 (s, 2H), 4.61 (s, 2H), 7.13 (d, 2H, J = 7.9 Hz), 7.44-7.55 (m, 4H), 7.61-7.64 (m, 1H), 7.91 (d, 2H, J = 7.3 Hz), 12.65 (bs, 1H). MS (ESI) m/z: 376 [M+1], 398 [M+Na]. Anal $C_{21}H_{17}N_3O_2S$

6-(1-(2,6-Dichlorophenyl)-ethyl)-2-(2-(4-methoxyphenyl)-vinylsulfanyl)-5-methylpyrimidin-4(3*H*)-one (35).

Yield 60%. Mp 197-198 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1523, 1632, 2925. ^{1}H NMR (DMSO-d_6): δ 1.52 (s, 3H), 1.58 (d, 3H, J = 7.1 Hz), 3.74 (s, 3H), 4.86 (q, 1H, J = 7.1 Hz), 6.78-6.95 (m, 3H), 7.22-7.43 (m, 6H). MS (ESI) m/z: 447 $[M + H]^+$, 469 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 7.58 min. Anal. ($C_{22}H_{20}Cl_2N_2O_2S$) C, H, S, N.

6-(2,6-Dichlorobenzyl)-2-(3-(4-nitrophenyl)-allylsulfanyl)-5-methylpyrimidin-4(3*H*)-one (37).

Yield 62%. Mp 220-222 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1524, 1653, 3002. ^{1}H NMR (DMSO-d_6): δ 2.05 (s, 3H), 3.15 (m, 2H), 3.59-3.68 (m, 1H), 4.11 (s, 2H), 5.12-5.21 (m, 1H), 7.22-7.45 (m, 5H), 8.07-8.12 (m, 2H). MS (ESI) m/z: 462 $[M + H]^+$, 484 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 6.22 min. Anal. ($C_{21}H_{17}Cl_2N_3O_3S$) C, H, S, N.

6-(2,6-Dichlorobenzyl)-2-(3-(4-dimethylaminophenyl)-allylsulfanyl)-5-methylpyrimidin-4(3*H*)-one (38).

Yield 63%. Mp 226-229 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1538, 1660, 2974. ^{1}H NMR (DMSO-d_6): δ 2.03 (s, 3H), 2.86 (s, 6H), 3.45 (d, 2H, J = 7.2 Hz), 4.17 (s, 2H), 5.50-5.71 (m, 1H, J = 7.2 Hz, J_{trans} =

15.7 Hz), 6.17 (d, 1H, J_{trans} = 15.7 Hz), 6.62 (d, 2H, J = 8.7 Hz), 7.04 (d, 2H, J = 8.7 Hz), 7.20 (t, 1H, J = 8.1 Hz), 7.42 (d, 2H, J = 8.1 Hz), 12.48 (br s, 1H). MS (ESI) *m/z*: 482 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 7.28 min. Anal. ($C_{23}H_{23}Cl_2N_3OS$) C, H, S, N.

6-(2,6-Dichlorobenzyl)-2-(3-(4-cyanophenyl)-allylsulfanyl)-5-ethylpyrimidin-4(3*H*)-one (39).

Yield 67%. Mp 203-205 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1532, 1653, 2928. ^1H NMR (DMSO-d_6): δ 1.07 (t, 3H, J = 7.0 Hz), 2.50 (q, 2H, J = 7.0 Hz), 3.49 (d, 2H, J = 6.9 Hz), 4.38 (s, 2H), 5.97 (dt, 1H, J = 6.9 Hz, J_{trans} = 15.8 Hz), 6.36 (d, 1H, J_{trans} = 15.8 Hz), 7.13-7.39 (m, 5H), 7.72-7.92 (m, 2H), 12.53 (br s, 1H). MS (ESI) *m/z*: 456 $[M + H]^+$, 478 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 5.12 min. Anal. ($C_{23}H_{19}Cl_2N_3OS$) C, H, S; N.

6-(2,6-Dichlorobenzyl)-2-(3-(4-methoxyphenyl)-allylsulfanyl)-5-ethylpyrimidin-4(3*H*)-one (40).

Yield 85%. Mp 261-263 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1537, 1657, 3006. ^1H NMR (DMSO-d_6): δ 1.07 (t, 3H, J = 7.2 Hz), 2.48 (q, 2H, J = 7.2 Hz), 3.43 (d, 2H, J = 7.3 Hz), 3.72 (s, 3H), 4.21 (s, 2H), 5.67 (dt, 1H, J = 7.3 Hz, J_{trans} = 15.7 Hz), 6.22 (d, 1H, J_{trans} = 15.7 Hz), 6.83-7.42 (m, 7H). MS (ESI) *m/z*: 461 $[M + H]^+$, 483 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 6.38 min. Anal. ($C_{23}H_{22}Cl_2N_2O_2S$) C, H, S; N.

6-(2,6-Dichlorobenzyl)-2-(3-(4-nitrophenyl)-allylsulfanyl)-5-ethylpyrimidin-4(3*H*)-one. (41).

Yield 75%. Mp 228-229 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1532, 1663, 2925. ^1H NMR (DMSO-d_6): δ 1.08 (t, 3H, J = 6.7 Hz), 2.54 (q, 2H, J = 6.7 Hz), 3.51 (d, 2H, J = 6.8 Hz), 4.22 (s, 2H), 6.06 (dt, 1H, J = 6.8 Hz, J_{trans} = 15.8 Hz), 6.42 (d, 1H, J_{trans} = 15.8 Hz), 7.17 (t, 1H, J = 8.3 Hz), 7.39 (d, 2H, J = 8.2 Hz), 7.46 (d, 2H, J = 8.3 Hz), 8.16 (d, 2H, J = 8.2 Hz), 12.53 (br s, 1H). MS (ESI) *m/z*: 476 $[M + H]^+$, 498 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 6.25 min. Anal. ($C_{22}H_{19}Cl_2N_3O_3S$) C, H, S, N.

6-(1-(2,6-Dichlorophenyl)-ethyl)-2-(3-(4-methoxyphenyl)-allylsulfanyl)-5-methylpyrimidin-4(3*H*)-one (42).

Yield 81%. Mp 211-213 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1644, 3011. ^1H NMR (DMSO-d_6): δ 1.44 (s, 3H), 1.58 (d, 3H, J = 7.1 Hz), 3.61 (s, 3H), 3.81-4.09 (m, 2H) 4.82 (q, 1H, J = 7.1 Hz), 6.21 (dt, 1H, , J = 6.8 Hz, J_{trans} = 15.1 Hz), 6.55 (d, 1H, J_{trans} = 15.1 Hz), 6.82-6.87 (m, 2H), 7.20-7.41 (m, 5H), 12.52 (br s, 1H). MS (ESI) *m/z*: 461 $[M + H]^+$, 483 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 6.36 min. Anal. ($C_{23}H_{22}Cl_2N_2O_2S$) C, H, S, N.

6-(1-(2,6-Dichlorophenyl)-ethyl)-2-(3-(4-nitrophenyl)-allylsulfanyl)-5-methylpyrimidin-4(3*H*)-one. (43).

Yield 80%. Mp 235-237 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1536, 1663, 2931. ^1H NMR (DMSO-d_6): δ 1.45 (s, 3H), 1.59 (d, 3H, J = 7.1 Hz), 3.81-4.09 (m, 2H) 4.83 (q, 1H, J = 7.1 Hz), 6.65 (dt, 1H, J = 6.1 Hz, J_{trans} = 15.8 Hz), 6.78 (d, 1H, J_{trans} = 15.8 Hz), 7.23 (t, 1H, J= 8.7 Hz), 7.41 (d, 2H, J = 8.7 Hz), 7.62 (d, 2H, J = 8.7 Hz), 8.14 (d, 2H, J = 8.7 Hz), 12.62 (br s, 1H). MS (ESI) *m/z*: 476 $[M + H]^+$, 498 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 6.30 min. Anal. ($C_{22}H_{19}Cl_2N_3O_3S$) C, H, S; N.

6-(2,6-Difluorobenzyl)-2-(3-(4-nitrophenyl)-allylsulfanyl)-5-methylpyrimidin-4(3*H*)-one (44).

Yield 47%. Mp 260-262 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1661, 2928. ^1H NMR ($CDCl_3$): δ 2.00 (s, 3H), 3.64 (d, 2H, J = 7.0 Hz), 3.91 (s, 2H), 6.20 (dt, 1H, J = 7.0 Hz, J_{trans} = 15.8 Hz), 6.48 (d, 1H, J_{trans} = 15.8 Hz), 6.98-7.49 (m, 5H), 8.12-8.17 (m, 2H), 12.48 (br s, 1H). MS (ESI) *m/z*: 430 $[M + H]^+$, 452 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 5.30 min. Anal. ($C_{21}H_{17}F_2N_3O_3S$) C, H, S, N.

6-(2,6-Difluorobenzyl)-2-(3-(4-methoxyphenyl)-allylsulfanyl)-5-methylpyrimidin-4(3*H*)-one. (45).

Yield 42%. Mp 177-179 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1660, 3007. ^1H NMR ($CDCl_3$): δ 2.16 (s, 3H), 3.67 (d, 2H, J = 7.2 Hz), 3.79 (s, 3H), 3.95 (s, 2H), 5.29-5.92 (m, 1H, J = 7.2 Hz, J_{trans} = 15.6 Hz), 6.35 (d, 1H, J_{trans} = 15.6 Hz), 6.79-6.87 (m, 3H), 7.09-7.25 (m, 4H). MS (ESI) *m/z*: 415 $[M + H]^+$, 437 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 4.34 min. Anal. ($C_{22}H_{20}F_2N_2O_2S$) C, H, S, N.

6-(1-(2,6-Difluorophenyl)-ethyl)-2-(3-(4-nitrophenyl)-allylsulfanyl)-5-methylpyrimidin-4(3*H*)-one. (46).

Yield 34%. Mp 240-242 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1532, 1644, 3011. ^1H NMR (DMSO-d_6): δ 1.50 (d, 3H, J = 7.3 Hz), 1.76 (s, 3H), 3.74-3.94 (m, 2H), 4.47 (q, 1H, J = 7.3 Hz), 6.31-6.43 (m, 1H), 6.56 (d, 1H, J_{trans} = 15.9 Hz), 6.91 (t, 1H, J = 8.6 Hz), 7.13-7.21 (m, 2H), 7.45 (d, 2H, J = 8.6 Hz), 8.06 (d, 2H, J = 8.7 Hz), 12.52 (br s,1H). MS (ESI) m/z: 444 $[M + H]^+$, 466 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 5.36 min. Anal. ($C_{22}H_{19}F_2N_3O_3S$) C, H, S, N.

6-(1-(2,6-Difluorophenyl)-ethyl)-2-(3-(4-methoxyphenyl)-allylsulfanyl)-5-methylpyrimidin-4(3*H*)-one. (47).

Yield 40%. Mp 179-181 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1654, 3008. ^1H NMR ($CDCl_3$): δ 1.68 (d, 3H, J = 7.7 Hz), 2.00 (s, 3H), 3.79 (s, 3H), 3.83-4.05 (m, 2H), 4.60 (q, 1H, J = 7.7 Hz), 5.97-6.12 (m,1H), 6.46 (d, 1H, J_{trans} = 15.7 Hz), 6.76-6.86 (m, 4H), 7.04-7.24 (m, 3H). MS (ESI) m/z: 429 $[M + H]^+$, 451 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R5.56 min. Anal. ($C_{23}H_{22}F_2N_2O_2S$) C, H, S, N.

6-(1-(2,6-Difluorophenyl)-ethyl)-2-(3-(4-cyanophenyl)-allylsulfanyl)-5-methylpyrimidin-4(3*H*)-one. (48).

Yield 30%. Mp 221-223 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1648, 3011. ^1H NMR δ (MeOD-d_3): 1.67 (d, 3H, J = 6.8 Hz), 1.96 (s, 3H), 3.86-4.15 (m, 2H), 4.67 (q, 1H, J = 6.8 Hz), 6.35-6.64 (m, 2H), 6.89 (t, 1H, J = 7.6 Hz), 7.15-7.25 (m, 2H), 7.42 (d, 2H, J = 7.6 Hz), 7.61-7.65 (m, 2H). MS (ESI) m/z: 424 $[M + H]^+$, 446 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 4.36 min. Anal. ($C_{23}H_{19}F_2N_3OS$) C, H, S, N.

6-(1-(2,6-Difluorophenyl)-ethyl)-2-(3-(4-methoxyphenyl)-allylsulfanyl)-5-ethylpyrimidin-4(3*H*)-one. (49).

Yield 58%. Mp 164-165 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1660, 3007. ^1H NMR ($CDCl_3$): δ 1.01 (t, 3H, J = 7.2 Hz), 1.70 (d, 3H, J = 7.2 Hz), 3.79 (s, 3H), 2.52 (q, 2H, J = 7.2 Hz), 3.85-4.05 (m, 2H), 5.15 (q, 1H, J = 7.2 Hz), 5.98-6.05 (m, 1H), 6.46 (d, 1H, J_{trans} = 15.8 Hz), 6.85-7.24 (m, 7H). MS (ESI)

m/z: 443 [M + H]$^+$, 465 [M + Na]$^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 8.48 min. Anal. ($C_{24}H_{24}F_2N_2O_2S$) C, H, S, N.

6-(1-(2,6-Difluorophenyl)-ethyl)-2-(3-(4-nitrophenyl)-allylsulfanyl)-5-ethylpyrimidin-4(3*H*)-one. (50).

Yield 38%. Mp 198-200 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1656, 3011. ^{1}H NMR ($CDCl_3$): δ 1.07 (t, 3H, *J* = 7.5 Hz), 1.69 (d, 3H, *J* = 6.8 Hz), 2.52 (q, 2H, *J* = 7.5 Hz), 3.76-4.13 (m, 2H), 4.54 (q, 1H, *J* = 6.8 Hz), 6.20-6.35 (m,1H), 6.57 (d, 1H, J_{trans} = 15.8 Hz), 6.79 (t, 1H, *J* = 8.6 Hz), 7.06-7.14 (m, 2H), 7.37 (d, 2H, *J* = 8.6 Hz), 8.13 (d, 2H, *J* = 8.7 Hz), 11.05 (br s,1H). MS (ESI) *m/z*: 458 [M + H]$^+$, 480 [M + Na]$^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 7.52 min. Anal. ($C_{23}H_{21}F_2N_3O_3S$) C, H, S, N.

6-(1-(2,6-Difluorophenyl)-ethyl)-2-(3-(4-cyanophenyl)-allylsulfanyl)-5-ethylpyrimidin-4(3*H*)-one. (51).

Yield 62%. Mp .198-199 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1644, 3011. ^{1}H NMR ($CDCl_3$): δ 1.00 (t, 3H, *J* = 7.5 Hz), 1.68 (d, 3H, *J* = 7.2 Hz), 2.51 (q, 2H, *J* = 7.5 Hz), 3.64-4.03 (m, 2H), 4.62 (q, 1H, *J* = 7.2 Hz), 6.22-6.37 (m,1H), 6.52 (d, 1H, J_{trans} = 15.8 Hz), 6.78 (t, 1H, *J* = 7.5 Hz), 7.06-7.14 (m, 2H), 7.32 (d, 2H, *J* = 7.5 Hz), 7.55 (d, 2H, *J* = 8.4 Hz). MS (ESI) *m/z*: 438 [M + H]$^+$, 460 [M + Na]$^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 4.48 min. Anal. ($C_{24}H_{21}F_2N_3OS$) C, H, S, N.

6-(2,6-Dichlorobenzyl)-2-(3-(4-methoxyphenyl)-propynylsulfanyl)-5-methylpyrimidin-4(3*H*)-one (52).

Yield 80%. Mp 194-196 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1645, 3012, 3369. ^{1}H NMR (DMSO-d_6): δ 2.04 (s, 3H), 3.74 (s, 3H), 3.75 (s, 2H), 4.17 (s, 2H), 6.86-7.41 (m, 7H), 12.59 (br s, 1H). MS (ESI) *m/z*: 445 [M + H]$^+$, 467 [M + Na]$^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 5.82 min. Anal. ($C_{22}H_{18}Cl_2N_2O_2S$) C, H, S, N.

6-(1-(2,6-Dichlorophenyl)-ethyl)-2-(3-(4-methoxyphenyl)-propynylsulfanyl)-5-methylpyrimidin-4(3*H*)-one (53).

Yield 68%. Mp 213-215 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1509, 1643, 2931, 3368. ^1H NMR (DMSO-d_6): δ 1.56 (s, 3H), 1.70 (d, 3H, J = 7.1 Hz), 3.77 (s, 3H), 4.17 (d, 1H, J = 16.5 Hz), 4.31 (d, 1H, J = 16.5 Hz), 4.96 (q, 1H, J = 7.1 Hz), 6.81-6.86 (m, 2H), 7.12-7.23 (m, 1H), 7.26-7.35 (m, 4H). MS (ESI) m/z: 459 $[M + H]^+$, 481 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 7.60 min. Anal. ($C_{23}H_{20}Cl_2N_2O_2S$) C, H, S; N.

6-(2,6-Dichlorobenzyl)-2-(2-(4-methoxybenzyloxy)-ethylsulfanyl)-5-methylpyrimidin-4(3*H*)-one (55).

Yield 70%. Mp 138-140 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1644, 2958. ^1H NMR (DMSO-d_6): δ 1.99 (s, 3H), 2.85 (t, 2H, J = 5.8 Hz), 3.12 (t, 2H, J = 5.8 Hz), 3.71 (s, 3H), 4.10 (s, 2H), 4.20 (s, 2H), 6.83-6.87 (m, 2H), 7.12-7.36 (m, 5H), 12.51 (br s, 1H). MS (ESI) m/z: 465 $[M + H]^+$, 487 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 6.24 min. Anal. ($C_{22}H_{22}Cl_2N_2O_3S$) C, H, S; N.

6-(1-(2,6-Dichlorophenyl)-ethyl)-2-(2-(4-methoxybenzyloxy)-ethylsulfanyl)-5-methylpyrimidin-4(3*H*)-one (56).

Yield 62%. Mp 150-151 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1643, 2946. ^1H NMR (DMSO-d_6): δ 1.44 (s, 3H), 1.50 (d, 3H, J = 8.2 Hz), 3.25-3.28 (m, 2H), 3.60-3.67 (m, 2H), 3.71 (s, 3H), 4.40 (s, 2H), 4.79 (q, 1H, J = 8.2 Hz), 6.87 (d, 2H, J = 8.7 Hz), 7.22 (d, 2H, J = 8.8 Hz), 7.27 (t, 3H, J = 8.7 Hz), 7.43 (d, 2H, J = 8.8 Hz). MS (ESI) m/z: 479 $[M + H]^+$, 501 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 7.56 min. Anal. ($C_{23}H_{24}Cl_2N_2O_3S$) C, H, S; N.

6-(2,6-Difluorobenzyl)-2-(2-(4-methoxybenzyloxy)-ethylsulfanyl)-5-methylpyrimidin-4(3*H*)-one (57).

Yield 21%. Mp 146-148 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1643, 2931, 3334. ^1H NMR ($CDCl_3$): δ 2.13 (s, 3H), 3.07 (t, 2H, J = 6.0 Hz), 3.40 (t, 2H, J = 6.0 Hz), 3.89 (s, 3H), 4.37 (s, 2H), 4.89 (s, 2H), 6.83-6.87 (m, 4H), 7.18-7.24 (m, 3H). MS (ESI) m/z: 455 $[M + H]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 5.32 min. Anal. ($C_{22}H_{22}F_2N_2O_3S$) C, H, S; N.

6-(1-(2,6-Difluorophenyl)-ethyl)-2-(2-(4-methoxybenzyloxy)-ethylsulfanyl)-5-methylpyrimidin-4(3*H*)-one (58).

Yield 54%. Mp 138-140 °C. IR ($CHCl_3$) (ν, cm^{-1}): 1643, 2931. ^{1}H NMR ($CDCl_3$): δ 1.48 (s, 3H), 1.61 (d, 3H, *J* = 7.0 Hz), 3.32-3.35 (m, 2H), 3.56-3.65 (m, 2H), 3.78 (s, 3H), 4.43 (s, 2H), 4.56 (q, 1H, *J* = 7.0 Hz), 6.86-7.20 (m, 7H). MS (ESI) *m/z*: 447 $[M + H]^+$, 469 $[M + Na]^+$. HPLC (C_8 column; CH_3OH/H_2O, 80/20) t_R 5.34 min. Anal. ($C_{23}H_{24}F_2N_2O_3S$) C, H, S, N.

6-(2,6-Dichloro-benzyl)-5-ethyl-2-thioxo-2,3-dihydro-1H-pyrimidin-4-one (61)

Yield 52%. Mp 264-267 °C. ^{1}H NMR (DMSO-d_6): δ 0.38 (t, 3H, *J* = 7.2 Hz), 1.92 (q, 2H, *J* = 7.2 Hz), 4.30 (s, 2H), 7.30-7.58 (m, 3H). MS (ESI) *m/z*: 315 $[M+H]^+$, 337 $[M + Na]^+$. Anal. ($C_{13}H_{12}Cl_2N_2OS$) C, H, S, N

6-(1-(2,6-Dichloro-phenyl)-ethyl)-5-methyl-2-thioxo-2,3-dihydro-1*H*-pyrimidin-4-one (62).

Yield 40%. Mp 296-298 °C. ^{1}H NMR (DMSO-d_6): δ 1.34 (s, 3H), 1.54 (d, 3H, *J* = 7.1 Hz), 4.78 (q, 1H, *J* = 7.1 Hz), 7.29-7.49 (m, 3H), 12.46 (br s, 1H). MS (ESI) *m/z*: 315 $[M+H]^+$, 337 $[M + Na]^+$. Anal. ($C_{13}H_{12}Cl_2N_2OS$) C, H, S, N.

6-(1-(2,6-Difluorophenyl)-ethyl)-5-ethyl-2-thioxo-2,3-dihydro-1*H*-pyrimidin-4-one (66).

Yield 42%. Mp 203-206 °C. ^{1}H NMR (DMSO-d_6): δ 0.46 (t, 3H, *J* = 7.0 Hz), 1.61 (d, 1H, *J* = 6.9 Hz), 2.30 (q, 2H, *J* = 7.0 Hz), 4.47 (q, 1H, *J* = 6.9 Hz), 7.04-7.13 (m, 2H), 7.30-7.98 (m, 1H). MS (ESI) *m/z*: 297 $[M+H]^+$, 319 $[M + Na]^+$. Anal. ($C_{14}H_{14}F_2N_2OS$) C, H, S, N.

6-(1-(2,6-Difluoro-phenyl)-propyl)-5-methyl-2-thioxo-2,3-dihydro-1*H*-pyrimidin-4-one (67).

Yield 54%. ^{1}H NMR ($CDCl_3$): δ 1.10 (t, 3H, *J* = 6.3 Hz), 1.98-2.15 (m, 5H), 4.33-4.41 (m, 1H), 6.89-7.32 (m, 3H). MS (ESI) *m/z*: 297 $[M+H]^+$, 319 $[M + Na]^+$. Anal. ($C_{14}H_{14}F_2N_2OS$) C, H, S; N.

6-(4-Cyano-benzyl)-5-methyl-2-thioxo-2,3-dihydro-1H-pyrimidin-4-one (68)

Yield 68%. Mp 283-285 °C. ^{1}H NMR (DMSO-d_6): δ 1.78 (s, 3H), 3.97 (s, 3H), 7.46 (d, 2H, *J* = 8.0 Hz), 7.83 (d, 2H, *J* = 8.1 Hz), 12.32 (s, 1H), 12.48 (s, 1H). MS (ESI) *m/z*: 256 [M-H]. Anal. ($C_{13}H_{11}N_3OS$) C, H, S, N.

4-(2,6-Dichlorophenyl)-2-ethyl-3-oxo-butyric acid ethyl ester (78).

Yield 75%. ^{1}H NMR ($CDCl_3$): δ 0.90 (t, 3H, *J* = 7.3 Hz), 1.23-1.46 (m, 3H), 1.72-1.99 (m, 2H), 3.37 (t, 1H, *J* = 7.8 Hz), 4.07-4.39 (m, 4H), 7.04-7.26 (m, 3H). MS (ESI) *m/z*: 325 $[M + Na]^+$. Anal. ($C_{14}H_{16}Cl_2O_3$) C, H.

4-(2,6-Dichlorophenyl)-2-methyl-3-oxo-pentanoic acid ethyl ester (79).

Yield 64%. ^{1}H NMR ($CDCl_3$): δ 1.18 (t, 3H, *J* = 7.0 Hz), 1.27 (d, 3H, *J* = 6.9 Hz), 1.42 (d, 3H, *J* = 6.8 Hz), 3.44 (q, 1H, *J* = 6.9 Hz), 4.06 (q, 2H, *J* = 7.0 Hz), 4.59 (q, 1H, *J* = 6.8 Hz), 7.11-7.33 (m, 3H). MS (ESI) *m/z*: 303 $[M+H]^+$, 325 $[M + Na]^+$. Anal. ($C_{14}H_{16}Cl_2O_3$) C, H.

4-(2,6-Difluorophenyl)-2-ethyl-3-oxo-pentanoic acid ethyl ester. (83).

Yield 60%. ^{1}H NMR ($CDCl_3$): δ 0.70-0.98 (m, 3H), 1.09-1.28 (m, 3H), 1.31-1.49 (m, 3H), 1.71-2.01 (m, 2H), 3.30-3.49 (m, 1H), 3.85-4.15 (m, 3H), 6.86-6.91 (m, 2H), 7.15-7.28 (m, 1H). MS (ESI) *m/z*: 285 $[M+H]^+$, 307 $[M + Na]^+$. Anal. ($C_{15}H_{18}F_2O_3$) C, H.

4-(2,6-Difluorophenyl)-2-methyl-3-oxo-hexanoic acid ethyl ester. (84) Yield 60%. ^{1}H NMR ($CDCl_3$): δ 0.82 (t, 3H, *J* = 7.4 Hz), 1.09-1.28 (m, 6H), 2.15-2.25 (m, 2H), 3.46-3.53 (m, 1H), 4.01-4.15 (m, 3H), 6.86-7.17 (m, 3H). MS (ESI) *m/z*: 285 $[M+H]^+$, 307 $[M + Na]^+$. Anal. ($C_{15}H_{18}F_2O_3$) C, H.

4-(4-Cyanophenyl)-2-methyl-3-oxo-butyric acid ethyl ester (85).

Yield 34%. ^{1}H NMR ($CDCl_3$): δ 1.24 (t, 3H, *J* = 7.2 Hz), 1.33 (d, 3H, *J* = 7.4 Hz), 3.58 (q, 1H, *J* = 7.1 Hz), 3.88 (d, 1H, *J* = 16.3 Hz), 3.90 (d, 1H, *J* = 16.4 Hz), 4.16 (q, 2H, *J* = 7.1 Hz), 7.28 (d, 2H, *J* = 8.0 Hz), 7.58 (d, 2H, 7.9 Hz). MS (ESI) *m/z*: 268 $[M + Na]^+$. Anal. ($C_{14}H_{15}NO_3$) C, H, N.

Elemental Analyses

compd	formula	C Calcd % Found %	H Calcd % Found %	N Calcd % Found %
1	$C_{21}H_{18}F_2N_2O_3S$	60.57	4.36	6.73
		60.55	4.39	6.77
2	$C_{21}H_{20}Cl_2N_2O_2S$	57.93	4.63	6.43
		57.90	4.67	6.49
3	$C_{21}H_{17}Cl_2N_3OS$	58.61	3.98	9.76
		58.59	3.93	9.80
4	$C_{20}H_{17}Cl_2N_3O_3S$	53.34	3.80	9.33
		53.38	3.82	9.38
5	$C_{21}H_{20}Cl_2N_2O_2S$	57.93	4.63	6.43
		57.97	4.65	6.48
6	$C_{20}H_{17}Cl_2N_3O_3S$	53.34	3.80	9.33
		53.38	3.86	9.29
7	$C_{21}H_{17}Cl_2N_3OS$	58.61	3.98	9.76
		58.65	4.03	9.78
8	$C_{22}H_{22}Cl_2N_2O_2S$	58.80	4.93	6.23
		58.86	4.91	6.26
9	$C_{22}H_{22}Cl_2N_2O_2S$	58.80	4.93	6.23
		58.75	4.97	6.28
10	$C_{23}H_{24}Cl_2N_2O_2S$	59.61	5.22	6.04
		59.65	4.27	6.01
11	$C_{21}H_{20}F_2N_2O_2S$	62.67	5.01	6.96
		62.63	5.07	6.92
12	$C_{21}H_{20}F_2N_2O_3S$	60.27	4.82	6.69
		60.21	4.84	6.74
13	$C_{20}H_{16}F_2N_2O_3S$	59.69	4.01	6.96
		59.74	4.08	6.92
14	$C_{21}H_{18}F_2N_2O_3S$	60.57	4.36	6.73
		60.63	4.37	6.70
15	$C_{21}H_{18}F_2N_2O_3S$	60.57	4.36	6.73
		60.61	4.30	6.76
16	$C_{21}H_{20}F_2N_2O_2S$	62.67	5.01	6.96
		62.72	5.06	7.01
17	$C_{21}H_{17}F_2N_3OS$	63.46	4.31	10.57
		63.50	4.26	10.64
18	$C_{20}H_{17}F_2N_3O_3S$	57.55	4.10	10.07
		57.61	4.14	10.12
19	$C_{21}H_{20}F_2N_2O_2S$	62.67	5.01	6.96
		62.62	4.97	6.94
20	$C_{21}H_{17}F_2N_3OS$	63.46	4.31	10.57
		63.50	4.34	10.52
21	$C_{20}H_{17}F_2N_3O_3S$	57.55	4.10	10.07
		57.58	4.15	10.13
22	$C_{22}H_{22}F_2N_2O_2S$	63.44	5.32	6.73
		63.50	5.36	6.68

23	$C_{21}H_{20}F_2N_2O_2S$	62.67	5.01	6.96
		62.70	5.07	6.92
24	$C_{22}H_{22}F_2N_2O_2S$	63.44	5.32	6.73
		63.40	5.37	6.70
25	$C_{21}H_{19}N_3O_2S$	66.82	5.07	11.13
		67.01	5.08	11.12
26	$C_{17}H_{19}N_3OS$	65.15	6.11	13.41
		65.32	6.12	13.39
27	$C_{20}H_{16}N_4O_3S$	61.21	4.11	14.28
		61.43	4.11	14.25
28	$C_{21}H_{16}N_4OS$	67.72	4.33	15.04
		67.82	4.32	15.09
29	$C_{21}H_{15}Cl_2N_3O_2S$	56.76	3.40	9.46
		56.64	3.41	9.39
30	$C_{20}H_{15}F_2N_3O_4S$	55.68	3.50	9.74
		55.74	3.51	9.72
31	$C_{20}H_{15}ClF_2N_2O_2S$	57.08	3.59	6.66
		56.99	3.59	6.65
32	$C_{21}H_{17}N_3O_2S$	67.18	4.56	11.19
		67.05	4.57	11.21
33	$C_{20}H_{15}Cl_2FN_2OS$	57.02	3.59	6.65
		56.84	3.59	6.66
34	$C_{21}H_{18}Cl_2N_2O_2S$	58.20	4.19	6.46
		58.25	4.17	6.51
35	$C_{22}H_{20}Cl_2N_2O_2S$	59.06	4.51	6.26
		59.02	4.56	6.28
36	$C_{22}H_{20}Cl_2N_2O_2S$	59.06	4.51	6.26
		59.03	4.56	6.22
37	$C_{21}H_{17}Cl_2N_3O_3S$	54.55	3.71	9.09
		54.50	3.72	9.11
38	$C_{23}H_{23}Cl_2N_3OS$	60.00	5.04	9.13
		60.03	5.07	9.17
39	$C_{23}H_{19}Cl_2N_3OS$	60.53	4.20	9.21
		60.52	4.25	9.24
40	$C_{23}H_{22}Cl_2N_2O_2S$	59.87	4.81	6.07
		59.90	4.84	6.12
41	$C_{22}H_{19}Cl_2N_3O_3S$	55.47	4.02	8.82
		55.50	4.00	8.84
42	$C_{23}H_{22}Cl_2N_2O_2S$	59.87	4.81	6.07
		59.90	4.85	6.03
43	$C_{22}H_{19}Cl_2N_3O_3S$	55.47	4.02	8.82
		55.52	4.04	8.80
44	$C_{21}H_{17}F_2N_3O_3S$	58.73	3.99	9.78
		58.72	3.96	9.74
45	$C_{22}H_{20}F_2N_2O_2S$	63.75	4.86	6.76
		63.71	4.83	6.79
46	$C_{22}H_{19}F_2N_3O_3S$	59.58	4.32	9.48
		59.53	4.36	9.49
47	$C_{23}H_{22}F_2N_2O_2S$	64.47	5.18	6.54
		64.44	5.15	6.58

48	$C_{23}H_{19}F_2N_3OS$	65.23	4.52	9.92
		65.25	4.56	9.88
49	$C_{24}H_{24}F_2N_2O_2S$	65.14	5.47	6.33
		65.10	5.49	6.38
50	$C_{23}H_{21}F_2N_3O_3S$	60.38	4.63	9.18
		60.39	4.66	9.13
51	$C_{24}H_{21}F_2N_3OS$	65.89	4.84	9.60
		65.86	4.80	9.65
52	$C_{22}H_{18}Cl_2N_2O_2S$	59.33	4.07	6.29
		59.30	4.10	6.24
53	$C_{23}H_{20}Cl_2N_2O_2S$	60.13	4.39	6.10
		60.16	4.34	6.14
54	$C_{21}H_{15}F_2N_3O_3S$	59.01	3.54	9.83
		59.05	3.57	9.88
55	$C_{22}H_{22}Cl_2N_2O_3S$	56.78	4.76	6.02
		56.74	4.78	6.06
56	$C_{23}H_{24}Cl_2N_2O_3S$	57.62	5.05	5.84
		57.60	5.07	5.82
57	$C_{22}H_{22}F_2N_2O_3S$	61.10	5.13	6.48
		61.15	5.17	6.43
58	$C_{23}H_{24}F_2N_2O_3S$	61.87	5.42	6.27
		61.85	5.47	6.22
59	$C_{24}H_{26}F_2N_2O_3S$	62.59	5.69	6.08
		62.55	5.67	6.06