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SYNTHETIC EXAMPLES

The following HPLC methods were used in the analysis of the compounds as specified in the Synthetic Examples set forth below. As used herein, the term "R_t" refers to the retention time observed for the compound using the HPLC method specified.

HPLC-Method A:

Column: C18, 3 um, 2.1 X 50 mm, "Lighting" by Jones Chromatography.
Gradient: 100% water (containing 1% acetonitrile, 0.1% TFA) to 100% acetonitrile (containing 0.1% TFA) over 4.0 min, hold at 100% acetonitrile for 1.4 min and return to initial conditions. Total run time 7.0 min. Flow rate: 0.8 mL/min.

HPLC-Method B:

Column: C18, 5 um, 4.6 X 150 mm "Dynamax" by Rainin
Gradient: 100% water (containing 1% acetonitrile, 0.1% TFA) to 100% acetonitrile (containing 0.1% TFA) over 20 min, hold at 100% acetonitrile for 7.0 min and return to initial conditions. Total run time 31.5 min. Flow rate: 1.0 mL/min.

HPLC-Method C:

Column: Cyano, 5 um, 4.6 X 150 mm "Microsorb" by Varian.
Gradient: 99% water (0.1% TFA), 1% acetonitrile (containing 0.1% TFA) to 50% water (0.1% TFA), 50% acetonitrile (containing 0.1% TFA) over 20 min, hold for 8.0 min and return to initial conditions. Total run time 30 min. Flow rate: 1.0 mL/min.

HPLC-Method D:

Column: Waters (YMC) ODS-AQ 2.0x50mm, S5, 120A.
Gradient: 90% water (0.2% Formic acid), 10% acetonitrile (containing 0.1% Formic acid) to 10% water (0.1% formic acid), 90% acetonitrile (containing 0.1% formic acid) over 5.0 min, hold for 0.8 min and return to initial conditions. Total run time 7.0 min.
Flow rate: 1.0 mL/min.

HPLC-Method E:

Column: 50x2.0mm Hypersil C18 BDS;5 μm
Gradient: elution 100% water (0.1% TFA), to 5% water (0.1% TFA), 95% acetonitrile (containing 0.1% TFA) over 2.1 min, returning to initial conditions after 2.3 min.
Flow rate: 1 mL/min.

Example 1 **[2-(2-Clorophenyl)-5,6-dimethylpyrimidin-4-yl]-(5-Methyl-2*H*-pyrazol-3-yl)-amine (II-1):** ^{1}HNMR (500 MHz, DMSO-d6) δ10.4 (s, br, 1H), 7.74 (m, 2H), 7.68 (m, 1H), 7.60 (m, 1H), 6.39 (s, 1H), 2.52 (s, 3H), 2.30 (s, 3H), 2.22 (s, 3H); MS 314.1 (M+H).

Example 2 **[2-(2-Chloro-phenyl)-6,7,8,9-tetrahydro-5*H*-cycloheptapyrimidin-4-yl]-(1*H*-indazol-3-yl)-amine (II-2):** Prepared in 30% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 1.72 (m, 4H), 1.91 (m, 2H), 3.02 (m, 4H), 7.05 (t, 1H), 7.33 (t, 1H), 7.39 (m, 1H), 7.47 (d, 1H), 7.55 (m, 3H), 7.59 (d, 1H), 10.4 (m, 1H), 13.11 (br. s, 1H); EI-MS 390.2 (M+H); HPLC-Method A, R_t 2.99 min.

Example 3 **(5-Fluoro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[3,4-**

d]pyrimidin-4-yl]-amine (II-3): Compound **II-18** (90 mg, 0.17 mmol) was treated with an equal weight of Pd/C (10%) in 4.4% formic acid in MeOH at room temperature for 14 h. The mixture was filtered through celite, the filtrate was evaporated, and crude product was purified by HPLC to provide 18 mg (24%) of the desired product as pale yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ12.9 (s, 1H), 9.51 (s, 1H), 9.26 (s, 2H), 7.72 (d, 1H), 7.63 (t, 1H), 7.58 (t, 1H), 7.49 (m, 2H), 7.21 (td, 1H), 7.15 (dd, 1H), 4.24 (s, 2H), 3.56 (m, 2H), 2.95 (m, 2H) ppm. MS (ES+): m/e= 429.22 (M+H); HPLC-Method A, R_t 2.88 min.

Example 4 **[2-(2-Chloro-phenyl)-6,7,8,9-tetrahydro-5*H*-cycloheptapyrimidin-4-yl]-(7-fluoro-1*H*-indazol-3-yl)-amine (II-4)**: Prepared in 52% yield to afford a white solid. ^{1}HNMR (500MHz, DMSO-d6) δ 1.72 (m, 4H), 1.92 (m, 2H), 3.00 (m, 4H), 7.02 (td, 1H), 7.20 (dd, 1H), 7.40 (m, 1H), 7.42 (d, 1H), 7.52 (m, 3H), 10.5 (m, 1H), 13.50 (br. s, 1H); EI-MS 408.2 (M+H); HPLC-Method A, R_t 3.00 min.

Example 5 **[2-(2-Chloro-phenyl)-6,7,8,9-tetrahydro-5*H*-cycloheptapyrimidin-4-yl]-(5-fluoro-1*H*-indazol-3-yl)-amine (II-5)**: Prepared in 51% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 1.71 (m, 4H), 1.91 (m, 2H), 3.01 (m, 4H), 7.24 (td, 1H), 7.41 (m, 2H), 7.54 (m, 4H), 10.5 (m, 1H), 13.1 (br. s, 1H); EI-MS 408.2 (M+H); HPLC-Method A, R_t 3.05 min.

Example 6 **[2-(2-Chloro-phenyl)-6,7,8,9-tetrahydro-5*H*-cycloheptapyrimidin-4-yl]-(5,7-difluoro-1*H*-indazol-3-yl)-amine (II-6)**: Prepared according to Method C in 72% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 1.72 (m, 4H), 1.91 (m, 2H), 3.01 (m, 4H), 7.31 (m, 2H), 7.41 (m, 1H), 7.54 (m, 3H), 10.5 (m, 1H), 13.6 (br. s, 1H); EI-MS 426.2 (M+H); HPLC-Method A, R_t 3.21 min.

Example 7 **(7-Fluoro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-5,6,7,8-tetrahydroquinazolin-4-yl]-amine (II-7)**: Prepared in 62% yield. ^{1}HNMR (500 MHz, DMSO-d6) δ13.5 (s, br, 1H), 10.1 (s, br, 1H), 7.75 (m, 4H), 7.33 (d, 1H), 7.17 (dd, 1H), 7.00 (td, 1H), 2.80 (m, 2H), 2.71 (m, 2H), 1.89 (br, 4H) ppm; LC-MS (ES+) 428.44 (M+H), (ES-) 426.43 (M-H); HPLC-Method A, R_t 3.02 min.

Example 8 **(5-Fluoro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-5,6,7,8-tetrahydroquinazolin-4-yl]-amine (II-8)**: Prepared in 53% yield. ^{1}HNMR (500 MHz, DMSO-d6) δ13.1 (s, 1H), 10.2 (s, br, 1H), 7.75 (m, 4H), 7.50 (dd, 1H), 7.27 (dd, 1H), 7.21 (td, 1H), 2.80 (m, 2H), 2.72 (m, 2H), 1.88 (m, 4H) ppm; MS (ES+) 428.43 (M+H), (ES-) 426.43 (M-H); HPLC-Method A, R_t 3.01 min.

Example 9 **(5,7-Difluoro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-5,6,7,8-tetrahydroquinazolin-4-yl]-amine (II-9)**: Prepared in 37% yield. ^{1}HNMR (500 MHz, DMSO-d6) δ13.7 (s, 1H), 10.2 (s, br, 1H), 7.80 (d, 1H), 7.76 (t, 1H), 7.69 (m, 2H), 7.31 (t, 1H), 7.18 (d, 1H), 2.81 (t, br, 2H), 2.72 (t, br, 2H), 1.90 (m, 4H) ppm; MS (ES+) 446.42 (M+H), (ES-) 444.37 (M-H); HPLC-Method A, R_t 3.09 min.

Example 10 **(5-Trifluoromethyl-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-5,6,7,8-tetrahydroquinazolin-4-yl]-amine (II-10)**: Prepared by Method C in ethanol in 35% yield. ^{1}HNMR (500 MHz, DMSO-d6) δ13.2 (s, 1H), 10.1 (s, br, 1H), 8.01 (s, 1H), 7.76 (d, 1H), 7.66 (m, 4H), 7.57 (d, 1H), 2.79 (m, 2H), 2.73 (m, 2H), 1.89 (m, 4H) ppm. MS (ES+) 478.45 (M+H), (ES-) 476.42 (M-H); HPLC-Method A, R_t 3.21 min.

Example 11 **(5,7-difluoro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-6,7,8,9-tetrahydro-5*H*-cycloheptapyrimidin-4-yl]-amine (II-11)**: Prepared in 60% yield. White solid. ^{1}HNMR (500MHz, DMSO-d6) δ 1.72 (m, 4H), 1.91 (m, 2H), 3.01 (m, 4H), 7.15 (dd, 1H), 7.30 (td, 1H), 7.66 (m, 2H), 7.72 (t, 1H), 7.78 (d, 1H), 10.2 (m, 1H), 13.5 (br. s, 1H); EI-MS 460.2 (M+H); HPLC-Method A, R_t 3.13 min.

Example 12 **(6-Benzyl-2-(2-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yl)-(5-fluoro-1*H*-indazol-3-yl)-amine (II-12)**: Prepared in 49% yield. ^{1}HNMR (500 MHz, DMSO-d6) δ12.8 (s, 1H), 9.11 (s, 1H), 7.68 (d, 1H), 7.58 (t, 1H), 7.53 (t, 1H), 7.44 (m, 4H), 7.37 (t, 2H), 7.29 (t, 1H), 7.19 (m, 2H), 3.78 (s, 2H), 3.61 (s, 2H), 2.81 (s, br, 4H) ppm; LC-MS (ES+) 519.24 (M+H); HPLC-Method A, R_t 3.11 min.

Example 13 **(1*H*-Indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-6,7,8,9-tetrahydro-5*H*-cycloheptapyrimidin-4-yl]-amine (II-13)**: Prepared in 40% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 1.70 (m, 4H), 1.90 (m, 2H), 3.00 (m, 4H), 7.01 (t, 1H), 7.30 (td, 1H), 7.44 (d, 1H), 7.49 (d, 1H), 7.68 (m, 3H), 7.77 (d, 1H), 10.01 (m, 1H), 12.83 (s, 1H); EI-MS 424.2 (M+H); HPLC-Method A, R_t 3.17 min.

Example 14 **(7-Fluoro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-6,7,8,9-tetrahydro-5*H*-cycloheptapyrimidin-4-yl]-amine (II-14)**: Prepared in 78% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 1.71 (m, 4H), 1.91 (m, 2H), 3.00 (m, 4H), 6.98 (td, 1H), 7.16 (dd, 1H), 7.31 (d, 1H), 7.68 (m, 3H), 7.77 (d, 1H), 10.25 (m, 1H), 13.40 (br. s, 1H); EI-MS 442.2 (M+H); HPLC-Method A, R_t 3.12

min.

Example 15 **(5-Fluoro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-6,7,8,9-tetrahydro-5*H*-cycloheptapyrimidin-4-yl]-amine (II-15)**: Prepared in 63% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 1.71 (m, 4H), 1.91 (m, 2H), 3.00 (m, 4H), 7.20 (td, 1H), 7.25 (dd, 1H), 7.49 (dd, 1H), 7.69 (br. t, 2H), 7.74 (m, 1H), 7.79 (d, 1H), 10.35 (m, 1H), 13.00 (br. s, 1H); EI-MS 442.2 (M+H); HPLC-Method A, R_t 3.21 min.

Example 16 **(5-Fluoro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yl]-amine (II-16)**: A solution of compound **II-12** (45mg, 0.087 mmol) in methanol (4.4% HCOOH) was treated with an equal weight of Pd/C (10%) at room temperature for 14 h. The mixture was filtered through celite, the filtrate evaporated, and the crude product was purified by preparative HPLC to provide 15 mg (41%) of the desired product as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ12.9 (s, 1H), 9.52 (s, 1H), 9.32 (s, 2H, TFA-OH), 7.72 (d, 1H), 7.59 (m, 2H), 7.49 (m, 2H), 7.21 (m, 1H), 7.15 (m, 1H), 4.31 (s, 2H), 3.55 (s, 2H), 3.00 (m, 2H) ppm; LC-MS (ES+) 429.20 (M+H); HPLC-Method A, R_t 2.79 min.

Example 17 **(1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-5,6,7,8-tetrahydroquinazolin-4-yl]-amine (II-17)**: Prepared in 58% yield. ^{1}HNMR (500 MHz, DMSO-d6) δ13.0 (s, 1H), 10.3 (s, br, 1H), 7.74 (m, 4H), 7.51 (d, 1H), 7.47 (d, 1H), 7.32 (t, 1H), 7.03 (t, 1H), 2.82 (m, 2H), 2.73 (m, 2H), 1.90 (m, 4H) ppm; LC-MS (ES+) 410.21 (M+H); HPLC-Method A, R_t 2.99 min.

Example 18 **(7-Benzyl-2-(2-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yl)-(5-fluoro-1*H*-indazol-3-yl)-amine (II-18)**: Prepared from compound **B11** in 92% yield. ^{1}HNMR (500 MHz, DMSO-d6) δ12.9 (s, 1H), 10.5 (s, br, 1H), 9.58 (s, 1H, TFA-OH), 7.71 (d, 1H), 7.52 (m, 9H), 7.19 (m, 2H), 4.57 (s, 2H), 4.20 (m, 2H), 3.70 (m, 2H), 3.00 (m, 2H) ppm; LC-MS (ES+) 519.23 (M+H); HPLC-Method A, R_t 3.23 min.

Example 19 **(1*H*-Indazol-3-yl)-[6-methyl-2-(2-trifluoromethyl-phenyl)-pyrimidin-4-yl]-amine (II-19)**: Prepared in 42% yield. Melting point 235-237°C; ^{1}HNMR (500 MHz, DMSO) δ 2.44 (3H, s), 7.09 (1H, J=7.5 Hz, t), 7.40 (1H, J=7.1 Hz, t), 7.49 (1H, J=8.3 Hz, d), 7.70 (3H, m), 7.79 (1H, J=7.3 Hz, t), 7.87 (1H, J=8.3 Hz, d), 8.03 (1H, J=7.7 Hz, d), 10.3 (1H, s), 12.6 (1H, s) ppm; HPLC-Method A, R_t 2.958 min; MS (FIA) 370.2 $(M+H)^+$.

Example 20 **(1*H*-Indazol-3-yl)-[6-phenyl-2-(2-trifluoromethyl-phenyl)-pyrimidin-4-yl]-amine (II-20)**: Prepared in 32% yield. ^{1}HNMR (500 MHz, DMSO) δ 6.94 (1H, J=7.4 Hz, t), 7.24 (1H, J=7.4 Hz, t), 7.33 (1H, J=8.4 Hz, d), 7.42 (3H, m), 7.57 (1H, J=7.3 Hz, t), 7.68 (2H, m), 7.75 (1H, J=7.9 Hz, d), 7.93 (3H, m), 8.18 (1H, br s), 10.45 (1H, br s), 12.5 (1H, br s) ppm; HPLC-Method A, R_t 4.0 min; MS (FIA) 432.2 $(M+H)^+$.

Example 21 **(1*H*-Indazol-3-yl)-[6-(pyridin-4-yl)-2-(2-trifluoromethyl-phenyl)-pyrimidin-4-yl]-amine (II-21)**: Prepared in 12% yield. ^{1}HNMR (500 MHz, DMSO) δ 7.16 (1H, J=7.4 Hz, t), 7.46 (1H, J=7.6 Hz, t), 7.56 (1H, J=8.3 Hz, d), 7.80 (1H, J=7.2 Hz, t), 7.90 (2H, m), 7.97 (1H, J=7.8

Hz, d), 8.09 (1H, br), 8.22 (2H, J=4.9 Hz, d), 8.45 (1H, br s), 8.93 (2H, J=4.8 Hz, d), 10.9 (1H, br s), 12.8 (1H, br s) ppm; HPLC-Method A, R_t 3.307 min; MS (FIA) 433.2 $(M+H)^+$

Example 22 **(1*H*-Indazol-3-yl)-[6-(pyridin-2-yl)-2-(2-trifluoromethyl-phenyl)-pyrimidin-4-yl]-amine (II-22):** Prepared in 42% yield. ^{1}HNMR (500 MHz, DMSO) δ 7.07 (1H, J=7.4 Hz, t), 7.36 (1H, J=7.4 Hz, t), 7.46 (1H, J=7.4 Hz, d), 7.53 (1H, J=5.0 Hz, t), 7.70 (1H, J=7.4 Hz, t), 7.79 (1H, J=7.1 Hz, t), 7.83 (1H, J=7.4 Hz, d), 7.88 (1H, J=7.8 Hz, d), 7.97 (1H, J=7.7 Hz, t), 8.02 (1H, J=5.5 Hz, br d), 8.36 (1H, J=7.8 Hz, d), 8.75 (2H, J=4.1 Hz, d), 10.5 (1H, br s), 12.7 (1H, br s) ppm; HPLC-Method A, R_t 3.677 min; MS (FIA) 433.2 $(M+H)^+$.

Example 23 **[6-(2-Chlorophenyl)-2-(2-trifluoromethyl-phenyl)-pyrimidin-4-yl]-(1*H*-indazol-3-yl)-amine (II-23):** Prepared in 44% yield; ^{1}HNMR (500 MHz, DMSO) δ 7.08 (1H, J=7.5 Hz, t), 7.37 (1H, J=7.5 Hz, t), 7.45 (1H, J=8.4 Hz, d), 7.51 (2H, m), 7.61 (1H, J=7.4, 1.9 Hz, dd), 7.69 (2H, m), 7.79 (2H, J=4.0 Hz, d), 7.86 (3H, J=7.8 Hz, d), 8.04 (2H, J=6.2 Hz, br d), 10.7 (1H, br s), 12.6 (1H, br s) ppm; HPLC-Method A, R_t 3.552 min; MS (FIA) 466.2 $(M+H)^+$.

Example 24 **[5,6-Dimethyl-2-(2-trifluoromethyl-phenyl)-pyrimidin-4-yl]-(1*H*-indazol-3-yl)-amine (II-24):** Prepared in 35% yield; mp 183-186°C; ^{1}HNMR (500 MHz, DMSO) δ 2.14 (3H, s), 2.27 (3H, s), 6.85 (1H, J=7.5 Hz, t), 7.15 (1H, J=7.6 Hz, t), 7.32 (3H, m), 7.38 (1H, J=7.5 Hz, t), 7.42 (1H, J=7.4 Hz, t), 7.53 (1H, J=7.6 Hz, d), 8.88 (1H, s), 12.5 (1H, s) ppm; HPLC-Method A, R_t 2.889 min.; MS (FIA) 384.2 $(M+H)^+$.

Example 25 **[5,6-Dimethyl-2-(2-trifluoromethyl-phenyl)-pyrimidin-4-yl]-(5-fluoro-1*H*-indazol-3-yl)-amine (II-25)**: Prepared in 44% yield. Melting point 160-163°C; ^{1}HNMR (500 MHz, DMSO) δ 2.27 (3H, s), 2.40 (3H, s), 7.16 (2H, m), 7.44 (2H, m), 7.52 (1H, J=7.4 Hz, t), 7.57 (1H, J=7.4 Hz, t), 7.67 (1H, J=7.8 Hz, d), 9.03 (1H, s), 12.75 (1H, s) ppm; *HPLC-Method A, R_t 2.790 min; MS (FIA) 402.2* $(M+H)^+$.

Example 26 **[2-(2-Chlorophenyl)-5,6-dimethyl-pyrimidin-4-yl]-(1*H*-indazol-3-yl)-amine (II-26)**: Prepared in 30% yield. ^{1}HNMR (500 MHz, DMSO) δ 2.14 (3H, s), 2.33 (3H, s), 6.84 (1H, J=7.4 Hz, t), 7.13 (1H, J=7.4 Hz, t), 7.19 (1H, J=6.9 Hz, br t), 7.27 (1H, J=7.4 Hz, d), 7.32 (3H, br m), 7.37 (1H, J=7.1 Hz, d), 10.0 (1H, br), 12.8 (1H, br s) ppm; δ 2.919 min; MS (FIA) 350.1 $(M+H)^+$.

Example 27 **[5,6-Dimethyl-2-(2-trifluoromethyl-phenyl)-pyrimidin-4-yl]-(7-fluoro-1*H*-indazol-3-yl)-amine (II-27)**: Prepared in 92% yield. ^{1}HNMR (500 MHz, DMSO) δ 2.33 (3H, s), 2.50 (3H, s), 6.97 (1H, m), 7.15 (1H, m), 7.30 (1H, *J=8.1 Hz*, d), 7.65 (3H, m), 7.76 (1H, *J=7.5 Hz*, d), 10.0 (1H, s), 13.4 (1H, s) ppm; HPLC-Method A, R_t 3.053 min; MS (FIA) 402.2 $(M+H)^+$.

Example 28 **(5,7-Difluoro-1*H*-indazol-3-yl)-[5,6-Dimethyl-2-(2-trifluoromethyl-phenyl)-pyrimidin-4-yl]-amine (II-28)**: Prepared in 50% yield. ^{1}HNMR (500 MHz, DMSO) δ 2.42 (3H, s), 2.63 (3H, s), 7.22 (1H, J=7.6 Hz, d), 7.38 (1H, J=9.3, 1.7 Hz, dt), 7.71 (1H, m), 7.75 (1H, J=7.0 Hz, d), 7.79 (1H, J=6.7 Hz, d), 7.86 (1H, J=8.0 Hz, d), 10.0 (1H,

s), 13.2 (1H, s) ppm; HPLC-Method A, R_t 3.111 min; MS (FIA) 420.2 $(M+H)^+$.

Example 29 **[2-(2-Chlorophenyl)-5,6-dimethyl-pyrimidin-4-yl]-(5,7-difluoro-1*H*-indazol-3-yl)-amine (II-29)**: Prepared in 58% yield. ^{1}HNMR (500 MHz, DMSO) δ 2.47 (3H, s), 2.66 (3H, s), 7.44 (2H, m), 7.53 (1H, m), 7.64 (3H, m), 10.4 (1H, br), 13.8 (1H, br s) ppm; HPLC-Method A, R_t 2.921 min; MS (FIA) 386.1 $(M+H)^+$.

Example 30 **[2-(2-Chlorophenyl)-5,6-dimethyl-pyrimidin-4-yl]-(7-fluoro-1*H*-indazol-3-yl)-amine (II-30)**: Prepared in 70% yield. ^{1}HNMR (500 MHz, DMSO) δ 2.35 (3H, s), 2.51 (3H, s), 7.03 (1H, J=7.8, 4.4 Hz, dt), 7.22 (1H, m), 7.33 (1H, J=7.4 Hz, t), 7.42 (1H, m), 9.19 (1H, s), 13.3 (1H, s) ppm; HPLC-Method A, R_t 2.859 min; MS (FIA) 368.2 $(M+H)^+$.

Example 31 **[2-(2-Chlorophenyl)-5,6-dimethyl-pyrimidin-4-yl]-(5-fluoro-1*H*-indazol-3-yl)-amine (II-31)**: Prepared in 86% yield. ^{1}HNMR (500 MHz, DMSO) δ 2.49 (3H, s), 2.68 (3H, s), 7.38 (1H, J=9.0 Hz, t), 7.54 (2H, m), 7.67 (4H, m), 10.5 (1H, br), 13.2 (1H, br s) ppm; HPLC-Method A, R_t 2.850 min; MS (FIA) 368.1 $(M+H)^+$.

Example 32 **[2-(2,4-Dichlorophenyl)-5,6-dimethyl-pyrimidin-4-yl]-(1*H*-indazol-3-yl)-amine (II-32)**: Prepared in 52% yield. ^{1}HNMR (500 MHz, DMSO) δ 2.46 (3H, s), 2.64 (3H, s), 7.16 (1H, J=7.5 Hz, t), 7.46 (1H, J=7.6 Hz, t), 7.61 (2H, m), 7.68 (2H, J=8.2 Hz, d), 7.82 (1H, m), 10.2 (1H, br), 13.0 (1H, br s) ppm; HPLC-Method A, R_t 2.983 min; MS (FIA) 384.1 (M+H).

Example 33 **(5-Methyl-2*H*-pyrazol-3-yl)-[2-(2-methylphenyl)-quinazolin-4-yl]-amine (II-33)**: ^{1}HNMR (DMSO) δ 1.21 (3H,s), 2.25 (3H, s), 6.53 (1H, s), 7.38 (4H, m), 7.62 (1H, d), 7.73 (1H, d), 7.81 (1H, d), 7.89 (1H, t), 8.70 (1H, s), 12.20 (1H, s); MS 316.3 $(M+H)^+$.

Example 34 **[2-(2,4-Difluorophenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (II-34)**: ^{1}HNMR (500 MHz, DMSO-d6) δ12.4 (br s, 1H), 10.8 (br s, 1H), 8.58 (d, 1H), 7.97 (m, 1H), 8.36 (m, 1H), 7.85 (m, 1H), 7.60 (m, 1H), 6.62 (s, 1H), 2.30 (s, 3H); MS 338.07 (M+H).

Example 35 **[2-(2,5-Dimethoxyphenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (II-35)**: ^{1}HNMR (500 MHz, DMSO-d6) δ12.5 (br s, 1H), 8.68 (br, 1H), 7.92 (t, J = 7.5 Hz, 1H), 7.86 (d, J = 8.2 Hz, 1H), 7.65 (t, J = 7.5 Hz, 1H), 7.45 (s, 1H), 7.14 (m, 2H), 6.51 (s, 1H), 3.79 (s, 3H), 3.67 (s, 3H), 2.14 (s, 3H); MS 362.2 (M+H).

Example 36 **[2-(2-Chlorophenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (II-36)**: ^{1}HNMR (500 MHz, DMSO-d6) δ11.8 (br, 1H), 8.80 (d, J = 8.3 Hz, 1H), 8.00 (t, J = 7.6 Hz, 1H), 7.82 (d, J = 8.3 Hz, 1H), 7.78 (m, 2H), 7.67 (d, J = 7.8 Hz, 1H), 7.61 (t, J = 7.0 Hz, 1H), 7.55 (t, J = 7.4 Hz, 1H), 6.56 (s, 1H), 2.18 (s, 3H); MS 336.1 (M+H).

Example 37 **[2-(2-Methoxyphenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (II-37)**: ^{1}HNMR (500 MHz, DMSO-d6) δ8.78 (s, br, 1H), 8.00 (t, J = 7.4 Hz, 1H), 7.90 (m, 2H), 7.74 (t, J = 7.5 Hz, 1H), 7.63 (t, J = 7.3 Hz, 1H), 7.30 (d, J = 8.4 Hz, 1H), 7.18 (t, J = 7.5 Hz,

1H), 6.58 (s, br, 1H), 3.90 (s. 3H), 2.21 (s, 3H); MS 332.1 (M+H).

Example 38 **[2-(2,6-Dimethylphenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (II-38)**: ^{1}HNMR (500 MHz, DMSO-d6) δ12.2 (s, br, 2H), 8.88 (d, J = 7.7 Hz, 1H), 8.05 (t, J = 7.7 Hz, 1H), 7.80 (m, 2H), 7.37 (t, J = 7.6 Hz, 1H), 7.21 (d, J = 7.7 Hz, 2H), 6.36 (s, 1H), 2.16 (s, 3H), 2.15 (s, 6H); MS 330.1 (M+H).

Example 39 **[2-(2-Acetylphenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (II-39)**: ^{1}HNMR (500 MHz, DMSO-d6) δ12.35 (s, br, 1H), 8.93 (d, J = 8.4 Hz, 1H), 8.37 (d, J = 8.6 Hz, 1H), 8.20 (d, J = 7.6 Hz, 1H), 8.11 (t, J = 8.0 Hz, 2H), 7.89 (m, 2H), 7.77 (m, 2H), 6.93 (s, 1H), 2.33 (s, 3H), 2.04 (s, 3H) MS 344.1 (M+H).

Example 40 **[2-(2,3-Dimethylphenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (II-40)**: ^{1}HNMR (500 MHz, DMSO-d6) δ12.6 (s, br, 1H), 12.1 (s, br, 1H), 8.91 (d, J = 7.7 Hz, 1H), 8.14 (t, J = 7.2 Hz, 1H), 7.95 (d, J = 8.4 Hz, 1H), 7.89 (t, J = 7.7 Hz, 1H), 7.58 (d, J = 7.6 Hz, 1H), 7.53 (d, J = 7.0 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 6.60 (s, 1H), 2.43 (s, 3H), 2.35 (s, 3H), 2.32 (s, 3H); MS 330.1 (M+H).

Example 41 **(5-Methyl-2*H*-pyrazol-3-yl)-[2-(2-trifluoromethylphenyl)-quinazolin-4-yl]-amine (II-41)**: ^{1}HNMR (500 MHz, DMSO-d6) δ12.3 (s, 1H), 10.5 (s, 1H), 8.77 (d, J = 8.2 Hz, 1H), 7.92 (m, 2H), 7.85 (m, 3H), 7.56 (t, J = 8.1 Hz, 1H), 7.67 (t, J = 7.4 Hz, 1H), 6.63 (s, 1H), 2.27 (s, 3H); MS 370.1 (M+H).

Example 42 **[2-(2-Ethylphenyl)-quinazolin-4-yl]-(5-Methyl-2*H*-pyrazol—3-yl)-amine (II-42):** ^{1}HNMR (500 MHz, DMSO-d6) δ8.80 (m, 1H), 8.02 (s, br, 1H), 7.82 (d, J = 8.4 Hz, 1H), 7.77 (m, 1H), 7.62 (d, J = 7.6 Hz, 1H), 7.54 (m, 1H), 7.41 (m, 2H), 6.40 (s, 1H), 2.75 (q, J = 7.1 Hz, 2H), 2.17 (s, 3H), 0.99 (t, J = 7.5 Hz, 3H); MS 330.1 (M+H).

Example 43 **(2-Biphenyl-2-yl-quinazolin-4-yl)-(5-methyl-2*H*-pyrazol-3-yl)-amine (II-43):** ^{1}HNMR (500 MHz, DMSO-d6) δ 8.76 (d, J = 7.6 Hz, 1H), 8.04 (m, 1H), 7.75 (m, 6H), 7.30 (m, 5H), 5.34 (s, 1H), 2.14 (s, 3H); MS 378.2 (M+H).

Example 44 **[2-(2-Hydroxyphenyl)-quinazolin-4-yl]-(5-Methyl-2*H*-pyrazol—3-yl)-amine (II-44):** ^{1}HNMR (500 MHz, DMSO-d6) δ10.9 (s, br, 1H), 8.62 (d, J = 8.2 Hz, 1H), 8.28 (d, J = 7.9 Hz, 1H), 7.87 (m, 2H), 7.60 (t, J = 7.9 Hz, 1H), 7.37 (t, J = 7.8 Hz, 1H), 6.92 (m, 2H), 6.45 (s, 1H), 2.27 (s, 3H); MS 318.1 (M+H).

Example 45 **[2-(2-Ethoxyphenyl)-quinazolin-4-yl]-(5-Methyl-2*H*-pyrazol—3-yl)-amine (II-45):** ^{1}HNMR (500 MHz, DMSO-d6) δ12.1 (s, br, 1H), 8.75 (d, J = 8.3 Hz, 1H), 7.97 (t, J = 7.8 Hz, 1H), 7.82 (d, J = 8.3 Hz, 1H), 7.78 (d, J = 7.5 Hz, 1H), 7.70 (t, J = 7.8 Hz, 1H), 7.56 (t, J = 7.8 Hz, 1H), 7.22 (d, J = 8.4 Hz, 1H), 7.12 (t, J = 7.6 Hz, 1H), 6.55 (s, 1H), 4.11 (q, J = 6.9 Hz, 2H), 2.16 (s, 3H), 1.22 (t, J = 6.9 Hz, 3H); MS 346.1 (M+H).

Example 46 **[5-(Thiophen-2-yl)-2*H*-pyrazol-3-yl]-[2-(2-trifluoromethylphenyl)-quinazolin-4-yl]-amine (II-46):** ^{1}HNMR (500 MHz, DMSO-d6) δ8.04 (d, J = 8.3 Hz, 1H), 8.05

(dd, J = 7.3, 8.2 Hz, 1H), 7.93 (d, J = 6.5 Hz, 1H), 7.81 (m, 5H), 7.34 (d, J = 5.0 Hz, 1H), 7.25 (m, 1H), 7.00 (m, 1H), 6.87 (s, 1H); MS 438.1 (M+H).

Example 47 **[4-(Thiophen-2-yl)-2*H*-pyrazol-3-yl]-[2-(2-trifluoromethylphenyl)-quinazolin-4-yl]-amine (II-47):** Prepared according to Method B. ^{1}HNMR (500MHz, DMSO-d6) δ 6.97 (m, 1H), 7.08 (m, 1H), 7.27 (m, 1H), 7.36 (m, 1H), 7.66 (m, 2H), 7.77 (m, 3H), 7.83 (m, 1H), 8.00 (m, 1H), 8.18 (s, 1H), 8.62 (d, J = 8.2 Hz, 1H), 10.7 (br. s, 1H); EI-MS 438.1 (M+H); HPLC-Method A, R_t 2.97 min.

Example 48 **(4-Phenyl-2*H*-pyrazol-3-yl)-[2-(2-trifluoromethylphenyl)-quinazolin-4-yl]-amine (II-48):** Prepared according to Method B. ^{1}HNMR (500MHz, DMSO-d6) δ 7.05 (br. s, 1H), 7.14 (t, J = 7.8 Hz, 1H), 7.25 (m, 3H), 7.43 (m, 2H), 7.60 (m, 2H), 7.73 (m, 2H), 7.80 (d, 1H), 7.95 (m, 1H), 8.12 (br. s, 1H), 8.60 (m, 1H), 10.6 (br. s, 1H); EI-MS 432.2 (M+H); HPLC-Method A, R_t 3.04 min.

Example 49 **(5-*tert*-Butyl-2*H*-pyrazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-49):** ^{1}HNMR (500 MHz, DMSO-d6) δ 8.76 (d, J = 8.3 Hz, 1H), 7.94 (m, 2H), 7.79 (m, 4H), 7.70 (t, J = 7.6 Hz, 1H), 6.51 (s, 1H), 1.16 (s, 9H); MS 412.2 (M+H).

Example 50 **(5-Phenyl-2*H*-pyrazol-3-yl)-[2-(2-trifluoromethylphenyl)-quinazolin-4-yl]-amine (II-50):** ^{1}HNMR (500MHz, DMSO-d6) δ 7.09 (s, 1H), 7.36 (td, J = 7.8, 1.1 Hz, 1H), 7.46 (t, J = 7.8 Hz, 2H), 7.65 (br. d, J = 8.1 Hz, 2H), 7.78 (m, 2H), 7.90 (m, 4H), 7.95 (d, J = 7.7 Hz, 1H), 8.00 (t, J = 7.8 Hz, 1H), 8.81 (d, J = 8.6 Hz, 1H), 11.29 (br. s, 1H); EI-MS 432.1 (M+H); HPLC-Method A, R_t 3.24 min.

Example 51 **(4,5-Diphenyl-2*H*-pyrazol-3-yl)-[2-(2-trifluoromethylphenyl)-quinazolin-4-yl]-amine (II-51):** ^{1}HNMR (500MHz, DMSO-d6) δ 7.13 (m, 1H), 7.18 (m, 5H), 7.36 (m, 5H), 7.62 (m, 3H), 7.73 (m, 2H), 7.85 (m, 1H), 8.48 (d, J = 8.7 Hz, 1H), 10.02 (s, 1H), 13.19 (s, 1H); EI-MS 508.2 (M+H); HPLC-Method A, R_t 3.39 min.

Example 52 **(4-Carbamoyl-2*H*-pyrazol-3-yl)-[2-(2-trifluoromethylphenyl)-quinazolin-4-yl]-amine (II-52):** Prepared in 40% yield. ^{1}HNMR (500MHz, DMSO-d6): δ 12.85 (s, 1H), 12.77 (s, 1H), 11.80 (s, 1H), 10.80 (s, 1H), 8.35-7.42 (m, 9H); MS 399.13 (M+H) HPLC-Method A, R_t 2.782 min.

Example 53 **(2*H*-Pyrazol-3-yl)-[2-(2-trifluoromethylphenyl)-quinazolin-4-yl]-amine (II-53):** Prepared in 38% yield. ^{1}HNMR (500 MHz, DMSO-d6) δ 12.52 (s, 1H), 10.65 (s, 1H), 8.75 (d, 1H), 7.91-7.68 (m, 8H), 6.87 (s, 1H). MS: (M+H) 356.17. HPLC-Method A, R_t 2.798 min.

Example 54 **(5-Hydroxy-2*H*-pyrazol-3-yl)-[2-(2-trifluoromethylphenyl)-quinazolin-4-yl]-amine (II-54):** Prepared in 36% yield; ^{1}HNMR (500 MHz, DMSO-d6) δ 10.61 (s, 1H), 8.75 (s, 1H), 8.03-7.75 (m, 9H), 5.97 (s, 1H); MS 372.18 (M+H); HPLC-Method A, R_t 2.766 min.

Example 55 **(5-Cyclopropyl-2*H*-pyrazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-55):** Prepared in 30% yield. ^{1}HNMR (500 MHz, DMSO-d6) δ12.21 (s, 1H), 10.45 (s, 1H), 8.68 (s, 1H), 7.89-7.45 (m, 8H),

6.48 (s, 1H), 0.89 (m, 2H), 0.62 (s, 2H). MS 396.18 (M+H); HPLC-Method A, R_t 3.069 min.

Example 56 **(5-Methoxymethyl-2*H*-pyrazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-56):** Prepared in 33% yield; ^{1}HNMR (500 MHz, DMSO-d6) δ 12.51 (s, 1H), 10.48 (s, 1H), 8.60 (s, 1H), 7.81-7.55 (m, 7H), 6.71 (s, 1H), 4.28 (s, 2H), 3.18 (s, 3H). MS 400.19 (M+H): HPLC-Method A, R_t 2.881 min.

Example 57 **(1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-57):** Prepared to afford 51 mg (78% yield) as pale yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ12.7 (s, 1H), 10.4 (s, 1H), 8.55 (d, 1H), 7.81 (t, 1H), 7.71 (d, 1H), 7.61 (d, 1H), 7.58 (t, 1H), 7.46 (m, 4H), 7.36 (d, 1H), 7.22 (t, 1H), 6.91 (t, 1H) ppm; LC-MS (ES+) 406.16 (M+H), (ES-) 404.19 (M-H); HPLC-Method A, R_t 3.00 min.

Example 58 **(4-Chloro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-58):** Prepared in DMF (70% yield) as pale yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.3 (s, br, 1H), 10.9 (s, br, 1H), 8.60 (d, 1H), 7.97 (t, 1H), 7.81 (d, 1H), 7.75 (t, 1H), 7.67 (d, 1H), 7.63 (dd, 1H), 7.57 (m, 2H), 7.43 (d, 1H), 7.28 (dd, 1H), 7.08 (d, 1H) ppm; LC-MS (ES+) 440.10 (M+H), (ES-) 438.12 (M-H); HPLC-Method A, R_t 3.08 min.

Example 59 **(5-Fluoro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-59):** Prepared in DMF (34% yield) as pale yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.0 (s, 1H), 10.6 (s, 1H), 8.72 (d, 1H), 7.99 (t, 1H), 7.89 (d, 1H), 7.79 (d, 1H), 7.75 (t, 1H), 7.68 (m, 3H), 7.56 (dd, 1H), 7.39 (d, 1H), 7.28 (t,

1H) ppm; LC-MS (ES+) 424.12 (M+H), (ES-) m/e= 422.13 (M-H); HPLC-Method A, R_t 3.05 min.

Example 60 **(7-Fluoro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-60):** Prepared in DMF (51% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.4 (s, 1H), 10.6 (s, 1H), 8.68 (d, 1H), 7.95 (t, 1H), 7.85 (d, 1H), 7.72 (m, 2H), 7.63 (m, 2H), 7.58 (m, 1H), 7.43 (d, 1H), 7.18 (dd, 1H), 7.00 (m, 1H) ppm; LC-MS (ES+) 424.11 (M+H), (ES-) 422.15 (M-H); HPLC-Method A, R_t 3.06 min.

Example 61 **(5-Methyl-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-61):** *Prepared in DMF (81% yield) as yellow solid.* ^{1}*HNMR (500* MHz, DMSO-d6) δ13.0 (s, br, 1H), 8.79 (br, 1H), 8.11 (br, 1H), 7.96 (d, 1H), 7.82 (m, 5H), 7.46 (s, 1H), 7.41 (d, 1H), 7.20 (d, 1H), 2.33 (s, 3H) ppm; MS (ES+) 420.15 (M+H), (ES-) 418.17 (M-H); HPLC-Method A, R_t 3.07 min.

Example 62 **[2-(2,6-Dichloro-phenyl)-quinazolin-4-yl]-(5-fluoro-1*H*-indazol-3-yl)-amine (II-62):** Prepared in DMF (37% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.0 (s, 1H), 10.8 (s, 1H), 8.72 (d, 1H), 7.97 (t, 1H), 7.90 (d, 1H), 7.75 (t, 1H), 7.53 (m, 3H), 7.43 (t, 1H), 7.35 (d, 1H), 7.23 (t, 1H) ppm; LCMS (ES+) 424.08 (M+H), (ES-) 422.10 (M-H); HPLC-Method A, R_t 3.06 min.

Example 63 **[2-(2-Chloro-phenyl)-quinazolin-4-yl]-(1*H*-indazol-3-yl)-amine (II-63):** Prepared in 91% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 7.06 (t, 1H), 7.36 (t, 1H), 7.39 (t, 1H), 7.52 (m, 3H), 7.62 (d, 1H), 7.72 (d, 1H), 7.82 (m, 1H), 7.90 (d, 1H), 8.05 (m, 1H), 8.76 (d, 1H), 11.5 (m, 1H), 13.02 (s, 1H); EI-MS 372.1 (M+1); HPLC-Method A, R_t

2.93 min.

Example 64 **(5-Trifluoromethyl-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-64):** Prepared in DMF (57% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.4 (s, br, 1H), 11.4 (br, 1H), 8.72 (d, 1H), 8.12 (s, 1H), 7.98 (t, 1H), 7.83 (d, 1H), 7.76 (d, 1H), 7.73 (dd, 1H), 7.60 (m, 4H), 7.52 (d, 1H) ppm; LC-MS (ES+) 474.12 (M+H), (ES-) 472.17 (M-H); HPLC-Method A, R_t 3.25 min.

Example 65 **(4-Trifluoromethyl-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-65):** Prepared in DMF (8% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.7 (s, br, 1H), 11.2 (br, 1H), 8.70 (d, 1H), 8.05 (s, 1H), 7.85 (m, 3H), 7.65 (m, 4H), 7.51 (m, 2H) ppm; LC-MS (ES+) 474.13 (M+H), (ES-) 472.17 (M-H); HPLC-Method A, R_t 3.15 min.

Example 66 **[2-(2,6-Dichloro-phenyl)-quinazolin-4-yl]-(1*H*-indazol-3-yl)-amine (II-66):** Prepared in DMF (30% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ12.9 (s, 1H), 11.1 (s, 1H), 8.69 (d, 1H), 7.95 (t, 1H), 7.82 (d, 1H), 7.73 (t, 1H), 7.56 (d, 1H), 7.47 (s, 1H), 7.45 (s, 1H), 7.39 (m, 2H), 7.26 (t, 1H), 6.92 (t, 1H) ppm; LC-MS (ES+) 406.11 (M+H), (ES-) 404.12 (M-H); HPLC-Method A, R_t 3.00 min.

Example 67 **(1*H*-indazol-3-yl)-[2-(2-methyl-phenyl)-quinazolin-4-yl]-amine (II-67):** Prepared in 55% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 2.15 (s, 3H), 7.09 (t, 1H), 7.26 (d, 1H), 7.31 (t, 1H), 7.39 (t, 1H), 7.42 (m, 1H), 7.55 (d 1H), 7.64 (d, 1H), 7.74 (d, 1H), 7.89 (m, 1H), 7.96

(d, 1H), 8.10 (m, 1H), 8.81 (d, 1H), 12.0 (m, 1H), 13.18 (s, 1H); EI-MS 352.2 (M+1); HPLC-Method A, R_t 2.93 min.

Example 68 **(7-Trifluoromethyl-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-68):** Prepared in DMF (75% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.5 (s, br, 1H), 11.2 (s, br, 1H), 8.68 (d, 1H), 7.97 (t, 1H), 7.92 (d, 1H), 7.82 (d, 1H), 7.74 (t, 1H), 7.70 (d, 1H), 7.68 (d, 1H), 7.64 (m, 2H), 7.57 (m, 1H), 7.14 (t, 1H) ppm; LC-MS (ES+) 474.11 (M+H), (ES-) 472.14 (M-H); HPLC-Method A, R_t 3.24 min.

Example 69 **(6-Trifluoromethyl-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-69):** Prepared by Method B in DMF (78% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ 13.4 (s, br, 1H), 11.1 (s, br, 1H), 8.67 (d, 1H), 7.95 (t, 1H), 7.82 (m, 3H), 7.72 (m, 2H), 7.63 (m, 2H), 7.57 (t, 1H), 7.23 (d, 1H) ppm; LC-MS (ES+) 474.12 (M+H), (ES-) 472.15 (M-H); HPLC-Method A, R_t 3.28 min.

Example 70 **(5-Nitro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-70):** Prepared in DMF (82% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.6 (s, br, 1H), 11.4 (s, br, 1H), 8.75 (s, 1H), 8.72 (d, 1H), 8.09 (dd, 1H), 7.98 (t, 1H), 7.83 (d, 1H), 7.75 (t, 1H), 7.70 (m, 2H), 7.61 (m, 3H) ppm; LC-MS (ES+) 451.14 (M+H), (ES-) 449.12 (M-H); HPLC-Method A, R_t 3.02 min.

Example 71 **(5,7-Difluoro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-71):** Prepared in DMF (60% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.7 (s, br, 1H), 11.2 (s, br, 1H), 8.73

(d, 1H), 8.03 (t, 1H), 7.88 (d, 1H), 7.80 (m, 2H), 7.70 (m, 3H), 7.32 (m, 2H) ppm; LC-MS (ES+) 442.14 (M+H), (ES-) 440.14 (M-H); HPLC-Method A, R_t 3.11 min.

Example 72 **(4-Pyrrol-1-yl-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-72)**: Prepared in DMF (33% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.4 (s, br, 1H), 11.0 (s, br, 1H), 8.53 (d, 1H), 7.98 (t, 1H), 7.75 (m, 4H), 7.62 (m, 2H), 7.52 (d, 1H), 7.43 (t, 1H), 7.05 (d, 1H), 6.80 (s, 2H), 5.61 (s, 2H) ppm; LC-MS (ES+) 471.18 (M+H), (ES-) 469.18 (M-H); HPLC-Method A, R_t 3.12 min.

Example 73 **(5-Amino-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-73)**: A solution of compound **II-70** (70 mg, 0.16 mmol) in MeOH (2 mL) was treated with Raney Ni until solution was colorless (about 1.5 g Raney Ni was added). After stirring at room temperature for 40 min, the mixture was filtered through celite, the resulting celite was washed with MeOH (5 times), and the solvent was evaporated *in vacuo* to provide a crude product that was then purified by HPLC to give the title compound as a yellow solid (10 mg, 15%). m.p. 221-223°C; ^{1}HNMR (500 MHz, DMSO-d6) δ13.2 (s, br, 1H), 10.7 (s, br, 1H), 9.80 (br, 2H), 8.68 (d, 1H), 7.97 (t, 1H), 7.87 (d, 1H), 7.75 (m, 2H), 7.65 (m, 5H), 7.30 (d, 1H) ppm; MS (ES+) 421.16 (M+H), (ES-) 419.17 (M-H); HPLC-Method A, R_t 2.41 min.

Example 74 **[2-(2-Chloro-phenyl)-quinazolin-4-yl]-(7-fluoro-1*H*-indazol-3-yl)-amine (II-74)**: Prepared in DMF (35% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.7 (s, 1H), 11.7 (s, br, 1H), 8.80 (d, 1H), 8.15 (t, 1H), 7.99 (d, 1H), 7.88 (t, 1H), 7.68 (d, 1H), 7.60 (m,

2H), 7.53 (t, 1H), 7.46 (t, 1H), 7.25 (dd, 1H), 7.04 (m, 1H) ppm; LC-MS (ES+) 390.16 (M+H); HPLC-Method A, R_t 3.00 min.

Example 75 **[2-(2-Chloro-phenyl)-quinazolin-4-yl]-(5-fluoro-1*H*-indazol-3-yl)-amine (II-75)**: Prepared in DMF. ^{1}HNMR (500 MHz, DMSO-d6) δ13.2 (s, 1H), 11.7 (s, br, 1H), 8.80 (d, 1H), 8.10 (t, 1H), 7.91 (m, 2H), 7.70 (d, 1H), 7.58 (m, 4H), 7.50 (t, 1H), 7.29 (t, 1H) ppm; LC-MS (ES+) 390.17 (M+H); HPLC-Method A, R_t 3.00 min.

Example 76 **[2-(2-Chloro-phenyl)-quinazolin-4-yl]-(5,7-difluoro-1*H*-indazol-3-yl)-amine (II-76)**: Prepared in DMF (55% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.8 (s, 1H), 11.5 (s, br, 1H), 8.76 (d, 1H), 8.08 (t, 1H), 7.93 (d, 1H), 7.84 (t, 1H), 7.64 (d, 1H), 7.55 (d, 1H), 7.50 (t, 1H), 7.44 (m, 2H), 7.36 (t, 1H) ppm; LC-MS (ES+) 408.15 (M+H), (ES-) 406.17 (M-H); HPLC-Method A, R_t 3.08 min.

Example 77 **[2-(2-Chloro-phenyl)-quinazolin-4-yl]-(5-trifluoromethyl-1*H*-indazol-3-yl)-amine (II-77)**: Prepared in DMF (66% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.5 (s, 1H), 11.4 (s, br, 1H), 8.79 (d, 1H), 8.29 (s, 1H), 8.07 (t, 1H), 7.93 (d, 1H), 7.84 (t, 1H), 7.72 (d, 1H), 7.63 (d, 2H), 7.53 (d, 1H), 7.48 (t, 1H), 7.36 (t, 1H) ppm; LC-MS (ES+): m/e= 440.16 (M+H); (ES-): m/e= 438.18 (M-H); HPLC-Method A, R_t 3.22 min.

Example 78 **[2-(2-cyano-phenyl)-quinazolin-4-yl]-(1*H*-indazol-3-yl)-amine (II-78)**: Prepared in 13% yield. ^{1}H-NMR (500 MHz, DMSO) δ 12.9 (br, 1H), 10.8 (br, 1H), 8.73 (br s, 1H), 7.97 (m, 4H), 7.74 (m, 1H), 7.5 (m, 4H), 7.42

(m, 1H), 7.08 (m, 1H) ppm; MS (FIA) 363.2 (M+H); HPLC-Method A, R_t 2.971 min.

Example 79 **(5-Bromo-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-79):** Prepared in DMF (64% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.4 (s, 1H), 11.6 (s, br, 1H), 8.93 (d, 1H), 8.21 (t, 1H), 8.14 (s, 1H), 8.05 (d, 1H), 7.95 (m, 4H), 7.86 (t, 1H), 7.65 (d, 1H), 7.59 (d, 1H) ppm; MS (ES+) 486.10 (M+H), (ES-) 484.09 (M-H); HPLC-Method A, R_t 3.22 min.

Example 80 **(6-Chloro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-80):** Prepared in DMF (94% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.1 (s, 1H), 11.2 (s, br, 1H), 8.73 (d, 1H), 8.03 (t, 1H), 7.87 (d, 1H), 7.79 (m, 2H), 7.73 (m, 2H), 7.67 (m, 2H), 7.58 (s, 1H), 7.04 (dd, 1H) ppm. LC-MS (ES+) 440.14 (M+H), (ES-) 438.16 (M-H); HPLC-Method A, R_t 3.25 min.

Example 81 **(7-Fluoro-6-trifluoromethyl-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-81):** Prepared in DMF (30% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.9 (s, 1H), 11.0 (s, br, 1H), 8.64 (d, 1H), 7.94 (t, 1H), 7.81 (d, 1H), 7.71 (m, 2H), 7.60 (m, 4H), 7.20 (dd, 1H) ppm. LC-MS (ES+) 492.18 (M+H), (ES-) 490.18 (M-H); HPLC-Method A, R_t 3.44 min.

Example 82 **(6-Bromo-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-82):** Prepared in DMF (40% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.1 (s, 1H), 11.2 (s, br, 1H), 8.73 (d, 1H), 8.03 (t, 1H), 7.87 (d, 1H), 7.80 (m, 2H), 7.73 (m,

3H), 7.67 (m, 1H), 7.61 (d, 1H), 7.15 (dd, 1H) ppm; MS (ES+) 486.07 (M+H); HPLC-Method A, R_t 3.28 min.

Example 83 **[2-(2,4-Bis-trifluoromethyl-phenyl)-quinazolin-4-yl]-(5,7-difluoro-1*H*-indazol-3-yl)-amine (II-83)**: Prepared in DMF in 28% yield. ^{1}HNMR (500MHz, MeOH-d4) δ 8.81 (d, J=8.4Hz, 1H), 8.35-8.20 (m, 3H), 8.19-7.96 (m, 3H), 7.40-7.34 (m, 1H), 7.29-7.14 (m, 1H); LC-MS (ES+) 510.14 (M+H); HPLC-Method C, R_t 8.29 min.

Example 84 **(5,7-Difluoro-1*H*-indazol-3-yl)-[2-(4-fluoro-2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-84)**: Prepared in 48% yield. ^{1}HNMR (500MHz, MeOH-d4) δ 8.74-8.63 (m, 1H), 8.23-8.10 (m, 1H), 7.99-7.90 (m, 2H), 7.89-7.80 (m, 1H), 7.71-7.61 (m, 1H), 7.61-7.50 (m, 1H), 7.24-7.15 (m, 1H), 7.14-7.02 (m, 1H); LC-MS (ES+) 460.14 (M+H); HPLC-Method C, R_t 7.59 min.

Example 85 **[2-(2-Bromo-phenyl)-quinazolin-4-yl]-(5,7-difluoro-1*H*-indazol-3-yl)-amine (II-85)**: Prepared in THF (21% yield). ^{1}HNMR (500MHz, MeOH-d4) δ 8.81 (d, J=8.4Hz, 1H), 8.35-8.20 (m, 3H), 8.19-7.96 (m, 3H), 7.40-7.34 (m, 1H), 7.29-7.14 (m, 1H); LC-MS (ES+) 510.14 (M+H); HPLC-Method C, R_t 8.29 min.

Example 86 **(5,7-Difluoro-1*H*-indazol-3-yl)-[2-(5-fluoro-2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-86)**: Prepared in THF (26% yield). ^{1}HNMR (500MHz, MeOH-d4) δ 8.62 (d, J=8.4Hz, 1H), 8.16-8.02 (m, 1H), 7.96-7.73 (m, 3H), 7.59-7.48 (m, 1H), 7.48-7.35 (m, 1H), 7.21-7.09 (m, 1H), 7.09-6.89 (m, 1H); LC-MS (ES+) 460.16 (M+H); HPLC-Method C, R_t 7.28 min.

Example 87 **[2-(2,4-Dichloro-phenyl)-quinazolin-4-yl]-(5,7-Difluoro-1*H*-indazol-3-yl)-amine (II-87)**: Prepared in THF (16% yield). ^{1}HNMR (500MHz, MeOH-d4) δ8.81 (d, J=8.4Hz, 1H), 8.35-8.20 (m, 3H), 8.19-7.96 (m, 3H), 7.40-7.34 (m, 1H), 7.29-7.14 (m, 1H); LC-MS (ES+) 510.14 (M+H); HPLC-Method C, R_t 8.29 min.

Example 88 **[2-(2-Chloro-5-trifluoromethyl-phenyl)-quinazolin-4-yl]-(5,7-Difluoro-1*H*-indazol-3-yl)-amine (II-88)**: Prepared in THF (33% yield). ^{1}HNMR (500MHz, DMSO-d6) δ 10.76 (s, 1H), 8.66 (d, J=8.3Hz, 1H), 8.06-7.84 (m, 3H), 7.81-7.63 (m, 3H), 7.48-7.16 (m, 2H); LC-MS (ES+) 476.16 (M+H); HPLC-Method C, R_t 19.28 min.

Example 89 **(4-Fluoro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-89)**: Prepared in NMP (79% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.2 (s, 1H), 10.8 (s, br, 1H), 8.63 (d, 1H), 7.97 (t, 1H), 7.85 (d, 1H), 7.74 (m, 2H), 7.64 (t, 1H), 7.57 (m, 2H), 7.32 (m, 2H), 6.82 (m, 1H) ppm; LC-MS (ES+) 424.17 (M+H); HPLC-Method A, R_t 3.14 min.

Example 90 **(1*H*-Indazol-3-yl)-[8-methoxy-2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-90)**: Prepared using THF as solvent to afford the title compound as a TFA salt (23% yield). HPLC-Method A, R_t 2.97 min (95%); ^{1}HNMR (DMSO-d6, 500 MHz) δ 12.9 (1H, bs), 11.0 - 10.7(1H, bs), 8.25 (1H, m), 7.75-7.50 (8H, s), 7.30 (1H, m), 6.90 (1H, m), 4.0 (3H, s); MS (m/z) 436.2 (M+H).

Example 91 **(5-Fluoro-1*H*-indazol-3-yl)-[8-methoxy-2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-91)**: Prepared using TFA as solvent to afford the title compound as a TFA salt (23% yield). HPLC-Method A, R_t

3.10 min. (99%); ^{1}HNMR (DMSO-d6, 500 MHz): 13.0 (1H, bs), 11.0 - 10.7(1H, bs), 8.25 (1H, m), 7.75-7.50 (7H, m), 7.35 (1H, m), 7.25 (1H, m), 4.0 (3H, s); MS (m/z) 454.2 (M+H).

Example 92 **(7-Fluoro-1*H*-indazol-3-yl)-[8-methoxy-2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-92)**: Prepared using THF as solvent to afford the title compound as a TFA salt (98 mg, 58% yield). HPLC-Method A, R_t 3.20 min (92%); ^{1}HNMR (DMSO-d6, 500 MHz) δ 13.45 (1H, bs), 11.0 - 10.7(1H, bs), 8.25 (1H, m), 7.75-7.60 (5H, m), 7.50 (1H, m), 7.40 (1H, m), 7.15 (1H, m), 6.95 (1H, m) 4.0 (3H, s); MS (m/z) 454.2 (M+H).

Example 93 **(5,7-Difluoro-1*H*-indazol-3-yl)-[8-methoxy-2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-93)**: Prepared using THF as solvent to afford the title compound as a TFA salt (36% yield). HPLC-Method A, R_t 3.27 min. (95%); ^{1}HNMR (DMSO-d6, 500 MHz): 13.65 (1H, bs), 11.0 - 10.7(1H, bs), 8.22 (1H, m), 7.75-7.60 (5H, m), 7.40 (1H, m), 7.35 (1H, m), 7.19 (1H, m), 4.0 (3H, s); MS (m/z) 472.2 (M+H).

Example 94 **[2-(2-Chloro-pyridin-3-yl)-quinazolin-4-yl]-(5,7-Difluoro-1*H*-indazol-3-yl)-amine (II-94)**: Prepared in DMF. ^{1}HNMR (500MHz, DMSO-d6) δ 13.62 (br s, 1H, 11.06-10.71 (m, 1H), 8.16-7.70 (m, 4H), 7.60-7.09 (m, 3H); LC-MS (ES+) 409.14 (M+H); HPLC-Method A, R_t 2.89 min.

Example 95 **[2-(2-Chloro-4-nitro-phenyl)-quinazolin-4-yl]-(5,7-difluoro-1*H*-indazol-3-yl)-amine (II-95)**: Prepared in THF. ^{1}HNMR (500MHz, DMSO-d6) δ 13.35 (s, 1H), 10.74 (s, 1H), 8.67 (d, J=8.4Hz, 1H), 8.29 (d, J=2.05Hz, 1H), 8.18-

8.08 (m, 1H), 8.07-7.60 (m, 4H), 7.53-7.10 (m, 2H). LC-MS (ES+) 453.15 (M+H); HPLC-Method D, R_t 3.63 min.

Example 96 **[2-(4-Amino-2-chloro-phenyl)-quinazolin-4-yl]-(5,7-Difluoro-1*H*-indazol-3-yl)-amine (II-96):** A solution of compound **II-95** (8mg, 0.018mmol) and tin chloride dihydrate (22mg, 0.1mmol) in ethanol (2mL) was heated at 100°C for 24h. The reaction was diluted with EtOAc (10mL), washed with 1N NaOH solution (2x10mL), brine, and dried over anhydrous sodium sulfate to afford the crude product. Purification was achieved by flash chromatography on silica gel (eluting with 1-3% MeOH in CH_2Cl_2.) The title compound was isolated as pale yellow solid (1.2mg, 16% yield). LC-MS (ES+) 423.12 (M+H), HPLC-Method C, R_t 13.78 min.

Example 97 **(4,5,6,7-Tetrahydro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-97):** Prepared in 34% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 1.58 (m, 2H), 1.66 (m, 2H), 2.24 (m, 2H), 2.54 (m 2H), 7.63 (m, 3H), 7.71 (t, 1H), 7.75 (d, 1H), 7.78 (d, 1H), 7.85 (t, 1H), 8.53 (d, 1H), 9.99 (s, 1H), 12.09 (s, 1H); EI-MS 410.2 (M+1); HPLC-Method A, R_t 3.05 min.

Example 98 **(1*H*-Pyrazolo[4,3-b]pyridin-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-98):** Prepared in DMF (37% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.1 (s, br, 1H), 11.2 (s, br, 1H), 8.73 (d, 1H), 8.54 (dd, 1H), 8.12 (d, 1H), 8.06 (t, 1H), 7.90 (d, 1H), 7.84 (t, 1H), 7.75 (d, 1H), 7.69 (m, 2H), 7.65 (t, 1H), 7.47 (dd, 1H) ppm; LC-MS (ES+) 407.18 (M+H); HPLC-Method A, R_t 2.77 min.

Example 99 **(1*H*-Pyrazolo[3,4-b]pyridin-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-99)**: Prepared in DMF (45% yield). ^{1}HNMR (500 MHz, DMSO-d6) δ13.5 (s, br, 1H), 11.3 (s, br, 1H), 8.78 (d, 1H), 8.49 (d, 1H), 8.17 (d, 1H), 8.03 (t, 1H), 7.89 (d, 1H), 7.80 (m, 2H), 7.74 (m, 2H), 7.68 (m, 1H), 7.08 (dd, 1H) ppm. MS (ES+) 407.16 (M+H), (ES-) 405.16 (M-H); HPLC-Method A, R_t 2.80 min.

Example 100 **(6-Methyl-1*H*-pyrazolo[3,4-b]pyridin-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-100)**: Prepared in DMF (11% yield). ^{1}HNMR (500 MHz, DMSO-d6) δ13.2 (s, br, 1H), 10.8 (s, br, 1H), 8.57 (d, 1H), 7.95 (t, 1H), 7.82 (d, 1H), 7.72 (t, 1H), 7.65 (m, 2H), 7.58 (m, 2H), 2.44 (s, 3H, buried by DMSO), 2.20 (s, 3H) ppm. LC-MS (ES+) 435.22 (M+H), (ES-) 433.25 (M-H); HPLC-Method A, R_t 2.94 min.

Example 101 **(6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine II-101**: Prepared in DMF (6% yield). ^{1}HNMR (500 MHz, DMSO-d6) δ12.6 (s, 1H), 11.0 (s, br, 1H), 8.60 (d, 1H), 7.95 (t, 1H), 7.88 (d, 1H), 7.80 (d, 1H), 7.68 (m, 4H), 7.40 (s, 3H), 7.22 (s, 2H), 6.61 (s, 1H) ppm. LC-MS (ES+) 500.21 (M+H), (ES-) 498.16 (M-H); HPLC-Method A, R_t 3.00 min.

Example 103 **[6-Methyl-2-(2-trifluoromethoxy-phenyl)-pyrimidin-4-yl]-(5-phenyl-2H-pyrazol-3-yl)-amine (II-103)**: MS 412.13 (M+H); HPLC-Method E R_t 1.248 min.

Example 104 **(5-Furan-2-yl-2H-pyrazol-3-yl)-[6-methyl-2-(2-trifluoromethoxy-phenyl)-pyrimidin-4-yl]-amine (II-104)**; MS 402.12 (M+H); HPLC-Method E, R_t 1.188 min.

Example 105 **[6-Ethyl-2-(2-trifluoromethoxy-phenyl)-pyrimidin-4-yl]-(5-methyl-2H-pyrazol-3-yl)-amine (II-105)**: MS 364.14 (M+H); HPLC-Method E, R_t 1.112 min.

Example 106 **[2-(2-Chloro-phenyl)-pyrido[2,3-*d*]pyrimidin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (II-106)**: ^{1}HNMR (500 MHz, DMSO) δ 12.23 (s, 1H), 10.78 (s, 1H), 7.73-7.47 (m, 7H), 6.72 (s, 1H), 2.21 (s, 3H). MS: (M+H) 337.02. HPLC-Method A, R_t 2.783 min.

Example 107 **(5-Fluoro-1H-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-6,7-dihydro-5H-cyclopentapyrimidin-4-yl]-amine (II-107)**: Prepared in 68% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 2.16 (t, 2H), 2.88 (m, 2H), 2.98 (t, 2H), 7.21 (td, 1H), 7.29 (dd, 1H), 7.50 (dd, 1H), 7.65 (t, 1H), 7.67 (t, 1H), 7.73 (t, 1H), 7.79 (d, 1H), 10.22 (br. s, 1H), 12.99 (br. s, 1H); EI-MS 414.2 (M+H); HPLC-Method A, R_t 2.92 min.

Example 108 **(1*H*-Indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-pyrido[2,3-*d*]pyrimidin-4-yl]-amine (II-108)**: HPLC-Method A, R_t 2.78 min. (95%); ^{1}HNMR (DMSO-d6, 500 MHz): 12.95 (1H, bs), 11.45 δ 11.15(1H, bs), 9.20 (2H, m), 7.85-7.70 (2H, m), 7.70-7.55 (4H, m), 7.50 (1H, m), 7.35 (1H, m), 7.05 (1H, m); MS (m/z) 407.03 (M+H).

Example 109 **(5,7-Difluoro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-pyrido[2,3-*d*]pyrimidin-4-yl]-amine (II-109)**: Yellow, di-TFA salt (25% yield). HPLC (Method A) 3.10 min. (95%); ^{1}HNMR (DMSO-d6, 500 MHz): 13.8-13.6 (1H, bs), 11.4 - 11.2(1H, bs), 9.15 (2H, m), 7.85-7.75 (2H, m), 7.75-7.62 (3H, m), 7.32 (2H, m); MS (m/z) 442.98 (M+H).

Example 110 **[2-(2-Chloro-phenyl)-pyrido[2,3-*d*]pyrimidin-4-yl]-(1*H*-indazol-3-yl)-amine (II-110):** Prepared from 2-aminonicotinic acid and 2-chlorobenzoyl chloride afforded the title compound as a di-TFA salt (28% yield). HPLC-Method A, R_t 2.85 min. (95%); ^{1}HNMR (DMSO-d6, 500 MHz): 12.90 (1H, s), 11.10 - 10.90 (1H, bs), 9.05 (2H, m), 7.75-7.60 (2H, m), 7.51 (1H, m), 7.45-7.25 (5H, m), 6.95 (1H, m); MS (m/z) 372.99(M+H).

Example 111 **(5-Fluoro-1H-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-5,6,7,8,9,10-hexahydro-cyclooctapyrimidin-4-yl]-amine (II-111).** Prepared in 43% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 1.46 (m, 2H), 1.53 (m, 2H), 1.77 (m, 4H), 2.95 (m, 2H), 3.04 (m, 2H), 7.22 (m, 2H), 7.50 (dd, 1H), 7.72 (m, 3H), 7.80 (d, 1H), 10.5 (m, 1H), 13.05 (br s, 1H); EI-MS 456.2 (M+H); HPLC-Method C, R_t 11.93 min.

Example 112 **[2-(2-Chloro-phenyl)-6,7-dihydro-5*H*-cyclopentapyrimidin-4-yl]-(5-fluoro-1*H*-indazol-3-yl)-amine (II-112):** Prepared in 67% yield. ^{1}HNMR (500MHz, DMSO-d6) δ2.18 (m, 2H), 2.89 (m, 2H), 3.02 (t, 2H), 7.24 (td, 1H), 7.42 (m, 2H), 7.49 (td, 1H), 7.52 (dd, 1H), 7.54 (d, 1H), 7.57 (dd, 1H), 10.50 (br. s, 1H), 13.06 (br. s, 1H); EI-MS 380.1 (M+1); HPLC-Method C, R_t 9.68 min.

Example 113 **(1H-Indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-6,7-dihydro-5H-cyclopentapyrimidin-4-yl]-amine (II-113):** Prepared in 37% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 2.65 (m, 2H), 2.85 (m, 2H), 2.99 (t, 2H), 7.02 (t, 1H), 7.32 (t, 1H), 7.47 (d, 1H), 7.55 (d, 1H), 7.68 (t, 1H),

7.74 (t, 1H), 7.80 (d, 1H), 10.37 (br. s, 1H), 12.91 (br. s, 1H); EI-MS 396.1 (M+H); HPLC-Method B, R_t 9.88 min.

Example 114 **(7-Fluoro-1H-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-6,7-dihydro-5*H*-cyclopentapyrimidin-4-yl]-amine (II-114)**: Prepared in 40% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 2.15 (m, 2H), 2.87 (m, 2H), 2.97 (t, 2H), 6.99 (td, 1H), 7.17 (dd, 1H), 7.38 (d, 1H), 7.65 (m, 2H), 7.71 (t, 1H), 7.78 (d, 1H), 10.21 (br. s, 1H), 13.40 (br. s, 1H); EI-MS 414.1 (M+H); HPLC-Method C, R_t 9.99 min.

Example 115 **(5,7-Difluoro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-6,7-dihydro-5*H*-cyclopentapyrimidin-4-yl]-amine (II-115)**: Prepared according to Method C in 52% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 2.16 (m, 2H), 2.89 (m, 2H), 2.97 (t, 2H), 7.19 (dd, 1H), 7.29 (td, 1H), 7.63 (t, 1H), 7.66 (d, 1H), 7.71 (t, 1H), 7.78 (d, 1H), 10.16 (br. s, 1H), 13.55 (br. s, 1H); EI-MS 432.1 (M+H); HPLC-Method C, R_t 10.09 min.

Example 116 **[2-(2-Chloro-phenyl)-6,7-dihydro-5*H*-cyclopentapyrimidin-4-yl]-(1*H*-indazol-3-yl)-amine (II-116)**: Prepared in 56% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 2.16 (m, 2H), 2.85 (m, 2H), 3.01 (t, 2H), 7.06 (t, 1H), 7.34 (t, 1H), 7.40 (t, 1H), 7.48 (m, 2H), 7.53 (d, 1H), 7.56 (d, 1H), 7.63 (d, 1H), 10.39 (br. s, 1H), 12.91 (s, 1H); EI-MS 362.1 (M+H); HPLC-Method A, R_t 3.09 min.

Example 117 **[2-(2-Chloro-phenyl)-6,7-dihydro-5*H*-cyclopentapyrimidin-4-yl]-(7-fluoro-1*H*-indazol-3-yl)-amine (II-117)**: Prepared in 63% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 2.15 (m, 2H), 2.87 (m, 2H), 3.00 (t, 2H), 7.01 (td, 1H), 7.19 (dd, 1H), 7.39 (t, 1H), 7.45 (m, 2H), 7.51

(d, 1H), 7.55 (d, 1H), 10.35 (br. s, 1H), 13.45 (br. s, 1H); EI-MS 380.1 (M+H); HPLC-Method A, R_t R_t 3.15 min.

Example 118 **[2-(2-Chloro-phenyl)-6,7-dihydro-5*H*-cyclopentapyrimidin-4-yl]-(5,7-difluoro-1*H*-indazol-3-yl)-amine (II-118)**: Prepared in 60% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 2.18 (m, 2H), 2.91 (m, 2H), 3.01 (t, 2H), 7.32 (t, 1H), 7.33 (td, 1H), 7.41 (t, 1H), 7.48 (t, 1H), 7.53 (d, 1H), 7.55 (dd, 1H), 10.35 (br. s, 1H), 13.45 (br. s, 1H); EI-MS 398.1 (M+H); HPLC-Method A, R_t R_t 3.24 min.

Example 119 **(1*H*-Indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-5,6,7,8,9,10-hexahydro-cyclooctapyrimidin-4-yl]-amine (II-119)**: Prepared in 36% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 1.47 (m, 2H), 1.53 (m, 2H), 1.78 (m, 4H), 2.96 (m, 2H), 3.06 (t, 2H), 7.03 (t, 1H), 7.47 (t, 1H), 7.72 (d, 1H), 7.73 (d, 1H), 7.72 (m, 3H), 7.81 (d, 1H), 10.52 (m, 1H), 12.97 (br. s, 1H); EI-MS 438.2 (M+1); HPLC-Method A, R_t 3.37 min.

Example 120 **(7-Fluoro-1H-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-5,6,7,8,9,10-hexahydro-cyclooctapyrimidin-4-yl]-amine (II-120)**: Prepared in 40% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 1.46 (m, 2H), 1.52 (m, 2H), 1.77 (m, 4H), 2.94 (m, 2H), 3.04 (m, 2H), 7.00 (td, 1H), 7.17 (dd, 1H), 7.30 (d, 1H), 7.70 (m, 3H), 7.79 (d, 1H), 10.5 (m, 1H), 13.49 (br s, 1H); EI-MS 456.1 (M+H); HPLC-Method A, R_t 3.43 min.

Example 121 **(5,7-Difluoro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-5,6,7,8,9,10-hexahydro-cyclooctapyrimidin-4-yl]-amine (II-121)**: Prepared in 48% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 1.46 (m, 2H), 1.52 (m, 2H), 1.77 (m, 4H), 2.95 (m, 2H), 3.03 (m, 2H), 7.14 (d,

1H), 7.30 (t, 1H), 7.73 (m, 3H), 7.80 (d, 1H), 10.5 (m, 1H), 13.62 (br. s, 1H); EI-MS 475.1 (M+1); HPLC-Method A, R_t 3.52 min.

Example 122 **[6-Cyclohexyl-2-(2-trifluoromethyl-phenyl)-pyrimidin-4-yl]- (1*H*-indazol-3-yl)-amine (II-122):** Prepared in 45% yield. ^{1}HNMR (500 MHz, CDCl3) δ 1.30 (2H, m), 1.46 (2H, m), 1.65 (2H, m), 1.76 (2H, m), 1.91 (2H, m), 2.61 (1H, br m), 7.08 (1H, t, J=7.4 Hz), 7.27 (1H, d, J=8.0 Hz), 7.35 (1H, t, J= 7.1 Hz), 7.50 (1H, t, J=7.0 Hz), 7.58 (1H, t, J=7.4 Hz), 7.66 (3H, m), 7.72 (1H, d, J=7.8 Hz), 8.0 (1H, br), 9.87 (1H, br) ppm; HPLC-Method D, R_t 3.57 min; LC-MS 438.17 $(M+H)^+$

Example 123 **[6-(2-Fluoro-phenyl)-2-(2-trifluoromethyl-phenyl)-pyrimidin-4-yl]-(1H-indazol-3-yl)-amine (II-123):** Prepared in 8% yield. ^{1}HNMR (500 MHz, $CDCl_3$) δ 7.18 (3H, m), 7.37 (1H, m), 7.43 (1H, t, J=7.9 Hz), 7.51 (1H, d, J=7.9 Hz), 7.55 (1H, t, J=7.6 Hz), 7.65 (1H, t, J=7.4 Hz), 7.79 (1H, d, J=7.9 Hz), 7.85 (1H, d, J= 7.6 Hz), 8.19 (2H, m), 8.70 (1H, d, J= 8.5 Hz) ppm; HPLC-Method D, R_t 4.93 min; LC-MS 450.13 $(M+H)^+$

Example 124 **(6-Fluoro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (II-124).** Prepared in DMF (87% yield) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.0 (s, 1H), 11.1 (s, br, 1H), 8.66 (d, 1H), 7.95 (t, 1H), 7.80 (d, 1H), 7.72 (m, 2H), 7.62 (m, 4H), 7.21 (dd, 1H), 6.84 (td, 1H) ppm. LC-MS (ES+) 424.15 (M+H); HPLC-Method A, R_t 3.05 min.

Example 125 **3-[2-(2-Trifluoromethyl-phenyl)-quinazolin-4-ylamino]-1*H*-indazole-5-carboxylic acid methyl ester (II-125):** To a solution of compound **II-79** (100 mg 0.21 mmol)

in DMF (2 mL) was added MeOH (1 mL), DIEA (54 uL, 0.31 mmol) and $PdCl_2$(dppf) (4 mg, 0.005 mmol). The flask was flushed with CO three times and then charged with a CO balloon. The reaction mixture was heated at 80°C for 14 h then poured into water. The resulting precipitate was collected and washed with water. The crude product was then purified first by flash column (silica gel, 50% ethyl acetate in hexanes) then by preparative HPLC to to afford **II-125** (32%) as yellow solid. ^{1}HNMR (500 MHz, DMSO-d6) δ13.3 (s, 1H), 11.3 (s, br, 1H), 8.70 (d, 1H), 8.36 (s, 1H), 7.97 (t, 1H), 7.82 (m, 2H), 7.71 (m, 3H), 7.58 (m, 2H), 7.51 (d, 1H), 3.75 (s, 3H) ppm; LC-MS (ES+) 464.13 (M+H); HPLC-Method A, R_t 3.12 min.

Example 208 **(5-Methyl-2*H*-pyrazol-3-yl)-[2-(2-naphthyl-1-yl)-quinazolin-4-yl]-amine (II-208):** ^{1}HNMR (500 MHz, DMSO-d6) δ8.92 (s, 1H), 8.73 (m, 1H), 8.39 (m, 1H), 8.09 (m, 2H), 7.95 (m, 3H), 7.62 (m, 3H), 6.78 (s, 1H), 2.32 (s, 3H); MS 352.2 (M+H).

Example 209 **[2-(2-Chloro-phenyl)-pyrido[2,3-*d*]pyrimidin-4-yl]-(7-fluoro-1*H*-indazol-3-yl)-amine (II-214):** Prepared from 4-Chloro-2-(2-chloro-phenyl)-pyrido[2,3-*d*]pyrimidine (100 mg, 0.36mmol) and 7-Fluoro-1*H*-indazol-3-ylamine (108mg, 0.72mmol). Purification by preparative HPLC afforded the title compound as a yellow, di-TFA salt (93 mg, 46% yield). HPLC-Method A, R_t 3.04 min; ^{1}H NMR (DMSO, 500 MHz): δ 13.67 (1H, s), 11.40-11.25 (1H, bs), 9.35-9.25 (2H, m), 7.95 (1H, m), 7.80-7.47 (5H, m), 7.35(1H, m), 7.15 (1H, m); MS (m/z), MH^+ 391.1.

Example 210 **[2-(2-Chloro-phenyl)-pyrido[2,3-*d*]pyrimidin-4-yl]-(5-fluoro-1*H*-indazol-3-yl)-amine (II-215):** Prepared from 4-Chloro-2-(2-chloro-phenyl)-pyrido[2,3-*d*]

pyrimidine (100 mg, 0.36mmol) and 5-Fluoro-1*H*-indazol-3-ylamine (108mg, 0.72mmol). Purification by preparative HPLC afforded the title compound as a yellow, di-TFA salt (45 mg, 22% yield). HPLC-Method A, R_t 3.00 min; ^{1}H NMR (DMSO, 500 MHz): δ 13.0 (1H, s), 10.90(1H, bs), 9.15-9.05 (2H, m), 7.70 (1H, m), 7.60-7.30 (6H, m), 7.20 (1H, m); MS (m/z), MH^+ 391.1.

Example 211 **[2-(2-Chloro-phenyl)-pyrido[2,3-*d*]pyrimidin-4-yl]-(5,7-difluoro-1*H*-indazol-3-yl)-amine (II-216)**: Prepared from 4-Chloro-2-(2-chloro-phenyl)-pyrido[2,3-*d*]pyrimidine (100 mg, 0.36mmol) and 7-Difluoro-1*H*-indazol-3-ylamine (112mg, 0.66mmol). Purification by preparative HPLC afforded the title compound as a yellow, di-TFA salt (130 mg, 62% yield). HPLC-Method A, R_t 3.12 min; ^{1}H NMR (DMSO, 500 MHz): 13.80-13.60 (1H, bs), 11.30-11.10 (1H, bs), 9.20-9.10 (2H, m), 7.80 (1H, m), 7.60-7.30 (6H, m); MS (m/z), MH^+ 409.1.

Example 212 **[2-(2-Chloro-phenyl)-pyrido[3,4-*d*]pyrimidin-4-yl]-(1*H*-indazol-3-yl)-amine (II-217)**: Prepared from 4-Chloro-2-(2-chloro-phenyl)-pyrido[3,4-*d*]pyrimidine (100 mg, 0.36mmol) and 1*H*-indazol-3-ylamine (88mg, 0.66mmol). Purification by preparative HPLC afforded the title compound as a yellow, di-TFA salt (72 mg, 33% yield). HPLC-Method A, R_t 3.21 min; ^{1}H NMR (DMSO, 500 MHz): δ 12.95 (1H, s), 10.90 (1H, bs), 9.25 (1H, s), 8.75 (1H, m), 8.55 (1H, m), 7.65 (1H, m), 7.55 (1H, m), 7.50-7.30 (5H, m), 7.00(1H, m); MS (m/z), MH^+ 373.1.

Example 213 **[2-(2-Chloro-phenyl)-pyrido[3,4-*d*]pyrimidin-4-yl]-(7-fluoro-1*H*-indazol-3-yl)-amine (II-218)**: Prepared from 4-Chloro-2-(2-chloro-phenyl)-pyrido[3,4-*d*]pyrimidine (100 mg, 0.36mmol) and 7-Fluoro-1*H*-indazol-3-ylamine

(108mg, 0.72mmol). Purification by preparative HPLC afforded the title compound as a yellow, di-TFA salt (48.7 mg, 22% yield). HPLC-Method A, R_t 3.35 min; ^{1}H NMR (DMSO, 500 MHz): δ 12.95 (1H, s), 10.90 (1H, bs), 9.25 (1H, s), 8.75 (1H, m), 8.55 (1H, m), 7.70-7.35 (5H, m), 7.25(1H, m), 6.95 (1H, m),; MS (m/z), MH^+ 391.08.

Example 214 **[2-(2-Chloro-phenyl)-pyrido[3,4-*d*]pyrimidin-4-yl]-(5-fluoro-1*H*-indazol-3-yl)-amine (II-219)**: Prepared from 4-chloro-2-(2-chloro-5-fluoro-1*H*-indazol-3-ylamine (108mg, 0.72mmol). Purification by preparative HPLC afforded the title compound as a yellow, di-TFA salt (57.2 mg, 26% yield). HPLC-Method A, R_t 3.27 min; ^{1}H NMR (DMSO, 500 MHz): δ 13.05 (1H, s), 10.95 (1H, s), 9.25 (1H, s), 8.75 (1H, m), 8.55 (1H, m), 7.60 (1H, m), 7.55 (1H, m), 7.50-7.30 (5H, m), 7.25(1H, m); MS (m/z), MH^+ 391.1.

Example 215 **[2-(2-Chloro-phenyl)-pyrido[3,4-*d*]pyrimidin-4-yl]-(5,7-difluoro-1*H*-indazol-3-yl)-amine (II-220)**: Prepared from 4-chloro-2-(2-chloro-7-difluoro-1*H*-indazol-3-ylamine (112mg, 0.66mmol). Purification by preparative HPLC afforded the title compound as a yellow, di-TFA salt (57.2 mg, 26% yield). HPLC-Method A, R_t 3.45 min; ^{1}H NMR (DMSO, 500 MHz): δ 13.65 (1H, s), 11.0 (1H, s), 9.25 (1H, s), 8.80 (1H, m), 8.50 (1H, m), 7.60 (1H, m), 7.55 (1H, m), 7.50-7.30 (5H, m); MS (m/z), MH^+ 409.1.

Example 216 **6-Fluoro-1*H*-indazol-3-ylamine (A1)**: ^{1}HNMR (500 MHz, DMSO-d6) δ11.4 (s, 1H), 7.68 (dd, 1H), 6.95 (dd, 1H), 6.75 (td, 1H), 5.45 (s, 2H) ppm; LC-MS (ES+) 152.03 (M+H); HPLC-Method A, R_t 2.00 min.

Example 217 **5-Fluoro-1*H*-indazol-3-ylamine (A2)**: ^{1}HNMR (500 MHz, DMSO-d6) δ11.3 (s, 1H), 7.43 (d, 1H), 7.22 (m, 1H), 7.08 (m, 1H), 5.29 (s, 2H) ppm; LC-MS (ES+) 152.01 (M+H); HPLC-Method A, R_t 1.93 min.

Example 218 **5,7-Difluoro-1H-indazol-3-yl-amine (A3)**: ^{1}HNMR (500 MHz, CD_3OD) δ7.22 (dd, J=2.0, 8.45Hz, 1H), 7.04-6.87 (m, 1H); LC-MS (ES+) 169.95 (M+H); HPLC-Method C, R_t 2.94 min

Example 219 **7-Fluoro-1*H*-indazol-3-ylamine (A4)**: ^{1}HNMR (500 MHz, DMSO-d6) δ11.8 (s, 1H), 7.42 (d, 1H), 6.97 (m, 1H), 6.78 (m, 1H), 5.40 (s, 2H) ppm; LCMS (ES+) 152.01 (M+H); HPLC-Method A, R_t 2.00 min.

Example 220 **7-Fluoro-6-trifluoromethyl-1*H*-indazol-3-ylamine (A5)**: ^{1}H-NMR (500 MHz, DMSO) δ 12.5 (s, 1H), 7.75 (d, 1H), 7.25 (m, 1H), 5.85 (m, 1H) ppm; MS (FIA) 220.0 (M+H); HPLC-Method A, R_t 2.899 min.

Example 221 **6-Bromo-1*H*-indazol-3-ylamine (A6)**: ^{1}H-NMR (500 MHz, DMSO) δ 11.5 (s, 1H), 7.65 (d, 1H), 7.40 (s, 1H), 7.00 (d, 1H), 5.45 (br s, 1H) ppm; MS (FIA) 213.8 (M+H); HPLC-Method A, R_t 2.441 min.

Example 222 **4-Fluoro-1*H*-indazol-3-ylamine (A7)**: ^{1}H-NMR (500 MHz, DMSO) δ 11.7 (s, 1H), 7.17 (m, 1H), 7.05 (d, 1H), 6.7 (br, 1H), 6.60 (dd, 1H), 5.20 (br s, 2H) ppm; MS (FIA) 152.0 (M+H); Method A, R_t 2.256 min.

Example 223 **5-Bromo-1*H*-indazol-3-ylamine (A8)**: ^{1}H-NMR (500 MHz, DMSO) δ 11.55 (br s, 1H), 7.95 (s, 1H), 7.30 (d,

1H), 7.20 (d, 1H), 5.45 (br s, 2H) ppm; MS (FIA) 213.8 (M+H); Method A, R_t 2.451 min.

Example 224 **5-Nitro-1*H*-indazol-3-ylamine (A9)**: ^{1}H-NMR (500 MHz, DMSO-d6) δ 9.00 (s, 1H), 8.20 (d, 1H), 7.45 (d, 1H), 6.15 (br s, 1H) ppm; Method A, R_t 2.184 min

Example 225 **4-Pyrrol-1-yl-1*H*-indazol-3-ylamine (A10)**: ^{1}H-NMR (500 MHz, DMSO) δ 7.20 (s, 2H), 7.00 (s, 2H), 6.75 (m, 1H), 6.25 (s, 2H), 4.30 (d, 1H) ppm; Method A, R_t 2.625 min.

Example 226 **4-Chloro-5,6-dimethyl-2-(2-trifluoromethyl-phenyl)-pyrimidine (B1)**: Prepared to afford a colorless oil in 75% yield. ^{1}H-NMR (500 MHz, CDCl3) δ 7.70 (d, J=7.8 Hz, 1H), 7.64 (d, J=7.6 Hz, 1H), 7.55 (t, J=7.6 Hz, 1H), 7.48 (t, J=7.5 Hz, 1H), 2.54 (s, 3H), 2.36 (s, 3H) ppm; MS (FIA) 287.0 (M+H); HPLC-Method A, R_t 3.891 min.

Example 227 **4-Chloro-2-(2-chloro-phenyl)-5,6-dimethyl-pyrimidine (B2)**: Prepared to afford a yellow-orange oil in 71% yield. ^{1}H-NMR (500 MHz, CDCl3) δ 7.73 (m, 1H), 7.52 (m, 1H), 7.39 (m, 2H), 2.66 (s, 3H), 2.45 (s, 3H) ppm; MS (FIA) 253.0 (M+H); HPLC-Method A, R_t R_t 4.156 min.

Example 228 **4-Chloro-6-methyl-2-(2-trifluoromethyl-phenyl)-pyrimidine (B3)**: Prepared to afford a pale yellow oil in 68% yield. ^{1}H-NMR (500 MHz, CDCl3) δ 7.72 (d, J=7.8 Hz, 1H), 7.65 (d, J=7.9 Hz, 1H), 7.57 (t, J=7.5 Hz, 1H), 7.52 (t, J=7.8 Hz, 1H), 7.16 (s, 1H), 2.54 (s, 3H) ppm; MS (FIA) 273.0 (M+H); HPLC-Method A, R_t 3.746 min.

Example 229 **4-Chloro-6-cyclohexyl-2-(2-trifluoromethyl-phenyl)-pyrimidine (B4)**: Prepared to afford a yellow oil in 22% yield. ^{1}H-NMR (500 MHz, CDCl3) δ 7.70 (m, 2H), 7.57 (t, J=7.5 Hz, 1H), 7.50 (t, J=7.5 Hz, 1H), 7.19 (s, 1H), 2.65 (m, 1H), 1.9 (m, 2H), 1.8 (m, 2H), 1.5 (m, 2H), 1.3 (m, 2H), 1.2 (m, 2H) ppm; MS (FIA) 341.0 (M+H).

Example 230 **4-Chloro-6-phenyl-2-(2-trifluoromethyl-phenyl)-pyrimidine (B5)**: Prepared to afford a yellow oil in 53% yield. ^{1}H-NMR (500 MHz, CDCl3) δ 8.08 (dd, J=7.9, 1.6 Hz, 2H), 7.80 (d, J=7.6 Hz, 1H), 7.77 (d, J=7.8 Hz, 1H), 7.67 (s, 1H), 7.61 (t, J=7.5 Hz, 1H), 7.54 (t, J=7.6 Hz, 1H), 7.47 (m, 3H) ppm; MS (FIA) 335.0 (M+H); HPLC-Method A, R_t 4.393 min.

Example 231 **4-Chloro-2-(2,4-dichloro-phenyl)-5,6-dimethyl-pyrimidine (B6)**: Prepared to afford a white solid in 91% yield. ^{1}H-NMR (500 MHz, CDCl3) δ 7.62 (d, J=8.3 Hz, 1H), 7.43 (d, J=7.0 Hz, 1H), 7.27 (dd, J=8.3, 2.0 Hz, 1H), 2.55 (s, 3H), 2.35 (s, 3H) ppm; MS (FIA) 287, 289 (M+H); HPLC-Method A, R_t 4.140 min.

Example 232 **4-Chloro-6-(2-chloro-phenyl)-2-(2-trifluoromethyl-phenyl)-pyrimidine (B7)**: Prepared to affod a yellow oil in 52% yield. ^{1}H-NMR (500 MHz, CDCl3) δ 7.75 (m, 3H), 7.65 (m, 2H), 7.53 (m, 1H), 7.44 (m, 1H), 7.36 (m, 2H) ppm; MS (FIA) 369.1 (M+H); HPLC-Method A, R_t 4.426 min.

Example 233 **4-Chloro-6-(2-fluoro-phenyl)-2-(2-trifluoromethyl-phenyl)-pyrimidine (B8)**: Prepared to afford a yellow oil in 95% yield. ^{1}H-NMR (500 MHz, CDCl3) δ 8.24 (t, J=7.9 Hz, 1H), 7.84 (s, 1H), 7.78 (d, J=7.7

Hz, 1H), 7.76 (d, J=8.0 Hz, 1H), 7.60 (t, J=7.5 Hz, 1H), 7.53 (t, J=7.6 Hz, 1H), 7.43 (m, 1H), 7.23 (t, J=7.6 Hz, 1H), 7.13 (m, 1H) ppm; MS (FIA) 353.0 (M+H).

Example 234 **4-Chloro-6-pyridin-2-yl-2-(2-trifluoromethyl-phenyl)-pyrimidine (B9)**: Prepared to afford a pale yellow solid in 50% yield. ^{1}H-NMR (500 MHz, CDCl3) δ 8.68 (m, 1H), 8.48 (dd, J=7.9, 0.8 Hz, 1H), 8.38 (d, J=2.3 Hz, 1H), 7.84 (m, 3H), 7.62 (t, J=7.6 Hz, 1H), 7.55 (t, J=7.6 Hz, 1H), 7.38 (m, 1H) ppm; MS (FIA) 336.0 (M+H); HPLC-Method A, R_t 4.575 min.

Example 235 **6-Benzyl-4-chloro-2-(2-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[4,3-*d*]pyrimidine (B10)**: ^{1}HNMR (500 MHz, $CDCl_3$) δ7.70 (d, 1H), 7.62 (d, 1H), 7.55 (t, 1H), 7.48 (t, 1H), 7.32 (m, 4H), 7.25 (m, 1H), 3.74 (s, 2H), 3.66 (s, 2H), 2.99 (t, 2H), 2.80 (t, 2H) ppm; LCMS (ES+) 404.17 (M+H); HPLC-Method A, R_t 3.18 min.

Example 236 **7-Benzyl-4-chloro-2-(2-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[3,4-*d*]pyrimidine (B11)**: ^{1}HNMR (500 MHz, $CDCl_3$) δ7.69 (d, 1H), 7.60 (d, 1H), 7.54 (t, 1H), 7.47 (t, 1H), 7.28 (m, 4H), 7.20 (m, 1H), 3.68 (s, 2H), 3.67 (s, 2H), 2.86 (t, 2H), 2.79 (t, 2H) ppm. MS (ES+) 404.18 (M+H); HPLC-Method A, R_t 3.12 min.

Example 237 **4-Chloro-2-(4-fluoro-2-trifluoromethyl-phenyl)-quinazoline (B12)**: ^{1}HNMR (500MHz, CD_3OD) δ 8.43 (d, J=8.1Hz, 1H), 8.20-8.05 (m, 2H), 8.05-7.82 (m, 2H), 7.71-7.51 (m, 2H). LC-MS (ES+) 327.09 (M+H). HPLC-Method D, R_t 4.56 min.

Example 238 **4-Chloro-2-(2-chloro-5-trifluoromethyl-phenyl)-quinazoline (B13)**: LC-MS (ES+) 342.97 (M+H). HPLC-Method D, R_t 4.91 min.

Example 239 **4-Chloro-2-(2-chloro-4-nitro-phenyl)-quinazoline (B14)**: LC-MS (ES+) 319.98 (M+H). HPLC-Method D, R_t 4.45 min.

Example 240 **4-Chloro-2-(2-trifluoromethyl-phenyl)-quinazoline (B15)**: Prepared in 57% yield. White solid. ^{1}HNMR (500MHz, DMSO-d6) δ 7.79 (t, 1H), 7.86 (t, 1H), 7.94 (m, 3H), 8.15 (dd, 1H), 8.20 (td, 1H), 8.37 (m, 1H); EI-MS 308.9 (M).

Example 241 **4-Chloro-2-(2-trifluoromethyl-phenyl)-6,7-dihydro-5*H*-cyclopentapyrimidine (B16)**: Prepared in 22% yield. ^{1}HNMR (500MHz, DMSO-d6) δ 2.19 (m, H), 3.01 (t, 2H), 3.08 (t, 2H), 7.49 (t, 1H), 7.55 (t, 1H), 7.62 (d, 1H), 7.71 (d, 1H). EI-MS 299.0 (M+H).

Example 242 **4-Chloro-2-(2-chloro-phenyl)-6,7,8,9-tetrahydro-5*H*-cycloheptapyrimidine (B17)**: Prepared according to Method C in 82% yield to afford a white solid. ^{1}HNMR (500MHz, $CDCl_3$) δ 1.67 (m 4H), 1.87 (m 2H), 3.02 (m 4H), 7.28 (m, 2H), 7.40 (m, 1H), 7.65 (m, 1H); EI-MS 293.0 (M+1).

Example 243 **4-Chloro-2-(2-trifluoromethyl-phenyl)-5,6,7,8,9,10-hexahydro-cyclooctapyrimidine (B18)**: Prepared in 38% yield to afford a brown oil. ^{1}HNMR (500MHz, $CDCl_3$) δ 1.35 (m 2H), 1.41 (m 2H), 1.76 (m 4H), 2.96 (m, 4H), 7.48 (t, 1H), 7.56 (t, 1H), 7.66 (d, 1H), 7.70 (d, 1H); EI-MS 341.0 (M+1).

Example 244 **4-Chloro-8-methoxy-2-(2-trifluoromethyl-phenyl)-quinazoline (B19)**: Prepared from 8-methoxy-2-(2-trifluoromethyl-phenyl)-3*H*-quinazolin-4-one (1.0g, 3.12mmol), triethylamine hydrochloride (472mg, 3.43mmol), and $POCl_3$. Purification by flash chromatography afforded a white solid (89% yield). HPLC-Method A, R_t 4.10 min, (98%), MS (m/z) 258.08 (M+H).

Example 245 **2-(4-Chloro-quinazolin-2-yl)-benzonitrile (B20)**: Prepared to afford a yellow solid in 1.5% yield. ^{1}H-NMR (500 MHz, CDCl3) δ 8.47 (d, 1H), 8.24 (d, 1H), 8.16 (d, 1H), 8.07 (impurity), 7.94 (t, 1H), 7.92 (impurity), 7.86 (d, 1H), 7.68 (m, 2H), 7.65 (impurity), 7.54 (impurity), 7.49 (t, 1H), 4.2 (impurity), 1.05 (impurity) ppm; MS (LC/MS) 266.05 (M+H); HPLC-Method A, R_t 3.88 min.

Example 246 **6-Methyl-2-(2-trifluoromethyl-phenyl)-3*H*-pyrimidin-4-one (D3)**: Prepared to afford a yellow solid in 50% yield. ^{1}H-NMR (500 MHz, DMSO-d6) δ 12.7 (br s, 1H), 7.9 (m, 1H), 7.8 (m, 2H), 7.7 (m, 1H), 6.3 (s, 1H), 2.21 (s, 3H) ppm; MS (FIA) 255.0 (M+H); HPLC-Method A, R_t 2.578 min.

Example 247 **6-Cyclohexyl-2-(2-trifluoromethyl-phenyl)-3*H*-pyrimidin-4-one (D4)**: Prepared to afford an off-white solid in 54% yield. ^{1}H-NMR (500 MHz, DMSO-d6) δ 12.9 (br s, 1H), 7.9 (m, 4H), 6.3 (s, 1H), 2.5 (m, 1H), 1.9 (m, 5H), 1.4 (m, 5H) ppm; MS (FIA) 323.1 (M+H); HPLC-Method A, R_t 3.842 min.

Example 248 **2-(2-Chloro-5-trifluoromethyl-phenyl)-3H-quinazoli-4-one (D10)**: ^{1}HNMR (500MHz, CD_3OD) δ 8.32-8.25 (m, 1H), 8.01 (s, 1H), 7.91-7.72 (m, 1H), 7.66-7.55 (m,

1H). LC-MS (ES+) 325.01 (M+H). HPLC-Method D, R_t 3.29 min.

Example 249 **2-(4-Fluoro-2-trifluoromethyl-phenyl)-3*H*-quinazolin-4-one (D14)**: ^{1}HNMR (500MHz, CD_3OD) δ 8.28 (d, 8.0Hz, 1H), 7.94-7.84 (m, 1H), 7.84-7.77 (m, 1H), 7.76-7.67 (m, 2H), 7.65-7.53 (m, 2H). LC-MS (ES+) 309.06 (M+H). HPLC-Method D, R_t 2.88 min.

Example 250 **2-(4-Nitro-2-chloro-phenyl)-3H-quinazolin-4-one (D15)**: LC-MS (ES+) 302.03 (M+H). HPLC-Method D, R_t 2.81 min.

Example 251 **2-(5-Fluoro-2-trifluoromethyl-phenyl)-3*H*-quinazolin-4-one (D17)**: ^{1}HNMR (500MHz, CD_3OD) δ 8.28 (d, R_t J=8.05Hz, 1H), 7.96 (dd, J=5.05, 8.55Hz, 1H), 7.89 (t, J=7.9Hz, 1H), 7.78-7.69 (m,1H), 7.66-7.46 (m, 3H). LC-MS (ES+) 309.14 (M+H). HPLC-Method D, R_t 2.90 min.

Example 252 **(1*H*-Indazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-1)**: Prepared by Method A in DMF to afford 70 mg (50% yield) as pale yellow solid. ^{1}H NMR (500 MHz, DMSO-d6) δ13.1 (s, br, 1H), 8.48 (d, 1H), 7.91 (d, 2H), 7.76 (br, 2H), 7.45 (m, 2H), 7.36 (d, 1H), 7.20 (m, 4H), 6.86 (t, 1H) ppm. MS (ES+) 338.07 (M+H); (ES-) 336.11 (M-H); HPLC-Method A, R_t 2.88 min.

Example 253 **(5-Methyl-2*H*-pyrazol-3-yl)-(2-phenyl-5,6,7,8-tetrahydroquinazolin-4-yl)-amine (III-7)**: Prepared according to Method A. ^{1}H NMR (500 MHz, DMSO-d6) δ12.1 (s, br, 1H), 8.70 (s, br, 1H), 8.37 (d, J = 6.7 Hz, 2H), 7.54 (m, 3H), 6.67 (s, 1H), 2.82 (m, 2H), 2.68 (m, 2H), 2.37 (s, 3H), 1.90 (s, br, 4H); MS 306.1 (M+H).

Example 254 **(5-Methyl-2*H*-pyrazol-3-yl)-(2-phenyl-6,7,8,9-tetrahydro-5*H*-cycloheptapyrimidin-4-yl)-amine (III-8):** MS 320.48 (M+H); HPLC-Method E, R_t 1.124 min.

Example 255 **(5-Methyl-2*H*-pyrazol-3-yl)-(2-pyridin-4-yl-quinazolin-4-yl)-amine (III-9):** Yellow solid, mp 286-289°C, ^{1}H NMR (DMSO) δ 2.35 (3H, s), 6.76 (1H, s), 7.61 (1H, m), 7.89 (2H, m), 8.32 (2H, d), 8.70 (1H, d), 8.78 (2H, d), 10.56 (1H, br s), 12.30 (1H, br s); IR (solid) 1620, 1598, 1571, 1554, 1483, 1413, 1370, 1328; MS 303.2 $(M+H)^+$

Example 256 **(7-Chloro-2-pyridin-4-yl-quinazolin-4-yl)-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-28):** ^{1}H NMR (DMSO-d6) δ 2.35 (3H,s), 6.75 (1H, s), 7.65 (1H, d), 7.93 (1H, s), 8.30 (2H, d), 8.73 (1H, d), 8.79 (2H, d), 10.69 (1H, s), 12.33 (1H, s); MS m/z 337.2 $(M+H)^+$.

Example 257 **(6-Chloro-2-pyridin-4-yl-quinazolin-4-yl)-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-29):** ^{1}H NMR (DMSO-d6) δ 2.31 (3H, s), 6.74 (1H,s), 7.89 (1H, s), 8.30 (2H, d), 8.80 (2H, d), 8.91 (1H, s), 10.63 (1H, s), 12.29 (1H, s); MS 337.2 $(M+H)^+$.

Example 258 **(2-Cyclohexyl-quinazolin-4-yl)-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-30):** ^{1}H NMR (DMSO) δ 2.35 (3H, s), 1.70 (3H, m), 1.87 (2H, d), 1.99 (2H, d), 2.95 (1H, t), 6.72 (1H, s), 7.75 (1H, d), 7.88 (1H, s), 7.96 (1H, s), 8.83 (1H, s), 11.95 (1H, s), 12.70 (1H, s); MS 308.4 $(M+H)^+$.

Example 259 **(5-Methyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-31):** mp 246°C; ^{1}H NMR (400MHz)

δ 2.35 (3H, s), 6.70 (1H, br s), 7.51-7.57 (4H, m), 7.83-7.84 (2H, d), 8.47-8.50 (2H, d), 8.65 (1H, d), 10.4 (1H, s), 12.2 (1H, bs); IR (solid) 3696, 3680, 2972, 2922, 2865; MS 302.1 (M+H)+.

Example 260 **[2-(4-Iodophenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-32)**: ^{1}H NMR (DMSO-d6) δ 2.34 (3H, s), 6.72 (1H, s), 7.56 (1H, d), 7.84 (2H, d), 7.93 (2H, d), 8.23 (2H, d), 8.65 (1H, s), 10.44 (1H, s), 12.24 (1H, s); MS 428.5 (M+H)+.

Example 261 **[2-(3,4-Dichlorophenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-33)**: A suspension of 2-(3,4-dichloro-phenyl)-3*H*-quinazolin-4-one (1g, 3.43 mmol) in phosphorus oxychloride (4 mL) was stirred at 110°C for 3 hours. The solvent was removed by evaporation and the residue is treated carefully with cold aqueous, saturated $NaHCO_3$. The resulting solid was collected by filtration and washed with ether to afford 4-chloro-2-(3,5-dichloro-phenyl)-quinazoline as a white solid (993 mg, 93%). To the above compound (400mg, 1.29 mmol) in THF (30 mL) was added 3-amino-5-methyl pyrazole (396 mg, 2.58 mmol) and the resulting mixture heated at 65°C overnight. The solvents were evaporated and the residue triturated with ethyl acetate, filtered, and washed with the minimum amount of ethanol to afford compound **III-33** as a white solid (311 mg 65%): mp 274°C; ^{1}H NMR (DMSO) δ 2.34 (3H, s), 6.69 (1H, s), 7.60 (1H, m), 7.84 (1H, d), 7.96 (2H, d), 8.39 (1H, dd), 8.60 (1H, d), 8.65 (1H, d), 10.51 (1H, s), 12.30 (1H, s); IR (solid) 1619, 1600, 1559, 1528, 1476, 1449, 1376, 1352, 797, 764, 738; MS 370.5 $(M+H)^+$.

Example 262 **[2-(4-Bromophenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-34)**: mp 262-265°C; ^{1}H NMR (DMSO) δ 2.34 (3S, s), 6.73 (1H, s), 7.55 (1H, m), 7.74 (2H, d), 7.83 (2H, m), 8.40 (2H, d), 8.65 (1H, d), 10.44 (1H, s), 12.25 (1H, s); IR (solid) 1603, 1579, 1546, 1484, 1408, 1365; MS 380.1/382.1 (M+H)+.

Example 263 **[2-(4-Chlorophenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-35)**: mp >300°C; ^{1}H NMR (DMSO) δ 2.34 (3H, s), 6.74 (1H, s), 7.53-7.62 (3H, m), 7.84 (2H, d), 8.47 (2H, d), 8.65 (1H, d), 10.44 (1H, s), 12.26 (1H, s); IR (solid) 1628, 1608, 1584, 1546, 1489, 1408, 1369, 1169; MS 336.2 (M+H)+.

Example 264 **[2-(3,5-Dichlorophenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-36)**: mp 228°C; ^{1}H NMR (DMSO) δ 2.34 (3H, s), 6.69 (1H, s), 7.96 (1H, d), 8.21 (3H, m), 8.56 (1H, d), 8.60 (2H, d), 10.51 (1H, s), 12.30 (1H, s); IR (solid) 1546, 1331, 802, 763, 729, 658, 652; MS 370.5 (M+H)+.

Example 265 **[2-(4-Cyanophenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-37)**: mp 263°C; ^{1}H NMR (DMSO) δ 2.34 (3H, s), 6.72 (1H, s), 7.61 (1H, d), 7.88 (2H, s), 8.04 (2H, d), 8.63 (2H, d), 8.67 (1H, s), 10.52 (1H, s), 12.27 (1H, s); IR (solid) 1739, 1436, 1366, 1229, 1217; MS 327.2 (M+H)+.

Example 266 **[2-(3-Iodophenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-38)**: mp 234-235°C; ^{1}H NMR (DMSO) δ 2.35 (3H, s), 6.73 (1H, s), 7.35 (1H, m), 7.56 (1H, m), 7.85 (3H, m), 8.47 (1H, m), 8.65 (1H, m), 8.86

(1H, s), 10.49 (1H, s), 12.28 (1H, br s); IR (solid) 1560, 1541, 1469, 1360; MS 428.1 (M+H)+.

Example 267 **[2-(4-Ethylsulfanylphenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-39)**: mp 229-231°C; ^{1}H NMR (DMSO) δ 1.29 (3H, t), 2.35 (3H, s), 3.07 (2H, q), 6.76 (1H, s), 7.43 (2H, d), 7.51 (1H, m), 7.81 (2H, m), 8.41 (2H, d), 8.64 (1H, d), 10.38 (1H, s), 12.24 (1H, br s); IR (solid) 1587, 1574, 1555, 1531, 1484, 1412, 1369; MS 362.1 (M+H)+.

Example 268 **(5-Cyclopropyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-40)**: mp 218-219°C; ^{1}H NMR (DMSO-d6) δ 0.70-0.80(2H, m), 0.90-1.00 (2H, m), 6.70 (1H, s), 7.45-7.55 (4H, m), 7.80-7.85 (2H, m), 8.45-8.55 (2H, m), 8.65 (1H, d), 10.40 (1H, s), 12.27 (1H, s); IR (solid) 1624, 1605, 1591, 1572, 1561, 1533, 1479, 1439, 1419, 1361, 1327, 997, 828, 803, 780, 762, 710; MS 328.2 $(M+H)^+$.

Example 269 **[2-(4-*tert*-Butylphenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-41)**: mp >300°C; ^{1}H NMR (DMSO-d6) δ 1.35 (9H, s), 2.34 (3H, s), 6.79 (1H, s), 7.55 (3H, d), 7.85 (2H, d), 8.39 (2H, d), 8.62 (1H, d), 10.35 (1H, s), 12.22 (1H, s); IR (solid) 1603, 1599, 1577, 1561, 1535, 1481, 1409, 1371, 1359, 998, 841, 825, 766, 757; MS 358.3 $(M+H)^+$.

Example 270 **[2-(4-Chlorophenyl)-quinazolin-4-yl]-(5-cyclopropyl-2*H*-pyrazol-3-yl)-amine (III-42)**: ^{1}H NMR (DMSO-d6) δ 0.77 (4H, br m) ,2.05 (1H, m), 6.59 (1H, s), 7.60 (1H, d), 7.85 (2H, d), 7.91 (2H, d), 8.22 (2H, d), 8.65 (1H, s), 10.51 (1H,s), 12.33 (1H,s); MS 362.1 $(M+H)^+$.

Example 271 **(2-Benzo[1,3]dioxol-5-yl-quinazolin-4-yl)-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-43)**: ^{1}H NMR (DMSO) δ 2.33 (3H, s), 6.13 (2H, s), 6.78 (1H,s), 7.11 (1H, d), 7.80 (1H, t), 7.94 (1H, s), 8.09 (3H, m), 8.25 (1H, d), 10.34 (1H, s), 12.21 (1H, s); MS 346.5 $(M+H)^+$.

Example 272 **[2-(4-Dimethylaminophenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-44)**: ^{1}H NMR (DMSO-d6) δ 2.02 (6H, s), 2.39 (3H, s), 6.83 (1H, s), 7.71 (1H, d), 7.98 (2H, s), 8.04 (2H, d), 8.33 (2H, d), 8.67 (1H, s), 11.82 (1H, s), 12.72 (1H, s); MS 345.3 $(M+H)^+$.

Example 273 **[2-(3-Methoxyphenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-45)**: mp 226°C; ^{1}H NMR (DMSO) δ 2.34 (3H,s), 3.92 (3H, s), 6.72 (1H, s), 7.21 (1H, d), 7.57 (1H, t), 7.79 (1H, t), 8.02 (3H, m), 8.14 (1H, s), 8.79 (1H, d), 10.39 (1H,s), 12.22 (1H, s); IR (solid) 1599, 1572, 1538, 1478, 1427, 1359, 833, 761, 661; MS 332.2 $(M+H)^+$.

Example 275 **(5-Cyclopropyl-2*H*-pyrazol-3-yl)-[2-(3,4-dichlorophenyl)-quinazolin-4-yl]-amine (III-46)**: ^{1}H NMR (DMSO-d6) δ 0.86 (2H, d), 1.02 (2H, d), 1.69 (1H, m), 6.56 (1H, s), 7.57 (1H, d), 7.84 (4H, m), 8.40 (1H, d), 8.58 (1H, s), 8.64 (1H, s), 10.53 (1H, s), 12.36 (1H, s); MS 396.0 $(M+H)^+$.

Example 276 **(2-Biphenyl-4-yl-quinazolin-4-yl)-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-47)**: To a mixture of [2-(4-bromo-phenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (**III-34**) (196 mg, 0.51 mmol) and phenylboronic acid (75 mg, 0.62 mmol) in THF:water (1:1, 4 mL) was added Na_2CO_3 (219 mg, 2.06 mmol), triphenylphosphine (9mg, 1/15 mol%) and palladium acetate (1 mg, 1:135 mol%). The

resulting mixture was heated at 80°C overnight, the solvents were evaporated and the residue purified by flash chromatography (gradient of dichloromethane:MeOH) to afford **III-21** as a yellow solid (99 mg, 51%): ^{1}H NMR (DMSO) δ 2.37 (3H, s), 6.82 (1H, s), 7.39-7.57 (4H, m), 7.73-7.87 (6H, m), 8.57 (2H, d), 8.67 (1H, d), 10.42 (1H, s), 12.27 (1H, s); MS 378.2 $(M+H)^+$.

Example 277 **[2-(4-Ethynylphenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-48)**: To a mixture of [2-(4-bromo-phenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (**III-34**) (114 mg, 0.3 mmol), and trimethylsilylacetylene (147 mg, 1.5 mmol)in DMF (2 mL) was added CuI (1.1 mg, 1:50 mol%), $Pd(PPh_3)_2Cl_2$ (4.2 mg, 1:50 mol%) and triethylamine (121 mg, 0.36 mmol). The resulting mixture was heated at 120°C overnight and the solvent evaporated. The residue was triturated in ethyl acetate and the resulting precipitate collected by filtration. The collected solid was suspended in THF (3 mL) and TBAF (1M in THF, 1.1eq) was added. The reaction mixture was stirred at room temperature for 2 hours and the solvent evaporated. The residue was purified by flash chromatography (silica gel, gradient of DCM:MeOH) to afford **III-48** as a white solid (68 mg, 70%): ^{1}H NMR (DMSO) δ 2.34 (3H, s), 4.36 (1H, s), 6.74 (1H, s), 7.55 (1H, m), 7.65 (2H, d), 7.84 (2H, m), 8.47 (2H, d), 8.65 (1H, d), 10.43 (1H, s), 12.24 (1H, s); MS 326.1 $(M+H)^+$.

Example 278 **[2-(3-Ethynylphenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-49)**: mp 204-207°C; ^{1}H NMR (DMSO) δ 2.34 (3H, s), 4.28 (1H, s), 6.74 (1H, s), 7.55-7.63 (3H, m), 7.83-7.87 (2H, m), 8.49 (1H, d), 8.57 (1H, s), 8.65 (1H, d), 10.46 (1H, s), 12.27 (1H, s); IR

(solid) 1598, 1574, 1541, 1489, 1474, 1422, 1365; MS 326.1 (M+H)+.

Example 279 **[2-(3-Methylphenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-50)**: A suspension of 1*H*-quinazoline-2,4-dione (10.0 g, 61.7 mmol) in $POCl_3$ (60 mL, 644 mmol) and N,N-dimethylaniline (8mL, 63.1 mmol) was heated under reflux for 2 h. The excess $POCl_3$ was removed *in vacuo*, the residue poured into ice, and the resulting precipitate collected by filtration. The crude solid product 2,4-dichloro-quinazoline (6.5 g, 53% yield) was washed with water and dried under vacuum for next step use without further purification. To a solution of the 2,4-dichloro-quinazoline (3.3 g, 16.6 mmol) in anhydrous ethanol (150 mL) was added 5-methyl-1*H*-pyrazol-3-yl amine (3.2 g, 32.9 mmol)and the resulting mixture was stirred at room temperature for 4 hours. The resulting precipitate was collected by filtration, washed with ethanol, and dried under vacuum to afford 4.0 g (93% yield) of (2-chloro-quinazolin-4-yl)-(5-methyl-1*H*-pyrazol-3-yl)-amine which was used in the next step without further purification. To a solution of the (2-chloro-quinazolin-4-yl)-(5-methyl-1*H*-pyrazol-3-yl)-amine (50 mg, 0.19 mmol) in DMF (1.0 mL) was added *m*-tolyl boronic acid (0.38 mmol), 2M Na_2CO_3 (0.96 mmol), and tri-t-butylphosphine (0.19 mmol). The flask was flushed with nitrogen and the catalyst $PdCl_2$(dppf) (0.011 mmol) added in one portion. The reaction mixture was then heated at 80°C for 10 hours, cooled to room temperature, and poured into water (2 mL). The resulting precipitate was collected by filtration, washed with water, and purified by HPLC to afford **III-50** as a pale yellow solid (61mg, 75%): ^{1}H NMR (500 MHz, DMSO-d6) δ12.3 (br s, 1H), 10.4 (br s, 1H), 8.75 (d, 1H), 8.30 (s, 1H), 8.25 (d, 1H),

7.78 (s, 2H), 7.55 (m, 1H), 7.45 (m, 1H), 7.35 (m, 1H), 6.80 (s, 1H), 2.47 (s, 3H), 2.30 (s, 3H); MS 316.1 (M+H).

Example 280 **[2-(3,5-Difluorophenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-51)**: ^{1}H NMR (500 MHz, DMSO-d6) δ12.3 (br s, 1H), 10.8 (br s, 1H), 8.63 (d, 1H), 7.95 (d, 2H), 7.85 (m, 2H), 7.58 (t, 1H), 7.41 (t, 1H), 6.59 (s, 1H), 2.27 (s, 3H); MS 338.1 (M+H).

Example 281 **[2-(3-Chloro-4-fluorophenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-52)**: ^{1}H NMR (500 MHz, DMSO-d6) δ12.4 (br s, 1H), 10.8 (br s, 1H), 8.65 (d, 1H), 8.50 (d, 1H), 8.36 (m, 1H), 7.85 (m, 1H), 7.60 (m, 1H), 6.62 (s, 1H), 2.30 (s, 3H); MS 354.1 (M+H).

Example 282 **(5-Methyl-2*H*-pyrazol-3-yl)-[2-(3-trifluoromethylphenyl)-quinazolin-4-yl]-amine (III-53)**: ^{1}H NMR (500 MHz, DMSO-d6) δ12.2 (br, 1H), 10.45(br, 1H), 7.53 (s, 1H), 7.43 (d, J = 7.2 Hz, 1H), 7.06 (d, J = 8.2 Hz, 1H), 6.65 (d, J = 8.3 Hz, 1H), 6.57 (t, J = 7.6 Hz, 1H), 6.51 (d, J = 7.8 Hz, 1H), 6.43 (t, J = 7.8 Hz, 1H), 6.32 (t, J = 7.6 Hz, 1H), 5.51 (s, 1H), 2.03 (s, 3H); MS 370.2 (M+H).

Example 283 **[2-(3-Cyanophenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-54)**: ^{1}H NMR (500 MHz, DMSO-d6) δ9.01 (s, 1H), 8.96 (m, 2H), 8.28 (d, J = 7.3 Hz, 1H), 8.16 (s, br, 2H), 8.06 (t, J = 7.8 Hz, 1H), 7.88 (m, 1H), 6.96 (S, 1H), 2.58 (s, 3H); MS 327.1 (M+H).

Example 284 **[2-(3-Isopropylphenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-55)**: ^{1}H NMR (500 MHz, DMSO-d6) δ8.89 (d, J = 7.5 Hz, 1H), 8.37 (s, 1H), 8.26

(s, 1H), 8.08 (m, 2H), 7.81 (t, br, 1H), 7.67 (m, 2H), 6.88 (s, 1H), 3.12 (m, 1H), 2.40 (s, 3H), 1.38 (d, J = 6.9 Hz, 6H); MS 344.2 (M+H).

Example 285 **(5-Methyl-2*H*-pyrazol-3-yl)-(2-pyridin-3-yl-quinazolin-4-yl)-amine (III-56)**: ^{1}H NMR (500 MHz, DMSO-d6) δ 9.50 (s, 1H), 8.84 (d, J = 7.3 Hz, 1H), 8.80 (d, J = 4.4 Hz, 1H), 8.66 (d, J = 8.2 Hz, 1H), 7.87 (m, 2H), 7.77 (m, 1H), 7.60 (t, J = 7.2 Hz, 1H), 6.67 (s, 1H), 2.28 (s, 3H); MS 303.1 (M+H).

Example 286 **[2-(3-Acetylphenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-57)**: ^{1}H NMR (500 MHz, DMSO-d6) δ 8.80 (s, 1H), 8.55 (d, J = 7.7 Hz, 1H), 8.42 (d, J = 7.6 Hz, 1H), 8.00 (d, J = 7.0 Hz, 1H), 7.76 (m, 2H), 7.58 (t, J = 7.7 Hz, 1H), 7.48 (s, br, 1H), 6.60 (s, 1H), 2.49 (s, 3H), 2.03 (s, 3H); MS 344.1 (M+H).

Example 287 **[2-(3,5-Ditrifluoromethylphenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-58)**: ^{1}H NMR (500 MHz, DMSO-d6) δ 10.7 (s, br, 1H), 8.95 (s, 2H), 8.63 (d, J = 8.2 Hz, 1H), 8.25 (s, 1H), 7.86 (m, 2H), 7.58 (t, J = 6.9 Hz, 1H), 6.62 (s, 1H), 2.26 (s, 3H); MS 438.1 (M+H).

Example 288 **[2-(3-Hydroxymethylphenyl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-59)**: ^{1}H NMR (500 MHz, DMSO-d6) δ 8.74 (d, J = 7.9 Hz, 1H), 8.33 (s, 1H), 8.17 (s, br, 1H), 7.95 (s, br, 1H), 7.89 (s, br, 1H), 7.62 (m, 3H), 6.72 (s, 1H), 5.53 (s, 1H), 4.60 (s, 2H), 2.28 (s, 3H); MS 332.1 (M+H).

Example 289 **(5-Methyl-2*H*-pyrazol-3-yl)-[2-(3-phenoxyphenyl)-quinazolin-4-yl]-amine (III-60)**: mp 231-

232°C; ^{1}H NMR (DMSO-d6) δ 2.21 (3H, s), 6.59 (1H, s), 7.10-7.22 (4H, m), 7.41-7.45 (2H, m), 7.54-7.59 (2H, m), 7.81 (2H, s), 8.09 (1H, s), 8.27 (1H, m), 8.64 (1H, m), 10.40 (1H, s), 12.20 (1H, s); IR (solid); IR (solid) 1589, 1560, 1541, 1536, 1484, 1360, 1227; MS 394.7 $(M+H)^+$.

Example 290 **(5-Cyclopropyl-2*H*-pyrazol-3-yl)-[2-(3-phenoxyphenyl)-quinazolin-4-yl]-amine (III-61)**: mp 193-195°C; ^{1}H NMR (DMSO-d6) δ 0.67 (2H, m), 0.93 (2H, m),1.87 (1H,m), 6.56 (1H, s), 7.06-7.20 (4H, m), 7.40-7.43 (2H, m), 7.55-7.59 (2H, m), 7.81 (2H, s), 8.11 (1H, s), 8.27 (1H, m), 8.63 (1H, m), 10.43 (1H, s), 12.26 (1H, s); IR (solid); IR (solid) 1589, 1574, 1527, 1483, 1369, 1226; MS 420.7 $(M+H)^+$.

Example 291 **(5-Methyl-2*H*-pyrazol-3-yl)-(2-thiophen-3-yl-quinazolin-4-yl)-amine (III-62)**: ^{1}H NMR (500 MHz, DMSO-d6) δ11.78 (s, br, 1H), 8.75 (d, J = 8.1 Hz, 1H), 8.68 (s, 1H), 7.98 (dd, J = 7.9, 7.5 Hz, 1H), 7.89 (m, 2H), 7.81 (m, 1H), 7.68 (t, J = 7.5 Hz, 1H), 6.69 (s, 1H), 2.30 (s, 3H); MS 308.1 (M+H).

Example 292 **(2-Phenyl-quinazolin-4-yl)-(2*H*-pyrazol-3-yl)-amine (III-63)**: mp 247-249°C; ^{1}H NMR (DMSO) δ 6.99 (1H, br s), 7.49-7.58 (5H, m), 7.81 (1H, br s), 7.83 (2H, m), 8.47-8.49 (2H, m), 8.66 (1H, d), 10.54 (1H, s), 12.59 (1H, s); IR (solid) 3145, 2922, 1622, 1597; MS 288.2 $(M+H)^+$.

Example 293 **(2*H*-Pyrazol-3-yl)-(2-pyridin-4-yl-quinazolin-4-yl)-amine (III-64)**: mp 285-286°C; ^{1}H NMR (DMSO) δ 6.99 (1H, br s), 7.65 (1H, m), 7.81-7.94 (3H, m), 8.3-8.35 (2H, m), 8.73 (1H, d), 8.84-8.90 (2H, m), 10.76 (1H, s),

12.6 (1H, s); IR (solid) 3180, 2972, 1600, 1574; MS 289.2 $(M+H)^+$.

Example 294 **5-Ethyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-65)**: mp 221-222°C; ^{1}H NMR (DMSO) δ 1.31 (3H, t), 2.68 (2H, d), 6.80 (1H, s), 7.50-7.60 (4H, m), 8.45-8.55 (2H, m), 8.65-8.75 (1H, m), 10.44 (1H,s), 12.27 (1H,s); IR (solid) 3190, 1622, 1595, 1575, 1533, 1482, 1441, 1420, 1403, 1361, 758, 711; MS 316.2 $(M+H)^+$.

Example 295 **(2-Phenyl-quinazolin-4-yl)-(5-propyl-2*H*-pyrazol-3-yl)-amine (III-66)**: mp 204-205°C; ^{1}H NMR (DMSO-d6) δ 1.02 (3H, t), 1.66-1.75 (2H, m), 2.69 (2H, t), 6.80 (1H, s), 7.45-7.60 (4H,m), 7.80-7.88 (2H, m), 8.45-8.50 (2H, m), 8.65 (1H, d), 10.39 (1H, s), 12.25 (1H, s); IR (solid) 1621, 1560, 1572, 1533, 1479, 1441, 1421, 1363, 1328, 999, 827, 808, 763, 709, 697; MS 330.2 $(M+H)^+$.

Example 296 **(5-Isopropyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-67)**: mp 218-219°C; ^{1}H NMR (DMSO-d6) δ 1.36 (6H, d), 3.05 (1H, m), 6.86 (1H, s), 7.48-7.59 (4H, m), 7.80-7.88 (2H, m), 8.49-8.58 (2H, m), 8.66 (1H, d), 10.47 (1H, s), 12.30 (1H, s); IR (solid) 3173, 2968, 1619, 1593, 1573, 1533, 1478, 1438, 1413, 1398, 1363, 1329, 995, 822, 798, 761, 707, 666, 659; MS 330.2 $(M+H)^+$.

Example 297 **(5-*tert*-Butyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-68)**: mp 136-137°C; ^{1}H NMR (DMSO-d6) δ 1.38 (9H, s), 6.87 (1H, br s), 7.51-7.57 (4H, m), 7.84-7.85 (2H, m), 8.49-8.51 (2H, m), 8.65 (1H, d), 10.43 (1H, s), 12.21 (1H, br s); IR (solid) 3162, 2963, 1621, 1590, 1572; MS 344.2$(M+H)^+$.

Example 298 **(5-*tert*-Butyl-2*H*-pyrazol-3-yl)-(2-pyridin-4-yl-quinazolin-4-yl)-amine (III-69)**: mp >300°C; ^{1}H NMR (DMSO) δ 1.38 (9H, s), 6.82 (1H, br s), 7.63 (1H, m), 7.86-7.91 (2H, m), 8.32-8.33 (2H, d), 8.69 (1H, d), 8.75-8.76 (2H, d), 10.60 (1H, s), 12.31 (1H, br s); IR (solid) 3683, 3149, 2963, 1621; MS 345.2(M+H)$^+$.

Example 299 **(5-Cyclopentyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-70)**: mp 240-241°C; ^{1}H NMR (DMSO-d6) δ 1.68-1.89 (6H, m), 2.03-2.17 (2H, m), 3.14-3.22 (1H, m), 6.80 (1H, s), 7.50-7.60 (4H, m), 7.80-7.89 (2H, m), 8.45-8.52 (2H, m), 8.67 (1H, d), 10.52 (1H, s), 12.26 (1H, s); IR (solid) 2957, 1621, 1591, 1571, 1531, 1476, 1438, 1405, 1370, 1325, 999, 951, 801, 775, 761, 747, 710695, 668, 654; MS 356.2(M+H)+.

Example 300 **(5-Phenyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-71)**: mp 207-209°C; ^{1}H NMR (DMSO) δ 7.38-7.40 (1H, m), 7.50-7.58 (6H, m), 7.82-7.88 (4H, m), 8.51 (2H, m), 8.67 (1H, s), 10.58 (1H, s), 13.11 (1H, br s); IR (solid) 3345, 3108, 1627, 1612; MS 364.2 (M+H)$^+$.

Example 301 **(5-Carboxy-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-72)**: (5-Methoxycarbonyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (**III-73**) (345mg, 1 mmole in THF, 6 mL) was treated with NaOH (1M, 4.0 mL), stirred at 50°C for 5 hours, cooled to room temperature, and neutralised with 1M HCl. The mixture was concentrated *in vacuo* to remove THF then diluted with water and the resulting precipitate filtered. The residual solid was dried at 80°C under vacuum to afford **III-72** as an off-white solid (312 mg, 94%): mp 289-291°C

(dec.); ^{1}H NMR (DMSO) δ 7.45 (1H, br s), 7.50-7.60 (5H, m), 7.80-7.88 (2H, m), 7.40-7.50 (2H, m), 8.60-8.70 (1H, d), 10.70 (1H, s), 13.00-13.80 (2H, br s); IR (solid) 1699, 1624, 1607, 1570,1539, 1506, 1486, 1398, 1333, 1256, 1177, 1004, 827, 764, 705; MS 332.3(M+H)$^+$.

Example 302 **(5-Methoxycarbonyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-73)**: mp 271-273°C; ^{1}H NMR (DMSO) δ 3.95 (3H, s), 7.50-7.65 (5H, m), 7.80-7.98 (2H, m), 8.40-8.50 (2H, m), 8.65-8.73 (1H, m), 10.80 (1H, s), 13.80 (1H, s); IR (solid) 3359, 1720, 1624, 1597, 1561, 1538, 1500, 1475, 1435, 1410, 1358, 1329, 1283, 1261, 1146, 1125, 1018, 1010, 944, 827, 806, 780, 763, 703, 690, 670; MS 346.3(M+H)$^+$.

Example 303 **(5-Hydroxymethyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-74)**: A solution of (5-Methoxycarbonyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (**III-73**) (345mg, 1mmol) in anhydrous THF (10mL) was treated with lithium borohydride (125mg, 5.75 mmol) at 65°C for 5 hours. The mixture was cooled to room temperature then combined with 2M HCl and ethyl acetate. Solid sodium hydrogen carbonate was added to achieve pH 8 and the resulting mixture extracted with ethyl acetate. The extracts were dried over magnesium sulphate and concentrated. Purification by flash chromatography (SiO_2, methanol-dichloromethane gradient) afforded **III-74** (95 mg, 30%) as an off-white solid: mp 238-239°C; ^{1}H NMR (DMSO) δ 4.58 (2H, d, CH2), 5.35 (1H, s, OH), 6.94 (1H, s), 7.50-7.60 (4H, m), 7.85-7.90 (2H, m), 8.48-8.54 (2H, m), 8.69 (1H, 1H), 10.40 (1H, s), 12.48 (1H, s); IR (solid) 1652, 1621, 1603, 1575, 1558, 1539, 1532, 1480, 1373, 1320, 1276, 1175, 1057, 1037, 1007, 951, 865, 843, 793, 780, 7124; MS 318.2(M+H)$^+$.

Example 304 **(5-Methoxymethyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-75)**: mp 190-191°C; ^{1}H NMR (DMSO) δ 3.34 (3H, s), 4.45 (2H, s), 7.00 (1H, s), 7.50-7.62 (4H, m), 7.82-7.90 (2H, m), 8.45-8.52 (2H, m), 8.65 (1H, br s), 10.50 (1H, s), 12.30 (1H, s); IR (solid) 3177, 1606, 1589, 1530, 1479, 1441, 1406, 1374, 1363, 1329, 1152, 1099, 999, 954, 834, 813, 766, 707, 691; MS 332.3(M+H)$^+$.

Example 305 **[5-(3-Hydroxyprop-1-yl)-2*H*-pyrazol-3-yl]-(2-phenyl-quinazolin-4-yl)-amine (III-76)**: A solution of (5-benzyloxypropyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (**III-78**) (200mg, 0.46mmol) in toluene (4mL) and acetonitrile (8mL) was stirred with trimethylsilyl iodide (0.64ml, 4.6mmol) at 55°C for 3 hours to afford an amber coloured solution. This mixture was diluted with ethyl acetate and aqueous sodium hydrogen carbonate. The resulting layers were separated, the organic layer was dried over magnesium sulphate and concentrated *in vacuo*. Purification by flash chromatography (SiO_2, methanol-dichloromethane gradient) affords a yellow oil (115mg). Trituration with dichloromethane affords **III-76** as an off-white solid dried at 75°C under vacuum (83mg, 52%): mp 164-165°C; ^{1}H NMR (DMSO) δ 1.80-1.90 (2H, m), 2.70-2.80 (2H, m), 3.50-3.60 (2H, m), 4.59 (1H, s), 6.80 (1H, s), 7.50-7.60 (4H, m), 7.82-7.90 (2H, m), 8.48-8.53 (2H, m), 8.63 (1H, s), 10.40 (1H, s), 12.25 (1H, s); IR (solid) 1622, 1587, 1574, 1562, 1528, 1480, 1440, 1421, 1368, 1329, 1173, 1052, 1030, 1006, 952, 833, 762, 734, 706, 690, 671, 665; MS 346.0(M+H)$^+$.

Example 306 **[5-(3-Methoxyprop-1-yl)-2*H*-pyrazol-3-yl]-(2-phenyl-quinazolin-4-yl)-amine (III-77)**: mp 169-170°C; ^{1}H

NMR (DMSO-d6) δ 1.86-1.97 (2H, m), 2.75 (2H, t), 3.30 (3H, s), 3.45 (2H, t), 6.80 (1H, s), 7.50-7.60 (4H, m), 7.80-7.90 (2H, m), 8.45-8.55 (2H, m), 8.67 (1H, d), 10.30 (1H, s), 12.25 (1H, s); IR (solid) 1620, 1591, 1572, 1532, 1476, 1425, 1408, 1373, 1326, 1117, 1003, 831, 764, 714, 695; MS 360.3$(M+H)^+$.

Example 307 **[5-(3-Benzyloxyprop-1-yl)-2*H*-pyrazol-3-yl]-(2-phenyl-quinazolin-4-yl)-amine (III-78)**: mp 177-178°C; ^{1}H NMR (DMSO) δ 1.92-2.03 (2H, m), 3.76-3.85 (2H, m), 3.52-3.62 (2H, m), 4.51 (2H, s), 6.82 (1H, s), 7.28-7.40 (5H, m), 7.46-7.58 (4H, m), 7.80-7.85 (2H, m), 8.47-8.52 (2H, m), 8.66 (1H, d), 10.45 (1H, s); IR (solid) 1621, 1591, 1562, 1532, 1479, 1454, 1426, 1408, 1374, 1101, 1006, 835, 766, 738, 712, 696; MS 436.3$(M+H)^+$.

Example 308 **[5-(3-Aminoprop-1-yl)-2*H*-pyrazol-3-yl]-(2-phenyl-quinazolin-4-yl)-amine (III-79)**: A solution of [5-(3-tert-butoxycarbonylaminoprop-1-yl)-2*H*-pyrazol-3-yl]-(2-phenyl-quinazolin-4-yl)-amine (**III-80**) (250mg, 0.56mmol), in dichloromethane (3mL) at 0°C was treated with TFA (2mL). The mixture was warmed to room temperature then concentrated *in vacuo*. The residue was triturated and concentrated from dichloromethane (3x5mL) and ether, then triturated with dichloromethane to crystallize the TFA salt. The resulting solid was collected by filtration and dissolved in a mixture of ethanol (3mL) and water (3mL). Potassium carbonate was added in portions to achieve pH 8 then the mixture allowed to crystallize. The product was collected by filtration and dried at 80°C under vacuum to afford **III-79** as an off-white powder (122mg, 63%): mp 205-207°C; ^{1}H NMR (DMSO) δ 1.68-1.83 (2H, m), 2.65-2.80(4H, m), 6.80 (1H, s), 7.50-7.60 (4H, m), 7.80-7.90 (2H, m), 8.45-8.53 (2H,

m), 8.65 (1H, d), 10.45 (1H, br s); IR (solid) 1621, 1598, 1568, 1533, 1484, 1414, 1364, 1327, 1169, 1030, 951, 830, 776, 764, 705, 677; MS 345.3$(M+H)^+$.

Example 309 **[5-(3-tert-Butoxycarbonylaminoprop-1-yl)-2*H*-pyrazol-3-yl]-(2-phenyl-quinazolin-4-yl)-amine (III-80)**: mp 199-200°C; ^{1}H NMR (DMSO) δ 1.37 (9H, s), 1.71-1.82 (2H,m), 2.67 (2H, t), 3.00-3.11 (2H, m), 7.81 (1H, s), 7.99 (1H, s), 7.50-7.60 (4H, m), 7.80-7.85 (2H, m), 8.48-8.52 (2H, m), 8.63 (1H, d), 10.40 (1H, s), 12.26 (1H, m); IR (solid) 2953, 1687, 1622, 1594, 1573, 1535, 1481, 1441, 1419, 1364, 1327, 1281, 1252, 1166, 1070, 1028, 998, 951, 848, 807, 768, 740, 728, 710,693; MS 445.3 $(M+H)^+$.

Example 310 **5-Isopropylcarbamoyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-81)**: ^{1}H NMR (500MHz, DMSO-d6) δ 1.20 (d, J = 6.6 Hz, 6H), 4.13 (m, 1H), 7.42 (br. s, 1H), 7.61 (dd, J = 7.0, 7.7 Hz, 2H), 7.66 (t, J = 7.1 Hz, 1H), 7.71 (m, 1H), 7.99 (m, 2H), 8.39 (m, 1H), 8.42 (d, J = 7.1 Hz, 2H), 8.74 (d, J = 8.2 Hz, 1H), 11.41 (br. s, 1H); EI-MS 373.2 (M+H); HPLC-Method C, R_t 14.09 min.

Example 311 **(5-Allylcarbamoyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-82)**: ^{1}H NMR (500MHz, DMSO-d6) δ 4.02 (m, 2H), 5.15 (m, 1H), 5.23 (m, 1H), 5.94 (m, 1H), 7.45 (br. s, 1H), 7.60 (t, J = 6.9 Hz, 2H), 7.64 (m, 1H), 7.72 (m, 1H), 7.98 (m, 2H), 8.43 (m 2H), 8.72 (d, J = 8.2 Hz, 1H), 8.84 (br. s, 1H), 11.34 (br. s, 1H); EI-MS 371.2 (M+H); HPLC-Method C, R_t 13.67 min.

Example 312 **[5-(2-Methoxyethylcarbamoyl)-2*H*-pyrazol-3-yl]-(2-phenyl-quinazolin-4-yl)-amine (III-83)**: ^{1}H NMR

(500MHz, DMSO-d6) δ 3.32 (s, 3H), 3.48 (m, 4H), 7.36 (br. s, 1H), 7.62 (m, 2H), 7.63 (m, 1H), 7.71 (m, 1H), 7.98 (m, 2H), 8.41 (dd, J = 1.4, 7.0, 2H), 8.70 (m, 2H), 11.30 (br. s, 1H); EI-MS 389.2 (M+H); HPLC-Method C, R_t 12.37 min.

Example 313 **(5-Benzylcarbamoyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-84)**: ^{1}H NMR (500MHz, DMSO-d6) δ 4.52 (d, J = 6.0 Hz, 2H), 7.29 (m, 1H), 7.38 (d, J = 4.2 Hz, 4H), 7.58 (t, J = 7.5 Hz, 2H), 7.63 (m, 1H), 7.72 (m, 1H), 7.98 (m, 2H), 8.43 (d, J = 7.7 Hz, 2H), 8.72 (d, J = 7.5 Hz, 1H), 9.23 (br. s, 2H), 11.34 (br. s, 1H); EI-MS 421.2 (M+H); HPLC-Method C, R_t 16.76 min.

Example 314 **(5-Cyclohexylcarbamoyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-85)**: ^{1}H NMR (500MHz, DMSO-d6) δ 1.16 (m, 1H), 1.34 (m, 4H), 1.62 (d, J = 2.6 Hz, 1H), 1.76 (m, 2H), 1.85 (m, 2H), 3.79 (m, 1H), 7.43 (m, 1H), 7.60 (t, J = 7.2 Hz, 2H), 7.65 (t, J = 7.1 Hz, 1H), 7.71 (ddd, J = 2.2, 5.4, 8.2 Hz, 1H), 7.98 (m, 2H), 8.35 (m, 1H), 8.43 (dd, J = 1.4, 7.2 Hz, 2H), 8.72 (d, J = 8.2 Hz, 1H), 11.34 (br. s, 1H); EI-MS 413.5 (M+H); HPLC-Method C, R_t 17.18 min.

Example 315 **(5-Diethylcarbamoyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-86)**: ^{1}H NMR (500MHz, DMSO-d6) δ 1.18 (br. s, 3H), 1.25 (br. s, 3H), 3.49 (br. s, 2H), 3.69 (b. s, 2H), 7.21 (s, 1H), 7.59 (t, J = 6.9 Hz, 2H), 7.62 (m, 1H), 7.70 (m, 1H), 7.96 (m, 2H), 8.39 (d, J = 7.1 Hz, 2H), 8.74 (d, J = 8.4 Hz, 1H), 11.37 (br. s, 1H); EI-MS 387.2 (M+H); HPLC-Method C, R_t 14.50 min.

Example 316 **[5-(Benzyl-methyl-carbamoyl)-2*H*-pyrazol-3-yl]-(2-phenyl-quinazolin-4-yl)-amine (III-87)**: ^{1}H NMR (500MHz, DMSO-d6) δ 3.33 (s, 3H), 4.75 (s, 2H), 7.26 (m, 1H), 7.31 (m, 1H), 7.38 (m, 4H), 7.58 (m, 2H), 7.70 (m, 1H), 7.95 (m, 3H), 8.26 (m, 1H), 8.40 (d, J = 7.8 Hz, 2H), 8.75 (m, 1H), 11.2 (br. s, 1H); EI-MS 435.2 (M+H); HPLC-Method C, R_t 16.77 min.

Example 317 **(2-Phenyl-quinazolin-4-yl)-(5-propylcarbamoyl-2*H*-pyrazol-3-yl)-amine (III-88)**: ^{1}H NMR (500MHz, DMSO-d6) δ 0.94 (t, J = 7.3 Hz, 3H), 1.57 (m, 2H), 3.24 (q, J = 6.5 Hz, 2H), 7.39 (br. s, 1H), 7.60 (t, J = 7.3 Hz, 2H), 7.64 (m, 1H), 7.71 (br. t, J = 6.5 Hz, 1H), 7.98 (m, 2H), 8.42 (d, J = 7.2 Hz, 2H), 8.61 (br. s, 1H), 8.72 (d, J = 8.5 Hz, 1H), 11.34 (br. s, 1H); EI-MS 373.3 (M+H); HPLC-Method C, R_t 13.51 min.

Example 318 **[5-(Ethyl-isopropyl-carbamoyl)-2*H*-pyrazol-3-yl]-(2-phenyl-quinazolin-4-yl)-amine (III-89)**: ^{1}H NMR (500MHz, DMSO-d6) δ 0.92 (t, J = 7.4 Hz, 6H), 1.52 (m, 2H), 1.59 (m, 1H), 3.79 (m, 2H), 7.53 (br. s, 1H), 7.57 (t, J = 7.5 Hz, 2H), 7.65 (t, J = 7.2 Hz, 1H), 7.71 (m, 1H), 7.99 (m, 2H), 8.23 (br. d, J = 8.8 Hz, 1H), 8.46 (d, J = 7.5 Hz, 2H), 8.74 (d, J = 8.4 Hz, 1H), 11.34 (br. s, 1H); EI-MS 401.2 (M+H); HPLC-Method C, R_t 15.51 min.

Example 319 **(5-Cyclopropylcarbamoyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-90)**: ^{1}H NMR (500MHz, DMSO-d6) δ 0.60 (m, 2H), 0.74 (m, 2H), 2.86 (m, 1H), 7.34 (br. s, 1H), 7.62 (m, 3H), 7.70 (m, 1H), 7.97 (m, 2H), 8.41 (d, J = 7.9 Hz, 2H), 8.63 (br. s, 1H), 8.72 (d, J = 7.8 Hz, 1H), 11.35 (br. s, 1H); EI-MS 371.2 (M+H); HPLC-Method C, R_t 12.64 min.

Example 320 **(5-Isobutylcarbamoyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-91)**: ^{1}H NMR (500MHz, DMSO-d6) δ 0.94 (d, J = 6.7 Hz, 6H), 1.88 (m, 1H), 3.12 (t, J = 6.4 Hz, 2H), 7.45 (br. s, 1H), 7.58 (t, J = 7.2 Hz, 3H), 7.64 (t, J = 7.1 Hz, 1H), 7.71 (m, 1H), 7.98 (m, 2H), 8.44 (dd, J = 1.3, 7.9 Hz, 2H), 8.62 (br. s, 1H), 8.72 (d, J = 8.3 Hz, 1H), 11.33 (br. s, 1H); EI-MS 387.2 (M+H); HPLC-Method C, R_t 14.70 min.

Example 321 **{5-[(3S)-3-Methoxymethyl-pyrrolidine-1-carbonyl]-2*H*-pyrazol-3-yl}-(2-phenyl-quinazolin-4-yl)-amine (III-93)**: ^{1}H NMR (500MHz, DMSO-d6) δ 2.00 (m, 2H), 2.12 (m, 1H), 3.29 (s, 3H), 3.45 (t, J = 8.7 Hz, 1H), 3.57 (dd, J = 3.2, 9.3 Hz, 1H), 3.86 (m, 1H), 3.92 (m, 1H), 4.36 (m, 2H), 7.45 (br. s, 1H), 7.59 (t, J = 7.2 Hz, 2H), 7.63 (m, 1H), 7.69 (m, 1H), 7.97 (m, 2H), 8.40 (d, J = 7.5 Hz, 2H), 8.74 (d, J = 7.6 Hz, 1H), 11.38 (br. s, 1H); EI-MS 429.2 (M+H); HPLC-Method C, R_t 13.84 min.

Example 322 **(2-Phenyl-quinazolin-4-yl)-(5-*m*-tolylcarbamoyl-2*H*-pyrazol-3-yl)-amine (III-94)**: ^{1}H NMR (500MHz, DMSO-d6) δ 2.33 (s, 3H), 6.97 (d, J = 7.5 Hz, 1H), 7.27 (t, J = 7.8 Hz, 1H), 7.62 (m, 7H), 7.72 (m, 1H), 7.98 (m, 2H), 8.46 (dd, J = 2.0, 7.9 Hz, 2H), 8.71 (m, 1H), 10.29 (s, 1H), 11.31 (br. s, 1H); EI-MS 421.2 (M+H); HPLC-Method C, R_t 17.11 min.

Example 323 **(2-Phenyl-quinazolin-4-yl)-(5-*p*-tolylcarbamoyl-2*H*-pyrazol-3-yl)-amine (III-95)**: ^{1}H NMR (500MHz, DMSO-d6) δ 2.30 (s, 3H), 7.20 (d, J = 8.3 Hz, 2H), 7.62 (m, 5H), 7.68 (d, J = 8.3 Hz, 2H), 7.72 (m, 1H), 7.98 (m, 2H), 8.46 (dd, J = 1.8, 7.0 Hz, 2H), 8.72 (m, 1H), 10.31 (s, 1H), 11.36 (br. s, 1H); EI-MS 421.2 (M+H); HPLC-Method C, R_t 16.95 min.

Example 324 **(5-Methylcarbamoyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-96)**: ^{1}H NMR (500MHz, DMSO-d6) δ 2.82 (d, J = 4.6 Hz, 3H), 7.31 (br. s, 1H), 7.62 (m, 3H), 7.69 (m, 1H), 7.97 (m, 2H), 8.42 (d, J = 7.1 Hz, 2H), 8.59 (br. s, 1H), 8.71 (d, J = 8.0 Hz, 1H), 11.30 (br. s, 1H); EI-MS 345.1 (M+H); HPLC-Method C, R_t 11.02 min.

Example 325 **[5-(Morpholine-4-carbonyl)-2*H*-pyrazol-3-yl]-(2-phenyl-quinazolin-4-yl)-amine (III-97)**: ^{1}H NMR (500MHz, DMSO-d6) δ 3.33 (m, 4H), 3.83 (m 4H), 7.34 (br. s, 1H), 7.53 (m, 4H), 7.86 (m, 2H), 8.43 (m, 2H), 8.67 (d, J = 8.6 Hz, 1H), 10.70 (s, 1H), 13.56 (s, 1H); EI-MS 401.2 (M+H); HPLC-Method A, R_t 2.68 min.

Example 326 **[5-(1-Methylpiperazine-4-carbonyl)-2*H*-pyrazol-3-yl]-(2-phenyl-quinazolin-4-yl)-amine (III-98)**: ^{1}H NMR (500MHz, DMSO-d6) δ 2.25 (s, 3H), 2.43 (m, 4H), 3.87 (m 4H), 7.33 (br. s, 1H), 7.53 (m, 4H), 7.87 (m, 2H), 8.45 (m, 2H), 8.67 (d, J = 7.6 Hz, 1H), 10.70 (s, 1H), 13.30 (s, 1H); EI-MS 414.2 (M+H); HPLC-Method A, R_t 2.38 min.

Example 327 **[5-(2-Hydroxyethylcarbamoyl-2*H*-pyrazol-3-yl]-(2-phenyl-quinazolin-4-yl)-amine (III-99)**: ^{1}H NMR (500MHz, DMSO-d6) δ 3.36 (m, 2H), 3.52 (m, 2H), 4.79 (m, 1H), 7.50 (m, 5H), 7.83 (m, 2H), 8.50 (m, 4H), 10.52 (br. s, 1H), 13.25 (s, 1H); EI-MS 375.1 (M+H); HPLC-Method A, R_t 2.51 min.

Example 328 **(5-Carbamoyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-100)**: To a solution of 5-(2-phenyl-quinazolin-4-ylamino)-1*H*-pyrazole-3-carboxylic

acid 2,5-dioxo-pyrrolidin-1-yl ester (270 mg, 0.63 mmol) in DMF (20 ml) was added a solution of ammonia in 1,4-dioxane (0.5 M, 10 ml). The resulting mixture was stirred at room temperature for 24 h. After concentration of the solvents, the residue was added to water (20 ml). The resulting precipitate was collected to afford **III-100** (168 mg, 80%)as a yellow solid. ^{1}H NMR (500MHz, DMSO-d6) δ 7.77-7.51 (m, 6H), 7.86 (br s, 2H), 8.11 (m, 1H), 8.50 (m, 2H), 8.63 (m, 1H), 10.52 (s, 1H), 11.25 (s, 1H); EI-MS 331.1 (M+H); HPLC-Method A, R_t 2.52 min.

Example 329 **(4-Bromo-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-101):** Prepared according to Method A to afford a yellow solid, mp 189°C; ^{1}H NMR (DMSO-d6) δ 7.44-7.46 (3H, m), 7.58 (1H, m), 7.87 (2H, d), 8.15 (1H, s), 8.31-8.34 (2H, m), 8.49 (1H, d), 10.08 (1H, s), 13.13 (1H, s); IR (solid) 3286, 2969, 1738, 1632; MS 366.2/368.2(M+H)$^+$.

Example 330 **(4-Bromo-5-methyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-102)**: mp 183-185°C; ^{1}H NMR (DMSO) δ 2.33 (3H, br s), 7.44-7.46 (3H, m), 7.57 (1H, m), 7.84-7.87 (2H, m), 8.31-8.34 (2H, m), 8.48 (1H, d), 10.05 (1H, s), 12.91 (1H, br s); IR (solid) 3362, 3065, 2831, 1619, 1578; MS 380.2/382.2(M+H)$^+$.

Example 331 **(4-Cyano-2*H*-pyrazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-103)**: mp >250°C; ^{1}H NMR (DMSO) δ 7.47-7.49 (3H, m), 7.64 (1H, m), 7.91 (2H, m), 8.40-8.43 (2H, m), 8.53 (1H, d), 8.71 (1H, d), 10.61 (1H, s), 13.60 (1H, s); IR (solid) 3277, 3069, 2855, 2231, 1625; MS 313.2(M+H)$^+$.

Example 332 **(5-Methyl-2*H*-pyrazol-3-yl)-(2-morpholin-4-yl-quinazolin-4-yl)-amine (III-104)**: mp 223-224°C; ^{1}H NMR (DMSO) δ 2.26(3H, s), 3.65(4H, m), 3.75(4H, m), 6.44(1H, s), 7.12(1H, d), 7.33(1H, d), 7.56(1H, t), 8.37(1H, d), 10.01(1H, s), 12.13(1H, br s); IR (solid) 1621, 1578, 1537, 1475, 1434, 1385; MS 311.0 $(M+H)^+$.

Example 333 **(5-Methyl-2*H*-pyrazol-3-yl)-(2-piperazin-1-yl-quinazolin-4-yl)-amine (III-105)**: mp 179-181°C; ^{1}H NMR (DMSO) δ 2.26(3H, s), 2.74 (4H, br s), 3.71(4H, br s), 6.43(1H, s), 7.08(1H, t), 7.30(1H, d), 7.53(1H, t), 8.34(1H, d), 9.50(1H, s), 12.08(1H, br s); IR (solid) 2853, 1619, 1603, 1566, 1549, 1539; MS 310.0 $(M+H)^+$

Example 334 **[2-(4-Methylpiperidin-1-yl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-106)**: mp 148-150°C; ^{1}H NMR (DMSO) δ 1.06(3H, d), 1.03(2H, m), 1.51-1.70(3H, m), 2.26(3H, s), 2.86(2H, m), 4.73(2H, d), 6.44(1H, s), 7.06(1H, d), 7.29(1H, d), 7.52(1H, t), 8.32(1H, d), 9.92(1H, s), 12.09(1H, br s); IR (solid) 2917, 2840, 1629, 1593, 1562, 1546, 1486; MS 323.0 $(M+H)^+$.

Example 335 **[2-(4-Methylpiperazin-1-yl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-107)**: mp 105-107°C; ^{1}H NMR (DMSO) δ 2.21(3H, s), 2.26(3H, s), 2.34(4H, m), 3.75(4H, m), 6.45(1H, s), 7.09(1H, t), 7.31(1H, d), 7.54(1H, t), 8.34(1H, d), 9.96(1H, s), 12.12(1H, br s); IR (solid) 2934, 2844, 2804, 1620, 1593, 1572, 1536, 1476; MS 324.0 $(M+H)^+$.

Example 336 **(5-Methyl-2*H*-pyrazol-3-yl)-(2-piperidin-1-yl-quinazolin-4-yl)-amine (III-108)**: mp 294°C; ^{1}H NMR (DMSO) δ 1.45-1.58 (4H, m), 1.63 (2H, m), 2.26 (3H, s), 3.79

(4H, m), 6.45 (1H, br s), 7.06 (1H, t), 7.29 (1H, d), 7.52 (1H, t), 8.33 (1H, d), 9.92 (1H, s), 12.11 (1H, br s); IR (solid) 2929, 2847, 1632, 1591, 1500, 1482, 1437, 1382; MS 309.3 $(M+H)^+$.

Example 337 **(2-Azepan-1-yl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-109)**: mp 269°C; ^{1}H NMR (DMSO) δ 1.50 (4H, br s), 1.76 (4H, br s), 2.25 (3H, s), 3.78 (4H, t), 6.55 (1H, br s), 7.03 (1H, t), 7.28 (1H, d), 7.50 (1H, t), 8.33 (1H, d), 9.92 (1H, s), 12.09 (1H, br s); IR (solid) 3427, 2963, 2927, 2909, 2872, 2850, 1623, 1595, 1586, 1568, 1504, 1486, 1468, 1386, 1427; MS 323.3 $(M+H)^+$.

Example 338 **[2-(4-(2-Hydroxyethylpiperidin-1-yl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-110)**: mp 175°C; ^{1}H NMR (DMSO) δ 1.08 (2H, m), 1.38 (2H, m), 1.57-1.83 (3H, m), 2.26 (3H, s), 2.85 (2H, t), 3.47 (2H, m), 4.38 (1H, t), 4.75 (2H, d), 6.45 (1H, br s), 7.06 (1H, t), 7.29 (1H, d), 7.52 (1H, t), 8.32 (1H, d), 9.93 (1H, s), 12.12 (1H, br s); IR (solid) 3365, 3073, 2972, 2868, 1622, 1604, 1586, 1568, 1486, 1463, 1440, 1394; MS 353.2 $(M+H)^+$.

Example 339 **(5-Cyclopropyl-2*H*-pyrazol-3-yl)-[2-(4-methylpiperidin-1-yl)-quinazolin-4-yl]-amine (III-111)**: To a solution of (5-cyclopropyl-1*H*-pyrazol-3-yl)-(2-chloro-quinazolin-4-yl)-amine (118 mg, 0.41 mmol) in *tert*-butanol (3.0 mL) was added 4-methylpiperidine (0.49 mL, 4.1 mmol) and the reaction mixture heated at reflux overnight. The reaction mixture was concentrated *in vacuo* and the residue dissolved in a mixture EtOH:water (1:3, 4 mL). Potassium carbonate (57mg, 0.41 mmol) was added and the mixture stirred at room temperature for 2

hours. The resulting suspension was filtered, washed with water (x2), and rinsed with Et_2O (x2) to afford **III-111** as a white solid (123mg, 85%): mp 190°C; ^1H NMR (DMSO) δ 0.66 (2H, s), 0.93 (5H, br s), 1.07 (2H, d), 1.66 (3H, s), 1.91 (1H, s), 2.85 (2H, t), 4.72 (2H, d), 6.33 (1H, s), 7.06 (1H, t), 7.29 (1H, d), 7.52 (1H, t), 8.31 (1H, d), 9.95 (1H, s), 12.18 (1H, br s); IR (solid) 2925, 2852, 1622, 1590, 1581, 1558, 1494, 1481, 1453, 1435, 1394; MS 349.2 $(M+H)^+$.

Example 340 **[2-(1,4-Dioxa-8-aza-spiro[4,5]dec-8-yl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-112)**: mp 191°C; ^1H NMR (DMSO) δ 1.65 (4H, s), 2.26 (3H, s), 3.90 (4H, s), 3.93 (4H, s), 6.43 (1H, br s), 7.09 (1H, t), 7.32 (1H, d), 7.54 (1H, t), 8.35 (1H, d), 9.99 (1H, br s), 12.13 (1H, br s); IR (solid) 3069, 2964, 2927, 2868, 1618, 1581, 1568, 1540, 1495, 1481, 1435, 1390; MS 367.3 $(M+H)^+$.

Example 341 **[2-(4-Cyclopentylamino-piperidin-1-yl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-113)**: mp 191°C; ^1H NMR (DMSO) δ 1.33 (2H, d), 1.65 (4H, s), 1.87 (2H, d), 2.20 (1H, s), 2.26 (3H, s), 2.49 (2H, s), 3.00 (2H, t), 3.36 (2H, s), 4.61 (2H, d), 6.45 (1H, br s), 7.07 (1H, s), 7.31 (1H, d), 7.52 (1H, s), 8.33 (1H, d), 9.94 (1H, br s), 12.12 (1H, br s); IR (solid) 3371, 2943, 1622, 1600, 1581, 1545, 1509, 1463, 1440, 1390; MS 378.2 $(M+H)^+$.

Example 342 **[2-(4-Hydroxypiperidin-1-yl)-quinazolin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (III-114)**: mp 123°C; ^1H NMR (DMSO) δ 1.34 (2H, d), 1.80 (2H, d), 2.26 (3H, s), 3.24 (2H, t), 3.72 (1H, br s), 4.39 (2H, d), 4.70 (1H, d), 6.44 (1H, br s), 7.07 (1H, t), 7.30 (1H, d), 7.53

(1H, t), 8.33 (1H, d), 9.94 (1H, br s), 12.11 (1H, br s); IR (solid) 3265, 3151, 2927, 2863, 1622, 1600, 1572, 1540, 1504, 1476, 1440, 1390, 1349, 1066, 1098; MS 325.3 $(M+H)^+$.

Example 343 **(5-Cyclopropyl-2*H*-pyrazol-3-yl)-[2-(4-hydroxy-4-phenylpiperidin-1-yl)-quinazolin-4-yl]-amine (III-115)**: mp 131°C; ^{1}H NMR (DMSO) δ 0.64 (2H, q), 0.93 (2H, q), 1.68 (2H, d), 1.83-1.97 (3H, m), 3.20-3.45 (2H, m), 4.69 (2H, d), 5.11 (1H, s), 6.37 (1H, br s), 7.08 (1H, t), 7.20 (1H, t), 7.31 (3H, t), 7.49 (2H, d), 7.53 (1H, t), 8.33 (1H, d), 9.98 (1H, br s), 12.18 (1H, br s); IR (solid) 3362, 2952, 2934, 2911, 2870, 2825, 1618, 1584, 1570, 1559, 1536, 1481, 1459, 1431, 1372, 1336, 1213, 994; MS 427.6 $(M+H)^+$.

Example 344 **(5-Cyclopropyl-2*H*-pyrazol-3-yl)-[2-(1,3-dihydro-isoindol-2-yl)-quinazolin-4-yl]-amine (III-116)**: Prepared according to Method E-I to afford an off-white solid, mp 237°C; ^{1}H NMR (DMSO-d6) δ 0.79 (2H, s), 1.00 (2H, d), 1.99 (1H, m), 4.92 (4H, d), 6.72 (1H, br s), 7.13 (1H, t), 7.33 (2H, s), 7.30-7.48 (3H, m), 7.58 (1H, t), 8.40 (1H, d), 10.12 (1H, s), 12.17 (1H, s); IR (solid) 3449, 3318, 2850, 1623, 1595, 1577, 1541, 1509, 1482, 1432, 1391, 1359, 1141, 1027, 877, 814; MS 369.4 $(M+H)^+$.

Example 345 **(2-Azepan-1-yl)-quinazolin-4-yl]-(5-cyclopropyl-2*H*-pyrazol-3-yl)-amine (III-117)**: mp 199-200°C; ^{1}H NMR (DMSO-d6) δ 0.60-0.70 (2H, m), 0.90-1.00 (2H, m), 1.45-1.57 (4H, m), 1.70-1.85 (4H, m), 1.88-1.97 (1H, m), 3.75-3.87 (4H, m), 6.42 (1H, s), 7.02 (1H, t), 7.27 (1H, d), 7.49 (1H, t), 8.29 (1H, d), 9.91 (1H, s), 12.19 (1H, br s); IR (solid) 2929, 1624, 1595, 1581,

1563, 1542, 1498, 1482, 1440, 1426, 1397, 1356, 1305, 1000, 825, 754; MS 349.2 $(M+H)^+$.

Example 346 **(5-Cyclopropyl-2*H*-pyrazol-3-yl)-[2-(3,4-dihydro-1*H*-isoquinolin-2-yl)-quinazolin-4-yl]-amine (III-118)**: mp 182-184°C; ^1H NMR (DMSO) δ 0.75 (2H, d), 1.02 (2H, d), 1.96 (1H, m), 2.89 (2H, m), 4.05 (2H, m), 4.94 (2H, s), 6.46 (1H, s), 7.10 (1H, t), 7.21 (4H, d), 7.37 (1H, d), 7.55 (1H, d), 8.36 (1H, d), 10.05 (1H, s), 12.23 (1H, br s); IR (solid) 1621, 1581, 1560, 1537, 1479, 1456, 1426, 1396, 1374, 1341, 1222; MS 383.3 $(M+H)^+$.

Example 347 **(5-Cyclopropyl-2*H*-pyrazol-3-yl)-[2-(2,3-dihydro-indol-1-yl)-quinazolin-4-yl]-amine (III-119)**: mp 150-153°C; ^1H NMR (DMSO) δ 0.74 (2H, d), 0.98 (2H, d), 1.96 (1H, m), 3.15 (2H, t), 4.25 (2H, t), 6.45 (1H, br s), 6.88 (1H, t), 7.09 (1H, t), 7.20 (2H, m), 7.53 (1H, d), 7.65 (1H, t), 8.43 (2H, br s), 10.09 (1H, s), 12.28 (1H, br s); IR (solid) 1621, 1588, 1577, 1564, 1537, 1487, 1455, 1425, 1386, 1259; MS 369.3 $(M+H)^+$.

Example 348 **(5-Cyclopropyl-2*H*-pyrazol-3-yl)-[2-(4-hydroxymethylpiperidin-1-yl)-quinazolin-4-yl]-amine (III-120)**: mp 142°C; ^1H NMR (DMSO) δ 0.67 (2H, d), 0.96 (2H, d), 1.10 (2H, q), 1.55-1.70 (3H, m), 1.91 (1H, m), 2.85 (2H, t), 3.28 (2H, s), 4.48 (1H, s), 4.76 (2H, d), 6.34 (1H, s), 7.06 (1H, t), 7.30 (1H, d), 7.52 (1H, t), 8.31 (1H, d), 9.96 (1H, s), 12.19 (1H, s); IR (solid) 3363, 3000, 2927, 2854, 1618, 1604, 1573, 1536, 1509, 1477, 1436, 1395, 1354, 1314, 1241, 1186, 1091, 995, 941, 823; MS 365.8 $(M+H)^+$.

Example 349 **(5-Cyclopropyl-2*H*-pyrazol-3-yl)-[2-(3,4-dihydro-2*H*-quinolin-1-yl)-quinazolin-4-yl]-amine (III-**

121): mp 137-145°C; ^{1}H NMR (DMSO-d6) δ 0.55 (2H, d), 0.88 (2H, d), 1.78 (1H, m), 1.92 (2H, t), 2.75 (2H, t), 4.04 (2H, t), 6.20 (1H, br s), 6.97 (1H, t), 7.14 (1H, m), 7.19 (1H, t), 7.42 (1H, d), 7.61 (1H, t), 7.67 (1H, d), 8.43 (1H, d), 10.04 (1H, s), 12.21 (1H, br s); IR (solid) 1622, 1572, 1539, 1493, 1454, 1420, 1373, 1249; MS 383.3 $(M+H)^+$.

Example 350 **(5-Methoxycarbonyl-2*H*-pyrazol-3-yl)-[2-(piperidine-1-yl)-quinazolin-4-yl]-amine (III-122):** ^{1}H NMR (500MHz, $CDCl_3$) δ1.7-1.8(6H,m), δ 3.8 (4H, m), δ 3.9 (3H, s), δ 5.5 (1H, s), δ 7.15 (1H, t), δ 7.4 (1H, d), δ 7.6 (1H, t), δ 8.0 (1H, d). HPLC-Method B, (starting with 95% H_2O) R_t 7.4 min; MS (ES+) 353.24 (M+H).

Example 351 **[5-(Piperidine-1-carbonyl)-2*H*-pyrazol-3-yl]-[2-(piperidine-1-yl)-quinazolin-4-yl]-amine (III-123):** HPLC-Method B, (starting with 95% H_2O:0.1% TFA) R_t 8.0 min; MS (ES+) 406.30, (ES-) 404.30.

Example 352 **(5-Hydroxymethyl-2*H*-pyrazol-3-yl)-[2-(piperidin-1-yl)-quinazolin-4-yl]-amine (III-124):** To a solution of **III-122** (10.0 mg, 0.028 mmol) in THF (6 mL) at ambient temperature was slowly added a 1M solution of $LiAlH_4$ in THF (0.05 mL, 0.05 mmol). After 15 minutes the solution was quenched with water and 1N HCl. The product was extracted from the aqueous layer with EtOAc. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by preparatory HPLC to afford **III-124** (4.0 mg, 44%). HPLC-Method B, (starting with 95% H_2O:0.1% TFA) R_t 6.1 min; MS (ES+) 325.13 (M+H), (ES-) 323.13 (M-H).

Example 353 **(5-Carbamoyl-2*H*-pyrazol-3-yl)-[2-(piperidin-1-yl)-quinazolin-4-yl]-amine (III-125)**: A solution of **III-122** (1.5 g, 4.3 mmol) in 2.0 M NH_3/MeOH (100 mL) was heated at 110°C for 2 days. The dark brown reaction mixture was concentrated *in vacuo* to afford a viscous oil which was purified by column chromatography to yield 0.7 g (50%) of **III-125**. ^{1}H NMR (500MHz, CD_3OD-d_3) δ1.6 (4H, m), δ1.7 (2H, m), δ 3.3 (1H, s), δ 3.8 (4H, m), δ 5.5 (1H, s), δ 7.15 (1H, t), δ 7.45 (1H, d), δ 7.55 (1H, t), δ 8.0 (1H, d); HPLC-Method B, (starting with 95% H_2O:0.1% TFA) R_t 5.9 min; MS (ES+) 338.13, (ES-) 336.15.

Example 354 **(5-Carbamoyl-2*H*-pyrazol-3-yl)-[2-(4-methylpiperidin-1-yl)-quinazolin-4-yl]-amine (III-126)**: HPLC-Method B, (starting with 95% H_2O:0.1% TFA) R_t 6.4 min; MS (ES+) 352.19, (ES-) 350.20.

Example 355 **(5,7-Difluoro-1*H*-indazol-3-yl)-(2-phenyl-5,6,7,8-tetrahydroquinazolin-4-yl)-amine (III-127)**: ^{1}H NMR (500 MHz, DMSO-d6) δ13.7 (s, 1H), 10.3 (s, br, 1H), 7.90 (d, 2H), 7.52 (t, 1H), 7.45 (m, 3H), 7.26 (d, 1H), 2.99 (m, 2H), 2.75 (m, 2H), 1.95 (br, 4H) ppm; MS (ES+) 378.24 (M+H); (ES-) 376.23 (M-H); HPLC-Method A, R_t 3.04 min.

Example 356 **(2-Phenyl-5,6,7,8-tetrahydroquinazolin-4-yl)-(5-trifluoromethyl-1*H*-indazol-3-yl)-amine (III-128)**: ^{1}H NMR (500 MHz, DMSO-d6) δ13.4 (s, 1H), 10.2 (s, br, 1H), 8.13 (s, 1H), 7.86 (d, 2H), 7.78 (d, 1H), 7.69 (d, 1H), 7.50 (t, 1H), 7.35 (dd, 2H), 2.89 (m, 2H), 2.72 (m, 2H), 1.90 (s, br, 4H) ppm; MS (ES+) 410.24 (M+H); (ES-) 408.23 (M-H); HPLC-Method A, R_t 3.19 min.

Example 357 **(7-Fluoro-1*H*-indazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-129)**: ^{1}H NMR (500 MHz, DMSO-d6) δ13.6 (s, 1H), 11.1 (s, br, 1H), 8.65 (d, 1H), 8.03 (d, 2H), 7.95 (s, 2H), 7.67 (m, 1H), 7.45 (m, 2H), 7.33 (t, 2H), 7.22 (dd, 1H), 6.99 (td, 1H) ppm. MS (ES+): m/e= 356.20 (M+H); HPLC-Method A R_t 3.00 min.

Example 358 **(5-Fluoro-1*H*-indazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-130)**: ^{1}H NMR (500 MHz, DMSO-d6) δ13.2 (s, 1H), 11.3 (s, br, 1H), 8.67 (d, 1H), 8.04 (d, 2H), 7.96 (s, 2H), 7.70 (m, 1H), 7.58 (dd, 1H), 7.43 (m, 4H), 7.28 (td, 1H) ppm. MS (ES+) 356.20 (M+H); HPLC-Method A, R_t 3.00 min.

Example 359 **(5,7-Difluoro-1*H*-indazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-131)**: ^{1}H NMR (500 MHz, DMSO-d6) δ13.7 (s, 1H), 8.65 (d, 1H), 8.04 (d, 2H), 7.95 (s, 2H), 7.68 (m, 1H), 7.45 (m, 1H), 7.35 (m, 4H) ppm. MS (ES+): m/e= 374.17 (M+H); HPLC-Method A, R_t 3.07 min.

Example 360 **(1*H*-Indazol-3-yl)-[2-(3-trifluoromethyl-phenyl)-quinazolin-4-yl]-amine (III-132)**: ^{1}H NMR (500MHz, DMSO-d6) δ 7.06 (t, 1H), 7.42 (t, 1H), 7.59 (d, 1H), 7.63 (t, 1H), 7.66 (d, 1H), 7.71 (m, 1H), 7.80 (d, 1H), 7.98 (m, 2H), 8.33 (s, 1H), 8.46 (d, 1H), 8.71 (d, 1H), 11.04 (br. s, 1H), 12.97 (s, 1H); EI-MS 406.1 (M+1); HPLC-Method A, R_t 3.15 min.

Example 361 **(2-Phenyl-quinazolin-4-yl)-(1*H*-pyrazolo[4,3-b]pyridin-3-yl)-amine (III-133)**: ^{1}H NMR (500 MHz, DMSO-d6) δ13.3 (s, br, 1H), 11.4 (s, br, 1H), 8.78 (d, 1H), 8.58 (dd, 1H), 8.24 (d, 1H), 8.10 (m, 2H), 7.95 (d, 2H), 7.86

(t, 1H), 7.56 (m, 2H), 7.44 (t, 2H) ppm. MS (ES+) 339.11 (M+H); HPLC-Method A, R_t 2.63 min.

Example 362 **[5-(3-Methoxy-phenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl]-(2-phenyl-quinazolin-4-yl)-amine (III-134)**: ^{1}H NMR (500 MHz, MeOH-d4) δ8.65 (d, 1H), 8.17 (m, 3H), 8.10 (d, 1H), 7.90 (t, 1H), 7.75 (t, 1H), 7.58 (m, 2H), 7.25 (t, 1H), 6.95 (m, 2H), 6.85 (d, 1H), 6.80 (s, 1H), 3.64 (s, 3H) ppm. MS (ES+): m/e= 462.2(M+H).

Example 363 **(6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (III-135)**: ^{1}H NMR (500 MHz, MeOH-d4) δ8.61 (d, 1H), 8.13 (m, 3H), 8.05 (d, 1H), 7.85 (t, 1H), 7.70 (t, 1H), 7.58 (m, 2H), 7.32 (m, 5H), 6.79 (s, 1H) ppm. MS (ES+): m/e= 432.2(M+H).

Example 364 **[5-(4-Methoxy-phenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl]-(2-phenyl-quinazolin-4-yl)-amine (III-136)**: MS (ES+) 462.2(M+H).

Example 365 **[5-(2,4-Dichloro-phenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl]-(2-phenyl-quinazolin-4-yl)-amine (III-137)**: ^{1}H NMR (500 MHz, MeOH-d4) δ8.63 (d, 1H), 8.17 (m, 4H), 7.89 (t, 1H), 7.73 (t, 1H), 7.61 (t, 2H), 7.57 (d, 1H), 7.32 (m, 1H), 7.21 (d, 1H), 6.84 (s, 1H) ppm. MS (ES+): m/e= 500.1(M+H).

Example 366 **[6-Oxo-5-(3-trifluoromethyl-phenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl]-(2-phenyl-quinazolin-4-yl)-amine (III-138)**: ^{1}H NMR (500 MHz, MeOH-d4) δ8.55 (d, 1H), 8.19 (d, 2H), 7.92 (m, 2H), 7.65 (m,

3H), 7.45 (t, 2H), 7.25 (t, 1H), 7.13 (t, 1H), 7.05 (t, 1H), 6.75 (s, 1H) ppm. MS (ES+): m/e= 500.2 (M+H).

Example 367 **[6-Oxo-5-(4-Phenoxy-phenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl]-(2-phenyl-quinazolin-4-yl)-amine (III-139)**: MS (ES+) 524.3(M+H).

Example 368 **[5-(4-Chloro-phenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl]-(2-phenyl-quinazolin-4-yl)-amine (III-140)**: MS (ES+) 466.2(M+H).

Example 369 **(2-imidazol-1-yl-quinazolin-4-yl)-(1*H*-indazol-3-yl)-amine (III-141)**: ^{1}H NMR (500MHz, DMSO-d6) δ 7.10 (t, 1H), 7.44 (t, 1H), 7.50 (br. s, 1H), 7.60 (d, 1H), 7.72 (m, 2H), 7.77 (m, 1H), 7.88 (d, 1H), 7.98 (t, 1H), 8.73 (d, 1H), 8.96 (s, 1H), 11.23 (s, 1H), 13.06 (s, 1H); EI-MS 328.1 (M+1); HPLC-Method A, R_t 2.93 min.

Example 370 **(1*H*-Indazol-3-yl)-[2-(2-methyl-imidazol-1-yl-quinazolin-4-yl]-amine (III-142)**: ^{1}H NMR (500MHz, DMSO-d6) δ 2.48 (s, 3H), 7.10 (t, 1H), 7.43 (t, 1H), 7.57 (d, 1H), 7.60 (d, 1H), 7.67 (d, 1H), 7.76 (td, 1H), 7.86 (d, 1H), 7.91 (d, 1H), 8.01 (td, 1H), 8.72 (d, 1H), 11.15 (s, 1H), 13.10 (s, 1H); EI-MS 342.1 (M+1); HPLC-Method A, R_t 3.06 min.

Example 371 **(1*H*-Indazol-3-yl)-(2-piperidin-1-yl-quinazolin-4-yl)-amine (III-143)**: ^{1}H NMR (500MHz, DMSO-d6) δ 1.48 (m, 6H), 3.60 (m, 4H), 7.11 (t, 1H), 7.52 (t, 1H), 7.55 (d, 1H), 7.64 (d, 1H), 7.69 (d, 1H), 7.75 (d, 1H), 7.90 (t, 1H), 8.58 (d, 1H), 11.82 (br. s, 1H), 13.25 (s, 1H); EI-MS 345.1 (M+1); HPLC-Method A, R_t 3.03 min.

Example 372 **(1*H*-Indazol-3-yl)-[2-(octahydro-quinolin-1-yl)-quinazolin-4-yl]-amine (III-144)**: ^{1}H NMR (500MHz, DMSO-d6) δ 0.6-1.9 (m, 13 H), 3.15 (m, 1H), 3.25 (m, 1H), 4.0 (m, 1H), 7.10 (t, 0.5H), 7.12 (t, 0.5H), 7.55 (m, 2H), 7.66 (d, 0.5 H), 7.69 (d, 0.5 H), 7.77 (d, 1H), 7.91 (t, 1H), 8.55 (d, 0.5 H), 8.59 (d, 0.5 H), 11.46 (s, 0.5 H), 11.54 (s, 0.5 H), 11.78 (s, 0.5 H), 11.84 (s, 0.5 H), 13.10 (s, 0.5 H), 13.12 (s, 0.5 H); EI-MS 399.3 (M+1); HPLC-Method A, R_t 3.37 min.

Example 373 **(1*H*-Indazol-3-yl)-[2-(2,6-dimethyl-morpholin-4-yl)-quinazolin-4-yl]-amine (III-145)**: ^{1}H NMR (500MHz, DMSO-d6) δ 1.0 (m, 6H), 4.0 (m, 6H), 7.12 (t, 1H), 7.41 (td, 1H), 7.56 (t, 1H), 7.58 (d, 1H), 7.68 (dd, 1H), 7.77 (t, 1H), 7.93 (t, 1H), 8.60 (d, 1H), 11.69 (s, 1H), 13.16 (s, 1H); EI-MS 375.3 (M+1); HPLC-Method A, R_t 2.93 min.

Example 374 **(5-Methyl-2*H*-pyrazol-3-yl)-(2-phenyl-pyrimidin-4-yl)-amine (IV-1)**: mp 245-246°C; ^{1}H NMR (DMSO) δ 2.26 (3H, s), 6.32 (1H, br s), 7.07 (1H, br s), 7.48-7.54 (3H, m), 8.33-8.39 (3H, m), 9.87 (1H, s), 12.03 (1H, s); IR (solid) 1628, 1589, 1579, 1522, 1479, 1441, 1393, 1336; MS 252.2 $(M+H)^+$.

Example 375 **[6-(4-Acetamidophenylsulfanyl)-2-phenyl-pyrimidin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (IV-3)**: A suspension of Fenclorim (4,6-dichloro-2-phenylpyrimidine) (0.1g, 0.44 mmol), 3-amino-5-methylpyrazole (0.045 g, 0.47 mmol), *N*, *N*-diisopropylethylamine (0.08 ml, 0.47 mmol) and sodium iodide (0.067 g, 0.44 mmol) in n-butanol (5 ml) were heated at 117 °C for 18 hours. The solvent was removed *in vacuo* and the crude product purified by flash chromatography (silica gel, 3:2 Petrol:EtOAc) to afford

0.037 g (29 % yield) of (6-Chloro-2-phenyl-pyrimidin-4-yl)-(5-methyl-2*H*-pyrazol—3-yl)-amine as a off-white solid. A suspension of the above pyrimidine (0.037 g, 0.13 mmol) and thioacetamidothiophenol (0.108 g, 0.64 mmol) in *tert*-butanol was heated at 85 °C under nitrogen for 2 days. The reaction mixture was cooled to room temperature and the solvent removed *in vacuo*. The concentrate was dissolved in EtOAc, and washed with $NaHCO_3$ (sat, aq.). The organic layer is concentrated *in vacuo*, and the crude product by preperative HPLC. The residual disulfide that still remained in the mixture after HPLC may be removed by precipitation from EtOAc and filtration. The mother liquor was concentrated to afford **IV-3** (7mg, 13 % yield) as an off-white solid: mp 235-236°C; ^{1}H NMR (DMSO) δ 2.10 (3H, s), 2.21 (3H, s), 6.33 (1H, br s), 7.50 (3H, m), 7.7-7.59 (2H, m), 7.76-7.78 (2H, m), 8.25 (2H, m), 9.72, 10.26 and 11.93 (3 H, 3 x br s); IR (solid) 1669, 1585, 1551, 1492, 1392, 1372, 1312, 1289, 1259, 1174, 1102, 1089, 1027, 1015, 984; MS 417.3 $(M+H)^+$.

Example 376 **[2-(4-Methylpiperidin-1-yl)-pyrimidin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (IV-4)**: mp 215-216°C; ^{1}H NMR (CD_3OD) δ 0.96 (3H, d), 1.16 (2H, m), 1.66 (3H, m), 2.27 (3H, s), 2.86 (2H, t), 4.58 (2H, m), 4.78 (2H, exch.protons), 6.13 (2H, m), 7.83 (1H, d); IR (solid) 1593, 1550, 1489, 1436, 1331, 1246, 1231; MS 273.1 $(M+H)^+$.

Example 377 **[2-(4-Methylpiperidin-1-yl)-5-nitropyrimidin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (IV-5)**: mp 185-187°C; ^{1}H NMR (DMSO) δ 0.93 (3H, d), 1.06-1.18 (2H, m), 1.68-1.80 (3H, m), 2.26 (3H, s), 3.01-3.12 (2H, m), 4.63 (1H, d), 4.80 (1H, d), 6.39 (1H, s), 9.00 (1H, s), 10.41

(1H, s), 12.36 (1H, s); IR (solid) 1589, 1517, 1479, 1446, 1346, 1317, 1246, 1222, 1055; MS 318.2 $(M+H)^+$.

Example 378 **[5-Amino-2-(4-Methylpiperidin-1-yl)-pyrimidin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (IV-6):** To a solution of **IV-5** (48 mg, 0.151 mmol) in ethanol (2.0 mL) was added tin dichloride dihydrate (171 mg, 0.756 mmol) and the resulting mixture heated at reflux for 3 hours. The reaction was cooled to room temperature and poured onto a mixture of 1M NaOH:dichloromethane:propanol (18:8:4mL) and stirred for 15 minutes. The layers were separated and the aqueous layer extracted twice with dichloromethane. The combined organic layers were concentrated *in vacuo* and the residue purified by flash chromatography (silica gel, gradient dichloromethane:MeOH) to afford **IV-6** as a grey solid (27mg, 63%): ^{1}H NMR (DMSO) δ 0.88-1.04 (5H, m), 1.55-1.62 (3H, m), 2.21 (3H, s), 2.70 (2H, m), 3.36 (2H, m), 4.40 (2H, m), 6.37 (1H, s), 7.49 (1H, s), 8.40 (1H, s), 11.92 (1H, br s); MS 288.2 $(M+H)^+$.

Example 379 **[5-Amino-6-methyl-2-(4-methylpiperidin-1-yl)-pyrimidin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (IV-7):** mp 172-175°C; ^{1}H NMR (DMSO) δ 0.90 (3H, d), 1.03 (2H, m), 1.52-1.62 (3H, m). 2.13 (3H, s), 2.20 (3H, s), 2.69 (2H, m), 3.92 (2H, br s), 4.44 (2H, d), 6.35 (1H, s), 8.41 (1H, s), 11.85 (1H, br s); IR (solid) 1612, 1589, 1489, 1446, 1317; MS 302.5 $(M+H)^+$.

Example 380 **[6-Methyl-2-(4-methyl-phenyl)-pyrimidin-4-yl]-(5-phenyl-2*H*-pyrazol-3-yl)-amine (IV-10):** MS 342.34 (M+H); HPLC-Method E, R_t 1.334 min.

Example 381 **[2-(4-Chloro-phenyl)-6-methyl-pyrimidin-4-yl]-(5-furan-2-yl-2*H*-pyrazol-3-yl)-amine (IV-11):** MS 352.11 (M+H); HPLC Method E, R_t 1.194 min.

Example 382 **5-Furan-2-yl-2*H*-pyrazol-3-yl)-(6-methyl-2-phenyl-pyrimidin-4-yl)-amine (IV-12):** MS 318.21 (M+H); HPLC-Method E, 1.192 min.

Example 383 **[6-Methyl-2-(4-trifluoromethyl-phenyl)-pyrimidin-4-yl]-(5-phenyl-2-yl-2*H*-pyrazol-3-yl)-amine (IV-13):** MS 396.24 (M+H); HPLC-Method E, R_t 1.419 min.

Example 384 **(5-Furan-2-yl-2*H*-pyrazol-3-yl)-[6-methyl-2-(4-trifluoromethyl-phenyl)-pyrimidin-4-yl]-amine (IV-14):** MS 386.08 (M+H); HPLC-Method E 1.347 min.

Example 385 **[2-(2,3-Dihydro-benzo[1,4]dioxin-2-yl)-6-methyl-pyrimidin-4-yl]-(5-furan-2-yl-2*H*-pyrazol-3-yl)-amine (IV-15):** MS 376.18 (M+H); HPLC-Method E, R_t 1.181 min.

Example 386 **[2-(2,3-Dihydro-bezo[1,4]dioxin-2-yl)-6-ethyl-pyrimidin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (IV-16):** MS 338.17 (M+H); HPLC-Method E, R_t 1.082 min.

Example 387 **(6-Ethyl-2-phenyl-pyrimidin-4-yl)-(5-methyl-2*H*-pyrazol-3-yl)-amine (IV-17):** MS 280.18 (M+H); HPLC-Method E, R_t 1.024 min.

Example 388 **(6-Methyl-2-phenyl-pyrimidin-4-yl)-(5-phenyl-2*H*-pyrazol-3-yl)-amine (IV-19):** MS 328.51 (M+H); HPLC-Method E, R_t 1.192 min.

Example 389 **[6-Ethyl-2-(4-trifluoromethyl-phenyl)-pyrimidin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (IV-20):** MS 348.5 (M+H); HPLC-Method E, R_t 1.224 min.

Example 390 **(5-Furan-2-yl-2*H*-pyrazol-3-yl)-[6-methyl-2-(4-methyl-phenyl)-pyrimidin-4-yl]-amine (IV-21):** MS 332.23 (M+H); HPLC-Method E, R_t 1.139 min.

Example 391 **(6-Methoxymethyl-2-phenyl-pyrimidin-4-yl)-(5-methyl-2*H*-pyrazol-3-yl)-amine (IV-22):** MS 296.31 (M+H); HPLC-Method E, R_t 0.971 min.

Example 392 **(5,6-Dimethyl-2-phenyl-pyrimidin-4-yl)-(5-methyl-2*H*-pyrazol-3-yl)-amine (IV-23):** MS 280.2 (M+H); HPLC-Method E, R_t 0.927 min.

Example 393 **(6-Methyl-2-phenyl-pyrimidin-4-yl)-(5-methyl-2*H*-pyrazol-3-yl)-amine (IV-24):** MS 266.18 (M+H); HPLC-Method E, R_t 0.925 min.

Example 394 **[6-Ethyl-2-(4-methyl-phenyl)-pyrimidin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (IV-25):** MS 294.46 (M+H); HPLC-Method E, R_t 1.174 min.

Example 395 **[2-(4-Chloro-phenyl)-6-ethyl-pyrimidin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (IV-26):** MS 314.42 (M+H); HPLC-Method E R_t 1.213 min.

Example 396 **(5-Methyl-1H-pyrazol-3-yl)-(6-methyl-2-p-tolyl-pyrimidin-4-yl)-amine (IV-27):** MS 280.45 (M+H); HPLC-Method E, R_t 1.135 min.

Example 397 **(1*H*-Indazol-3-yl)-(6-methoxymethyl-2-phenyl-pyrimidin-4-yl)-amine (IV-28):** ^{1}H NMR (500 MHz, DMSO) δ

3.57 (3H, s), 4.65 (2H, s), 7.23 (1H, J=7.5 Hz, t), 7.52 (1H, J=7.6 Hz, t), 7.63 (4H, m), 7.75 (1H, br), 8.13 (1H, J=5.5 Hz, br d), 8.44 (1H, J=5.7 Hz, br d), 10.6 (1H, br), 12.8 (1H, br s) ppm; HPLC-Method A, R_t 2.944 min; MS (FIA) 332.1 $(M+H)^+$.

Example 398 **(5-Methyl-2*H*-pyrazol-3-yl)-(2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-yl)-amine (IV-29)**: ^{1}H NMR (DMSO) δ 2.34 (3H, s), 6.66 (1H, s), 7.53 (1H, d), 7.84 (1H, d), 8.32 (2H, d), 8.70 (2H, d); MS 309.6 $(M+H)^+$.

Example 399 **(5-Methyl-2*H*-pyrazol-3-yl)-(2-phenyl-pyrido[3,4-d]pyrimidin -4-yl)-amine (IV-30)**: mp 225°C; ^{1}H NMR (DMSO) δ 2.35 (3H, s), 6.81 (1H, s), 7.50-7.63 (3H, m), 8.45-8.52 (2H, m), 8.54 (1H, d), 8.62 (1H, d), 9.20 (1H, s), 10.79 (1H, s), 12.38 (1H, br s); IR (solid) 2958, 2917, 2852, 1593, 1565, 1524, 1467, 1450; MS 303.2 $(M+H)^+$.

Example 400 **(5-Methyl-2*H*-pyrazol-3-yl)-(2-phenyl-pyrido[2,3-d]pyrimidin-4-yl)-amine (IV-31)**:
To a solution of 4-chloro-2-phenyl-pyrido[2,3-d]pyrimidine (J. Pharm. Belg., 29, 1974, 145-148) (109mg, 0.45 mmol) in THF (15 mL) was added 3-amino-5-methyl pyrazole (48 mg, 0.5 mmol) and the resulting mixture heated at 65 °C overnight. The mixture was cooled to room temperature and the resulting suspension was filtered and washed with Et_2O. The solid was dissolved in a mixture EtOH:water and the pH adjusted to pH 7. The aqueous was extracted twice with ethyl acetate and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, DCM-MeOH gradient) to afford **IV-31** as an off-white solid (69 mg, 50%): mp 234°C; ^{1}H NMR

(DMSO) δ 2.14 (3H, s), 5.99 (1H, s), 7.20-7.40 (3H, m), 7.40-7.50 (3H, m), 8.60 (1H, d), 8.79 (1H, d), 12.82 (1H, br s); IR (solid) 2957, 2921, 2857, 1644, 1560, 1459, 1427; MS 303.2 $(M+H)^+$.

Example 401 **(5-Cyclopropyl-2*H*-pyrazol-3-yl)-(2-phenyl-pyrido[3,4-d]pyrimidin-4-yl)-amine (IV-32)**: off-white solid, mp 232-233°C; ^{1}H NMR (DMSO) δ 0.70-0.85 (2H, m), 0.90-1.05 (2H, m), 1.05-2.07 (1H, m), 6.75 (1H, s), 7.50-7.75 (3H, m), 8.40-8.70 (4H, m), 9.20 (1H, s), 10.80 (1H, s), 12.41 (1H); IR (solid) 3178, 1601, 1573, 1532, 1484, 1452, 1409, 1367, 1328, 802, 781, 667; MS 329.2 $(M+H)^+$.

Example 402 **[2-(4-Methylpiperidin-1-yl)-purin-4-yl]-(5-methyl-2*H*-pyrazol-3-yl)-amine (IV-33)**: To a suspension of 2,4-dichloro-purine (2.0 g, 10.6 mmol) in anhydrous ethanol (10 mL) was added 5-methyl-1*H*-pyrazol-3-yl amine (2.05 g, 21.2 mmol). The resulting mixture was stirred at room temperature for 48 h. The resulting precipitate was collected by filtration, washed with ethanol, and dried under vacuum to afford 1.524 g (58% yield) of (2-chloro-purin-4-yl)-(5-methyl-1*H*-pyrazol-3-yl)-amine which was used in the next step without further purification. To a solution of (2-chloro-purin-4-yl)-(5-methyl-1*H*-pyrazol-3-yl)-amine (200 mg, 0.80 mmol) was added 4-methylpiperidine (4 mL, 8.01 mmol) and the reaction mixture heated at reflux overnight. The solvent was evaporated and the residue dissolved in a mixture EtOH:water (1:3, 4 mL). Potassium carbonate (57mg, 0.41 mmol) was added and the mixture was stirred at room temperature for 2 hours. The resulting suspension was filtered, washed with water (x2) and rinsed with Et_2O (x2) to afford **IV-33** as a white solid (225mg, 90%): mp >300°C; ^{1}H NMR (DMSO) δ 0.91 (3H, d), 1.10 (2H, m), 1.65 (3H, m),

2.24 (3H, s), 2.84 (2H, m), 4.60 (2H, m), 6.40 (1H, s), 7.87 (1H, m), 9.37-9.59 (1H, m), 12.03-12.39 (2H, m); IR (solid) 1651, 1612, 1574, 1484, 1446, 1327, 1317, 1255, 1203; MS 313.3 $(M+H)^+$.

Example 403 **(5-Cyclopropyl-2*H*-pyrazol-3-yl)-[2-(4-methylpiperidin-1-yl)-pyrrolo[3,2-d]pyrimidin-4-yl]-amine (IV-34)**: white solid; ^1H NMR (DMSO) δ 0.65 (2H, m), 0.91-0.96 (5H, m), 1.08 (2H, m), 1.58-1.64 (3H, m), 1.89 (1H, m), 2.77 (2H, t), 4.57 (2H, d), 6.09 (1H, s), 6.38 (1H, s), 7.33 (1H, s), 9.42 (1H, s), 10.65 (1H, s), 12.02 (1H, br s); MS 338.3 $(M+H)^+$.

Example 404 **[6-Benzyl-2-phenyl-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yl]-(5-fluoro-1*H*-indazol-3-yl)-amine (IV-35)**: ^1H NMR (500 MHz, DMSO-d6) δ13.0 (s, 1H), 10.4 (s, br, 1H), 9.73 (s, 1H, TFA-OH), 8.00 (d, 2H), 7.64 (m, 2H), 7.59 (dd, 1H), 7.52 (m, 3H), 7.41 (t, 1H), 7.31 (m, 3H), 7.14 (dd, 1H), 4.58 (s, 2H), 4.35 (br, 2H), 3.74 (m, 2H), 3.17 (s, 2H) ppm. MS (ES+): m/e= 451.30 (M+H); HPLC-Method A, T_{ret} 2.96 min.

Example 405 **(5-Fluoro-1*H*-indazol-3-yl)-(2-phenyl-5,6,7,8-tetrahydro-pyrido[4,3-d]pyrimidin-4-yl)-amine (IV-36)**: Prepared from **IV-35** (0.13 mmol) by treatment with an equal weight of Pd/C (10%) in 4.4% HCOOH in MeOH at room temperature for 12 h. The mixture was filtered through celite, the filtrate was evaporated, and crude product was purified by HPLC to afford **IV-36** as yellow solid in 35% yield. ^1H NMR (500 MHz, DMSO-d6) δ12.9 (s, 1H), 9.06 (s, 1H), 7.99 (d, 2H), 7.57 (dd, 1H), 7.34 (m, 1H), 7.28 (m, 3H), 7.22 (d, 1H), 3.83 (s, 2H), 3.05 (m, 2H), 2.72 (m, 2H) ppm. MS (ES+): m/e= 361.20 (M+H); HPLC-Method A, T_{ret} 2.68 min.

Example 406 **(5-Methyl-2*H*-pyrazol-3-yl)-(3-phenyl-isoquinolin-1-yl)-amine (V-1)**: To a solution of 1-chloro-3-phenylisoquinoline (J. Het. Chem., 20, 1983, 121-128)(0.33g, 1.37 mmol) in DMF (anhydrous, 5 mL) was added 3-amino-5-methylpyrazole (0.27g, 2.74 mmol) and potassium carbonate (0.57g, 4.13 mmol)and the resulting mixture was heated at reflux for 6 hours. The reaction mixture was then cooled and solvent removed *in vacuo*. The residue was extracted twice with ethyl acetate and the combined organic layers washed with brine, dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography (SiO_2, gradient DCM-MeOH) to afford **V-1** as a colourless oil; ^1H NMR (MeOD) δ 2.23 (3H, s), 5.61 (1H, s), 7.41 (1H, m), 7.52(2H, m), 7.62(1H, m), 7.81(1H, m), 8.07(1H, d), 8.19(2H, m), 8.29(1H, s), 8.54 (1H, d); MS 301.2 $(M+H)^+$.

Example 407 **(1*H*-Indazol-3-yl)-[3-(2-trifluoromethyl-phenyl)-isoquinoline-1-yl]-amine (V-2)**: A solution of 1-chloro-3-(2-trifluoromethyl-phenyl)-isoquinoline (100 mg, 0.326 mmol) and 1*H*-indazol-3-ylamine (86 mg, 0.651 mmol) in ethanol (3 mL) was heated at 160 C and the solvent evaporated with a stream of nitrogen. The remaining oil was then heated at 160 C for 18 hours under nitrogen. The resulting melt was dissolved in 5% methanol:dichloromethane (50 mL), washed with saturated aqueous sodium bicarbonate (1 x 25 mL) then dried over magnesium sulfate. Purification by silica gel chromatography (25% to 50% hexane:ethyl acetate) afforded **V-2** as a yellow solid (35 mg, 27%). ^1H NMR (500 MHz, d_6-DMSO) δ 9.78 (br s, 1H), 8.62 (d, 1H), 7.9-7.85 (m, 1H), 7.78-7.72 (m, 1H), 7.70-7.68 (m, 1H), 7.65-7.62 (m, 1H), 7.60-7.55 (m, 1H), 7.52-7.45 (m, 3H), 7.41-7.38 (m, 1H),

7.28-7.25 (m, 1H), 7.18 (s, 1H), 6.95-6.92 (m, 1H), 5:76 (s, 1H); LC-MS (ES+) m/e= 405.18 (M+H); HPLC-Method D R_t 2.74 min.

Example 408 **(5,7-Difluoro-1*H*-indazol-3-yl)-[3-(2-trifluoromethyl-phenyl)-isoquinolin-1-yl]-amine (V-3)**: Prepared from 5,7-difluoro-1*H*-indazol-3-ylamineto afford compound **V-3** as a yellow solid (90 mg, 63%). ^{1}H NMR (500 MHz, d_6-DMSO) δ 13.25 (s, 1H), 9.92 (br s, 1H), 8.61 (d, 1H), 7.9 (d, 1H), 7.81-7.49 (m, 6H), 7.26-7.2 (m, 2H), 7.12-7.10 (m, 1H); LC-MS (ES+) m/e= 441.16 (M+H); HPLC-Method D, R_t 3.58 min.

Example 409 **(5-Methyl-2*H*-pyrazol-3-yl)-(2-phenyl-quinolin-4-yl)-amine (V-4)**: To a mixture of 4-chloro-2-phenylquinoline (J. Het. Chem., 20, 1983, 121-128)(0.53g, 2.21 mmol) in diphenylether (5 mL) was added 3-amino-5-methylpyrazole (0.43g, 4.42 mmol) and the resulting mixture heated at 200°C overnight with stirring. The reaction mixture was cooled to ambient temperature then petroleum ether (20 mL) was added and the resulting precipitate was isolated by filtration. The crude solid was purified by flash chromatography (SiO_2, gradient DCM-MeOH) to afford **V-4** as a white solid: mp 242-244°C; ^{1}H NMR (DMSO) δ 2.27(3H, s), 6.02(1H, s), 7.47(2H, d), 7.53-7.40(2H, br m), 7.67(1H, m), 7.92(1H, m), 8.09(2H, d), 8.48(2H, m), 9.20(1H, s), 12.17(1H, br s); IR (solid) 1584, 1559, 1554, 1483, 1447, 1430, 1389; MS 301.2 $(M+H)^+$.

Example 410 **(1*H*-Indazol-3-yl)-(2-phenyl-quinolin-4-yl)-amine (V-5)**: ^{1}H NMR (500 MHz, d_6-DMSO) δ 12.78 (s, 1H), 9.50 (s, 1H), 8.65 (d, 1H), 8.15 (s, 1H), 8.04-7.98 (m, 3H), 7.94 (s, 1H), 7.78-7.75 (m, 1H), 7.60-7.40 (m, 6H),

7.15-7.10 (m, 1H). LC-MS (ES+) m/e= 337.11 (M+H); HPLC-Method D, R_t 2.10 min.

Example 411 **(2-Phenyl-quinolin-4-yl)-(1*H*-pyrazolo[4,3-b]pyridin-3-yl)-amine (V-6)**: ^{1}H NMR (500 MHz, DMSO-d6) δ13.6 (s, 1H), 11.4 (s, 1H), 8.94 (d, 1H), 8.61 (dd, 1H), 8.23 (d, 1H), 8.16 (dd, 1H), 8.12 (t, 1H), 7.89 (t, 1H), 7.86 (d, 1H), 7.65 (m, 4H), 7.54 (s, 1H), 7.52 (dd, 1H) ppm. MS (ES+): m/e= 338.11 (M+H); HPLC-Method A, HPLC-Method D, R_t 2.91 min.

Example 412 **(1*H*-Indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinolin-4-yl]-amine (V-7)**: ^{1}H NMR (500 MHz, d_6-DMSO) δ 12.68 (s, 1H), 9.51 (s, 1H), 8.7 (d, 1H), 7.95-7.89 (m, 2H), 7.83-7.70 (m, 3H), 7.68-7.62 (m, 2H), 7.60 (s, 1H), 7.55-7.52 (m, 1H), 7.49-7.45 (m, 1H), 7.40-7.37 (m, 1H), 7.12-7.09 (m, 1H); LC-MS (ES+) m/e= 405.15 (M+H); HPLC-Method D R_t 2.25 min.

Example 413 **(5,7-Difluoro-1*H*-indazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinolin-4-yl]-amine (V-8)**: ^{1}H NMR (500 MHz, d_6-DMSO) δ 13.31 (s, 1H), 9.49 (s, 1H), 8.70-8.67 (m, 1H), 7.96-7.92 (m, 1H), 7.85-7.66 (m, 7H), 7.63-7.60 (m, 1H), 7.42-7.40 (m, 1H). LC-MS (ES+) m/e= 441.18 (M+H); HPLC-Method D R_t 2.39 min.

Example 414 **[2-(2-trifluoromethyl-phenyl)-quinolin-4-yl]-(1*H*-pyrazolo[4,3-b]pyridin-3-yl)-amine (V-9)**: ^{1}H NMR (500 MHz, DMSO-d6) δ13.6 (s, 1H), 11.6 (s, br, 1H), 8.98 (d, 1H), 8.57 (dd, 1H), 8.12 (m, 3H), 7.97 (m, 2H), 7.86 (m, 3H), 7.49 (dd, 1H), 7.23 (s, 1H) ppm. MS (ES+): m/e= 406.20 (M+H); HPLC-Method A R_t 2.91 min.

Example 415 **(2-Phenyl-quinazolin-4-yl)-(2*H*-[1,2,4]triazol-3-yl)-amine (IX-154)**: off-white solid, mp 266-267°C; ^{1}H NMR (DMSO) δ 7.50-7.70 (4H, m), 7.85-8.00 (2H, m), 8.15-8.25 (2H, m), 8.37-8.45 (2H, m), 8.58 (1H, d), 13.90 (1H, br s); IR (solid) 3344, 3059, 1630, 1609, 1570, 1557, 1543, 1501, 1495, 1445, 1411, 1355, 1326, 1267, 1182, 1053, 1038, 760, 676, 667, 654; MS 289.2 $(M+H)^+$.

Example 416 **(5-Methyl-2*H*-[1,2,4]triazol-3-yl)-(2-phenyl-quinazolin-4-yl)-amine (IX-155)**: *^{1}H NMR (500 MHz, DMSO-d6)* δ 8.59 (s, 1H), 8.42 (d, J = 6.7 Hz, 2H), 7.79 (m, 4H), 8.03 (m, 2H), 7.74 (m, 4H), 2.51 (s, 3H) ppm. MS (ES+): m/e= 303.08 (M+H); HPLC-Method A, R_t 2.64 min.

Example 417 **(2*H*-[1,2,4]-Triazol-3-yl)-[2-(2-trifluoromethylphenyl)-quinazolin-4-yl]-amine (IX-47)**: Pale yellow solid (52% yield). ^{1}H NMR (500 MHz, DMSO-d6) δ 8.54 (s, 1H), 8.15 (s, br, 1H), 7.91 (t, 1H), 7.85 (m, 2H), 7.76 (m, 3H), 7.66 (t, 1H) ppm. MS (ES+): m/e= 357.13 (M+H); (ES-): m/e= 355.15 (M-H); HPLC-Method A, R_t 2.81 min.

Example 418 **(5-Methyl-2*H*-[1,2,4]triazol-3-yl)-[2-(2-trifluoromethylphenyl)-quinazolin-4-yl]-amine (IX-38)**: Pale yellow solid (54% yield). ^{1}H NMR (500 MHz, DMSO-d6) δ 8.44 (s, br, 1H), 7.92 (m, 3H), 7.84 (m, 1H), 7.77 (m, 2H), 7.68 (t, 1H), 2.28 (s, 3H) ppm. MS (ES+): m/e= 371.14 (M+H); (ES-): m/e= 369.18 (M-H); HPLC-Method A, R_t 2.89 min.

Example 419 **(5-Methylsulfanyl-2*H*-[1,2,4]triazol-3-yl)-[2-(2-trifluoromethylphenyl)-quinazolin-4-yl]-amine (IX-156)**: Pale yellow solid (65% yield). ^{1}H NMR (500 MHz,

DMSO-d6) δ 8.56 (br, 1H), 7.90 (t, 1H), 7.84 (m, 2H), 7.78 (m, 2H), 7.67 (m, 2H), 2.51 (s, 3H, buried by DMSO) ppm. MS (ES+): m/e= 403.12 (M+H); (ES-): m/e= 401.16 (M-H); HPLC-Method A, R_t 3.20 min.

Example 420 **(1*H*-[1,2,4]Triazol-3-yl)-[3-(2-trifluoromethyl-phenyl)-isoquinolin-1-yl]-amine (IX-175):** A solution of 1-chloro-3-(2-trifluoromethyl-phenyl)-isoquinoline (0.326 mmol) and 1*H*-[1,2,4]triazol-3-ylamine (0.651 mmol) in ethanol (3 mL) was heated at 160°C and the solvent evaporated with a stream of nitrogen. The remaining oil was then heated at 160°C for 18 hours under nitrogen. The resulting melt was dissolved in 5% methanol/dichloromethane (50 mL), washed with saturated aqueous sodium bicarbonate (1 x 25 mL) then dried over magnesium sulfate. Purification by silica gel chromatography afforded **IX-175** as a colorless oil (4% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.18 (d, 1H), 8.82 (s, 1H), 7.90 (d, 1H), 7.85-7.75 (m, 3H), 7.71-7.62 (m, 3H), 7.60-7.55 (m, 2H), 4.42-4.35 (m, 1H). LC-MS (ES+) 356.16 (M+H); HPLC-Method D, R_t 3.55 min.

Example 421 **(2-Phenyl-quinolin-4-yl)-(1*H*-[1,2,4]triazol-3-yl)-amine (IX-176):** Pale yellow solid (30% yield). ^{1}H NMR (500 MHz, d_6-DMSO) δ 13.82 (s, 1H), 9.91 (s, 1H), 8.80 (s, 1H), 8.70-8.65 (m, 1H), 8.55 (s, 1H), 8.15-8.12 (m, 2H), 8.03-7.98 (m, 1H), 7.75-7.72 (m, 1H), 7.57-7.49 (m, 3H). LC-MS (ES+) m/e= 288.11 (M+H); HPLC-Method D, R_t 1.55 min.

Example 422 **(1*H*-[1,2,4]triazol-3-yl)-[2-(2-trifluoromethyl-phenyl)-quinolin-4-yl]-amine (IX-177):** Pale yellow solid (46% yield). ^{1}H NMR (500 MHz, d_6-DMSO) δ 13.70 (s, 1H), 9.98 (s, 1H), 8.70 (d, 1H), 8.49 (s,

1H), 8.30 (s, 1H), 7.94-7.88 (m, 2H), 7.80-7.68 (m, 3H), 7.64-7.56 (m, 2H). LC-MS (ES+) m/e= 356.18 (M+H); HPLC-Method D, R_t 1.68 min.

Example 423 **(1-H-Indazol-3-yl)-[5-methyl-6-morpholin-4-yl-2-(2-trifluoromethyl-phenyl)-pyrimidin-4-yl]-amine (II-251):** Colorless film; 2 % yield; ^{1}H-NMR (500 MHz, CD_3OD) δ 7.84 (m, 2H), 7.71 (m, 3H), 7.41 (t, 2H), 7.14 (m, 1H), 3.74 (m, 4H), 3.69 (m, 4H), 1.24 (s, 3H) ppm; HPLC-Method A R_t 3.26 min; MS (FIA) 455.1 (M+H).

BIOLOGICAL TESTING

The activity of the compounds as protein kinase inhibitors may be assayed *in vitro, in vivo* or in a cell line. *In vitro* assays include assays that determine inhibition of either the phosphorylation activity or ATPase activity of the activated protein kinase. Alternate *in vitro* assays quantitate the ability of the inhibitor to bind to the protein kinase. Inhibitor binding may be measured by radiolabelling the inhibitor prior to binding, isolating the inhibitor/protein kinase complex and determining the amount of radiolabel bound. Alternatively, inhibitor binding may be determined by running a competition experiment where new inhibitors are incubated with the protein kinase bound to known radioligands.

BIOLOGICAL TESTING EXAMPLE 1

K_i DETERMINATION FOR THE INHIBITION OF GSK-3

Compounds were screened for their ability to inhibit GSK-3β (AA 1-420) activity using a standard coupled enzyme system (Fox et al. (1998) *Protein Sci.* 7, 2249). Reactions were carried out in a solution containing 100 mM HEPES (pH 7.5), 10 mM $MgCl_2$, 25 mM NaCl,

300 μM NADH, 1 mM DTT and 1.5% DMSO. Final substrate concentrations in the assay were 20 μM ATP (Sigma Chemicals, St Louis, MO) and 300 μM peptide (HSSPHQS(PO_3H_2)EDEEE, American Peptide, Sunnyvale, CA). Reactions were carried out at 30 °C and 20 nM GSK-3β. Final concentrations of the components of the coupled enzyme system were 2.5 mM phosphoenolpyruvate, 300 μM NADH, 30 μg/ml pyruvate kinase and 10 μg/ml lactate dehydrogenase.

An assay stock buffer solution was prepared containing all of the reagents listed above with the exception of ATP and the test compound of interest. The assay stock buffer solution (175 μl) was incubated in a 96 well plate with 5 μl of the test compound of interest at final concentrations spanning 0.002 μM to 30 μM at 30 °C for 10 min. Typically, a 12 point titration was conducted by preparing serial dilutions (from 10 mM compound stocks) with DMSO of the test compounds in daughter plates. The reaction was initiated by the addition of 20 μl of ATP (final concentration 20 μM). Rates of reaction were obtained using a Molecular Devices Spectramax plate reader (Sunnyvale, CA) over 10 min at 30 °C. The K_i values were determined from the rate data as a function of inhibitor concentration.

The following compounds were shown to have K_i values less than 0.1 μM for GSK-3: compounds II-1, II-105, II-33, II-34, II-36, II-39, II-38, II-39, II-40, II-41, II-42, II-46, II-57, II-59, II-60, II-61, II-62, II-63, II-64, II-66, II-67, II-69, II-70, II-53, II-71, II-99, II-73, II-74, II-75, II-76, II-77, II-7, II-8, II-9, II-10, II-24, II-19, II-78, II-54, II-79, II-80, II-81, II-82, II-83, II-84, II-56, II-86, II-20, II-25, II-26, II-85, II-21, II-27, II-28, II-87, II-88, II-29, II-11, II-12, II-30, II-31, II-13, II-14, II-15, II-16, II-17,

II-18, II-79, II-23, II-2, II-90, II-91, II-92, II-93, II-3, II-4, II-5, II-6, II-94, II-95, II-96, II-107, II-108, II-109, II-110, II-124, II-125, II-111, II-112, II-113, II-114, II-115, II-116, II-117, II-118, II-119, II-120, II-121, II-208, III-8, III-7, III-9, III-37, III-38, III-39, III-40, III-42, III-45, III-46, III-47, III-48, III-49, III-51, III-52, III-53, III-54, III-55, III-56, III-57, III-58, III-59, III-60, III-61, III-62, III-63, III-30, III-65, III-66, III-67, III-70, III-73, III-31, III-75, III-76, III-77, III-33, III-34, III-106, III-108, III-109, III-111, III-35, III-116, III-117, III-118, III-119, III-120, III-121, III-127, III-128, III-141, III-130, III-131, IV-15, IV-16, IV-17, IV-20, IV-25, IV-26, IV-30, IV-34, V-3, and IX-47.

The following compounds were shown to have K_i values between 0.1 and 1.0 μM for GSK-3: compounds II-103, II-104, II-35, II-44, II-45, II-49, II-50, II-97, II-101, II-22, II-32, III-41, III-43, III-44, III-28, III-50, III-29, III-64, III-71, III-74, III-78, III-82, III-88, III-90, III-102, III-105, III-107, III-110, III-112, III-114, III-115, III-122, III-124, III-124, IV-1, III-1, III-138, III-140, III-142, III-129, III-132, III-134, III-135, III-136, IV-1, IV-10, IV-11, IV-12, IV-13, IV-14, IV-19, IV-21, IV-22, IV-23, IV-24, IV-3, IV-4, IV-6, IV-7, IV-8, IV-29, IV-31, IV-32, IV-33, IV-36, V-2, V-7, IX-38, IX-154, and IX-177.

The following compounds were shown to have K_i values between 1.0 and 20 μM for GSK-3: compounds II-43, II-65, II-48, II-47, II-51, II-68, II-52, II-72, II-100, II-98, II-89, III-68, III-81, III-83, III-91, III-94, III-95, III-96, III-97, III-98, III-99, III-100, III-101, III-103, III-123, III-137, III-139, III-143, III-145, III-146, V-4, V-8, IX-156, and IX-176.

BIOLOGICAL TESTING EXAMPLE 2

K_I DETERMINATION FOR THE INHIBITION OF AURORA-2

Compounds were screened in the following manner for their ability to inhibit Aurora-2 using a standard coupled enzyme assay (Fox et al (1998) *Protein Sci* 7, 2249).

To an assay stock buffer solution containing 0.1M HEPES 7.5, 10 mM $MgCl_2$, 1 mM DTT, 25 mM NaCl, 2.5 mM phosphoenolpyruvate, 300 mM NADH, 30 mg/ml pyruvate kinase, 10 mg/ml lactate dehydrogenase, 40 mM ATP, and 800 μM peptide (LRRASLG, American Peptide, Sunnyvale, CA) was added a DMSO solution of a compound of the present invention to a final concentration of 30 μM. The resulting mixture was incubated at 30 °C for 10 min. The reaction was initiated by the addition of 10 μL of Aurora-2 stock solution to give a final concentration of 70 nM in the assay. The rates of reaction were obtained by monitoring absorbance at 340 nm over a 5 minute read time at 30 °C using a BioRad Ultramark plate reader (Hercules, CA). The K_i values were determined from the rate data as a function of inhibitor concentration.

The following compounds were shown to have K_i values less than 0.1 μM for Aurora-2: compounds II-33, II-34, II-36, II-37, II-40, II-41, II-55, III-7, III-9, III-37, III-38, III-39, III-40, III-41, III-42, III-44, III-45, III-46, III-47, III-48, III-49, III-50, III-51, III-52, III-53, III-54, III-55, III-56, III-57, III-59, III-60, III-61, III-63, III-30, III-65, III-66, III-67, III-70, III-31, III-76, III-77, III-78, III-80, III-32, III-33, III-34, III-106, III-108, III-109, III-110, III-111, III-112, III-114, III-35, III-115, III-116, III-117, III-118, III-119, III-120, III-121, IV-7, IV-30, IV-32, and IV-34.

The following compounds were shown to have K_i values between 0.1 and 1.0 μM for Aurora-2: compounds II-1, II-105, II-35, II-38, II-39, II-42, II-64, II-70, II-53, II-99, II-77, II-79, II-86, II-20, II-93, II-94, III-28, III-58, III-64, III-71, III-73, III-74, III-75, III-102, III-105, III-107, III-113, III-124, III-1, III-130, IV-1, IV-3, IV-4, IV-6, IV-29, IV-33, and V-4.

The following compounds were shown to have K_i values between 1.0 and 20 μM for Aurora-2: compounds II-103, II-104, II-57, II-59, II-61, II-63, II-67, II-69, II-75, II-76, II-10, II-19, II-78, II-54, II-80, II-82, II-21, II-90, II-91, II-96, II-107, III-68, III-79, III-82, III-101, III-103, III-127, III-141, III-129, III-132, IV-31, V-2, IX-47, IX-154, and IX-177.

BIOLOGICAL TESTING EXAMPLE 3

CDK-2 INHIBITION ASSAY

Compounds were screened in the following manner for their ability to inhibit CDK-2 using a standard coupled enzyme assay (Fox et al (1998) *Protein Sci* 7, 2249).

To an assay stock buffer solution containing 0.1M HEPES 7.5, 10 mM $MgCl_2$, 1 mM DTT, 25 mM NaCl, 2.5 mM phosphoenolpyruvate, 300 mM NADH, 30 mg/ml pyruvate kinase, 10 mg/ml lactate dehydrogenase, 100 mM ATP, and 100 μM peptide (MAHHHRSPRKRAKKK, American Peptide, Sunnyvale, CA) was added a DMSO solution of a compound of the present invention to a final concentration of 30 μM. The resulting mixture was incubated at 30 °C for 10 min.

The reaction was initiated by the addition of 10 μL of CDK-2/Cyclin A stock solution to give a final concentration of 25 nM in the assay. The rates of reaction were obtained by monitoring absorbance at 340 nm over a 5-minute read time at 30 °C using a BioRad

Ultramark plate reader (Hercules, CA). The K_i values were determined from the rate data as a function of inhibitor concentration.

BIOLOGICAL TESTING EXAMPLE 4

ERK INHIBITION ASSAY

Compounds were assayed for the inhibition of ERK2 by a spectrophotometric coupled-enzyme assay (Fox et al (1998) *Protein Sci* 7, 2249). In this assay, a fixed concentration of activated ERK2 (10 nM) was incubated with various concentrations of the compound in DMSO (2.5 %) for 10 min. at 30°C in 0.1 M HEPES buffer, pH 7.5, containing 10 mM $MgCl_2$, 2.5 mM phosphoenolpyruvate, 200 µM NADH, 150 µg/mL pyruvate kinase, 50 µg/mL lactate dehydrogenase, and 200 µM erktide peptide. The reaction was initiated by the addition of 65 µM ATP. The rate of decrease of absorbance at 340 nM was monitored. The IC_{50} was evaluated from the rate data as a function of inhibitor concentration.

The following compounds were shown to have a K_i value of <1µM for ERK-2: III-109, III-111, III-115, III-117, III-118, III-120, and IV-4.

The following compounds were shown to have a K_i value of between 1µM and 12µM for ERK-2: III-63, III-40, and III-108.

BIOLOGICAL TESTING EXAMPLE 5

AKT INHIBITION ASSAY

Compounds were screened for their ability to inhibit AKT using a standard coupled enzyme assay (Fox et al., Protein Sci., (1998) **7**, 2249). Assays were carried out in a mixture of 100 mM HEPES 7.5, 10 mM MgCl2, 25 mM NaCl , 1 mM DTT and 1.5% DMSO. Final substrate concentrations in the assay were 170 µM ATP (Sigma

Chemicals) and 200 µM peptide (RPRAATF, American Peptide, Sunnyvale, CA). Assays were carried out at 30 °C and 45 nM AKT. Final concentrations of the components of the coupled enzyme system were 2.5 mM phosphoenolpyruvate, 300 µM NADH, 30 µg/ML pyruvate kinase and 10 µg/ml lactate dehydrogenase.

An assay stock buffer solution was prepared containing all of the reagents listed above, with the exception of AKT, DTT, and the test compound of interest. 56 µl of the stock solution was placed in a 384 well plate followed by addition of 1 µl of 2 mM DMSO stock containing the test compound (final compound concentration 30 µM). The plate was preincubated for about 10 minutes at 30°C and the reaction initiated by addition of 10 µl of enzyme (final concentration 45 nM) and 1 mM DTT. Rates of reaction were obtained using a BioRad Ultramark plate reader (Hercules, CA) over a 5 minute read time at 30°C. Compounds showing greater than 50% inhibition versus standard wells containing the assay mixture and DMSO without test compound were titrated to determine IC_{50} values.

BIOLOGICAL TESTING EXAMPLE 6

SRC INHIBITION ASSAY

The compounds were evaluated as inhibitors of human Src kinase using either a radioactivity-based assay or spectrophotometric assay.

Src Inhibition Assay A: Radioactivity-based Assay

The compounds were assayed as inhibitors of full length recombinant human Src kinase (from Upstate Biotechnology, cat. no. 14-117) expressed and purified from baculo viral cells. Src kinase activity was monitored by following the incorporation of ^{33}P from ATP into the tyrosine of a random poly Glu-Tyr polymer substrate of composition, Glu:Tyr = 4:1 (Sigma, cat. no.

P-0275). The following were the final concentrations of the assay components: 0.05 M HEPES, pH 7.6, 10 mM $MgCl_2$, 2 mM DTT, 0.25 mg/ml BSA, 10 µM ATP (1-2 µCi ^{33}P-ATP per reaction), 5 mg/ml poly Glu-Tyr, and 1-2 units of recombinant human Src kinase. In a typical assay, all the reaction components with the exception of ATP were pre-mixed and aliquoted into assay plate wells. Inhibitors dissolved in DMSO were added to the wells to give a final DMSO concentration of 2.5%. The assay plate was incubated at 30 °C for 10 min before initiating the reaction with ^{33}P-ATP. After 20 min of reaction, the reactions were quenched with 150 µl of 10% trichloroacetic acid (TCA) containing 20 mM Na_3PO_4. The quenched samples were then transferred to a 96-well filter plate (Whatman, UNI-Filter GF/F Glass Fiber Filter, cat no. 7700-3310) installed on a filter plate vacuum manifold. Filter plates were washed four times with 10% TCA containing 20 mM Na_3PO_4 and then 4 times with methanol. 200µl of scintillation fluid was then added to each well. The plates were sealed and the amount of radioactivity associated with the filters was quantified on a TopCount scintillation counter. The radioactivity incorporated was plotted as a function of the inhibitor concentration. The data was fitted to a competitive inhibition kinetics model to get the K_i for the compound.

Src Inhibition Assay B: Spectrophotometric Assay

The ADP produced from ATP by the human recombinant Src kinase-catalyzed phosphorylation of poly Glu-Tyr substrate was quanitified using a coupled enzyme assay (Fox et al (1998) *Protein Sci* 7, 2249). In this assay one molecule of NADH is oxidised to NAD for every molecule of ADP produced in the kinase reaction. The

disappearance of NADH can be conveniently followed at 340 nm.

The following were the final concentrations of the assay components: 0.025 M HEPES, pH 7.6, 10 mM MgCl2, 2 mM DTT, 0.25 mg/ml poly Glu-Tyr, and 25 nM of recombinant human Src kinase. Final concentrations of the components of the coupled enzyme system were 2.5 mM phosphoenolpyruvate, 200 µM NADH, 30 µg/ml pyruvate kinase and 10 µg/ml lactate dehydrogenase.

In a typical assay, all the reaction components with the exception of ATP were pre-mixed and aliquoted into assay plate wells. Inhibitors dissolved in DMSO were added to the wells to give a final DMSO concentration of 2.5%. The assay plate was incubated at 30°C for 10 min before initiating the reaction with 100 µM ATP. The absorbance change at 340 nm with time, the rate of the reaction, was monitored on a molecular devices plate reader. The data of rate as a function of the inhibitor concentration was fitted to compettive inhibition kinetics model to get the K_i for the compound.

The following compounds were shown to have a K_i value of <100nM on SRC: III-31, III-32, III-33, III-34, III-35, III-47, III-65, III-66, III-37, III-38, III-39, III-40, III-42, III-44, III-48, III-49, III-70, III-45, III-78, III-76, and IV- 32.

The following compounds were shown to have a K_i value of between 100nM and 1µM for SRC: III-63, III-71, III-75, III-73, III-72, III-74, III-80, III-50, IV-30.

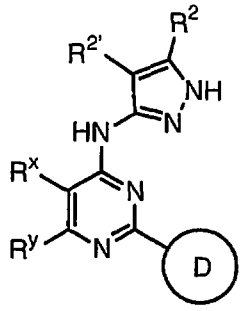
The following compounds were shown to have a K_i value of between 1µM and 6µM for SRC: III-79, IV-1, and IV-31.

While we have hereinbefore presented a number of embodiments of this invention, it is apparent that our basic construction can be altered to provide other

embodiments which utilize the compounds and methods of this invention. Therefore, it will be appreciated that the scope of this invention is to be defined by the appended claims rather than by the specific embodiments which have been represented by way of example.

We claim:

1. A compound of formula **III**:



III

or a pharmaceutically acceptable derivative or prodrug thereof, wherein:

Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl, said heteroaryl or heterocyclyl ring having 1-4 ring heteroatoms selected from nitrogen, oxygen or sulfur, wherein Ring D is substituted at any substitutable ring carbon by oxo or $-R^5$, and at any substitutable ring nitrogen by $-R^4$, provided that when Ring D is a six-membered aryl or heteroaryl ring, $-R^5$ is hydrogen at each ortho carbon position of Ring D;

R^x and R^y are taken together with their intervening atoms to form a fused, unsaturated or partially unsaturated, 5-8 membered carbocyclo ring, wherein any substitutable carbon on said fused ring formed by R^x and R^y is substituted by oxo or $T-R^3$;

T is a valence bond or a C_{1-4} alkylidene chain;

R^2 and $R^{2'}$ are independently selected from -R, $-T-W-R^6$, or R^2 and $R^{2'}$ are taken together with their intervening atoms to form a fused, 5-8 membered, unsaturated or partially unsaturated, ring having 0-3 ring heteroatoms selected from nitrogen, oxygen, or sulfur, wherein each substitutable carbon on said fused ring formed by R^2

and $R^{2'}$ is substituted by halo, oxo, -CN, $-NO_2$, $-R^7$, or $-V-R^6$, and any substitutable nitrogen on said ring formed by R^2 and $R^{2'}$ is substituted by R^4;

R^3 is selected from -R, -halo, =O, -OR, $-C(=O)R$, $-CO_2R$, -COCOR, $-COCH_2COR$, $-NO_2$, -CN, $-S(O)R$, $-S(O)_2R$, -SR, $-N(R^4)_2$, $-CON(R^4)_2$, $-SO_2N(R^4)_2$, $-OC(=O)R$, $-N(R^4)COR$, $-N(R^4)CO_2$(optionally substituted C_{1-6} aliphatic), $-N(R^4)N(R^4)_2$, $-C=NN(R^4)_2$, -C=N-OR, $-N(R^4)CON(R^4)_2$, $-N(R^4)SO_2N(R^4)_2$, $-N(R^4)SO_2R$, or $-OC(=O)N(R^4)_2$;

each R is independently selected from hydrogen or an optionally substituted group selected from C_{1-6} aliphatic, C_{6-10} aryl, a heteroaryl ring having 5-10 ring atoms, or a heterocyclyl ring having 5-10 ring atoms;

each R^4 is independently selected from $-R^7$, $-COR^7$, $-CO_2$(optionally substituted C_{1-6} aliphatic), $-CON(R^7)_2$, or $-SO_2R^7$, or two R^4 on the same nitrogen are taken together to form a 5-8 membered heterocyclyl or heteroaryl ring;

each R^5 is independently selected from -R, halo, -OR, $-C(=O)R$, $-CO_2R$, -COCOR, $-NO_2$, -CN, $-S(O)R$, $-SO_2R$, -SR, $-N(R^4)_2$, $-CON(R^4)_2$, $-SO_2N(R^4)_2$, $-OC(=O)R$, $-N(R^4)COR$, $-N(R^4)CO_2$(optionally substituted C_{1-6} aliphatic), $-N(R^4)N(R^4)_2$, $-C=NN(R^4)_2$, -C=N-OR, $-N(R^4)CON(R^4)_2$, $-N(R^4)SO_2N(R^4)_2$, $-N(R^4)SO_2R$, or $-OC(=O)N(R^4)_2$;

V is -O-, -S-, -SO-, $-SO_2-$, $-N(R^6)SO_2-$, $-SO_2N(R^6)-$, $-N(R^6)-$, -CO-, $-CO_2-$, $-N(R^6)CO-$, $-N(R^6)C(O)O-$, $-N(R^6)CON(R^6)-$, $-N(R^6)SO_2N(R^6)-$, $-N(R^6)N(R^6)-$, $-C(O)N(R^6)-$, $-OC(O)N(R^6)-$, $-C(R^6)_2O-$, $-C(R^6)_2S-$, $-C(R^6)_2SO-$, $-C(R^6)_2SO_2-$, $-C(R^6)_2SO_2N(R^6)-$, $-C(R^6)_2N(R^6)-$, $-C(R^6)_2N(R^6)C(O)-$, $-C(R^6)_2N(R^6)C(O)O-$, $-C(R^6)=NN(R^6)-$, $-C(R^6)=N-O-$, $-C(R^6)_2N(R^6)N(R^6)-$, $-C(R^6)_2N(R^6)SO_2N(R^6)-$, or $-C(R^6)_2N(R^6)CON(R^6)-$;

W is $-C(R^6)_2O-$, $-C(R^6)_2S-$, $-C(R^6)_2SO-$, $-C(R^6)_2SO_2-$, $-C(R^6)_2SO_2N(R^6)-$, $-C(R^6)_2N(R^6)-$, $-CO-$, $-CO_2-$, $-C(R^6)OC(O)-$, $-C(R^6)OC(O)N(R^6)-$, $-C(R^6)_2N(R^6)CO-$, $-C(R^6)_2N(R^6)C(O)O-$, $-C(R^6)=NN(R^6)-$, $-C(R^6)=N-O-$, $-C(R^6)_2N(R^6)N(R^6)-$, $-C(R^6)_2N(R^6)SO_2N(R^6)-$, $-C(R^6)_2N(R^6)CON(R^6)-$, or $-CON(R^6)-$;

each R^6 is independently selected from hydrogen or an optionally substituted C_{1-4} aliphatic group, or two R^6 groups on the same nitrogen atom are taken together with the nitrogen atom to form a 5-6 membered heterocyclyl or heteroaryl ring; and

each R^7 is independently selected from hydrogen or an optionally substituted C_{1-6} aliphatic group, or two R^7 on the same nitrogen are taken together with the nitrogen to form a 5-8 membered heterocyclyl or heteroaryl ring.

2. The compound according to claim 1, wherein said compound has one or more features selected from the group consisting of:

(a) Ring D is an optionally substituted ring selected from a phenyl, pyridinyl, piperidinyl, piperazinyl, pyrrolidinyl, thienyl, azepanyl, morpholinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, 2,3-dihydro-1*H*-isoindolyl, 2,3-dihydro-1*H*-indolyl, isoquinolinyl, quinolinyl, or naphthyl ring;

(b) R^x and R^y are taken together with their intervening atoms to form an optionally substituted 5-7 membered unsaturated or partially unsaturated ring; and

(c) $R^{2'}$ is hydrogen or methyl and R^2 is T-W-R^6 or R, wherein W is $-C(R^6)_2O-$, $-C(R^6)_2N(R^6)-$, $-CO-$, $-CO_2-$, $-C(R^6)OC(O)-$, $-C(R^6)_2N(R^6)CO-$, $-C(R^6)_2N(R^6)C(O)O-$, or $-CON(R^6)-$, and R is an optionally substituted group

selected from C_{1-6} aliphatic or phenyl, or R^2 and $R^{2'}$ are taken together with their intervening atoms to form a substituted or unsubstituted benzo, pyrido, pyrimido, or partially unsaturated 6-membered carbocyclo ring.

3. The compound according to claim 2, wherein:

(a) Ring D is an optionally substituted ring selected from a phenyl, pyridinyl, piperidinyl, piperazinyl, pyrrolidinyl, thienyl, azepanyl, morpholinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, 2,3-dihydro-1*H*-isoindolyl, 2,3-dihydro-1*H*-indolyl, isoquinolinyl, quinolinyl, or naphthyl ring;

(b) R^x and R^y are taken together with their intervening atoms to form an optionally substituted 5-7 membered unsaturated or partially unsaturated ring; and

(c) $R^{2'}$ is hydrogen or methyl and R^2 is T-W-R^6 or R, wherein W is $-C(R^6)_2O-$, $-C(R^6)_2N(R^6)-$, -CO-, $-CO_2-$, $-C(R^6)OC(O)-$, $-C(R^6)_2N(R^6)CO-$, $-C(R^6)_2N(R^6)C(O)O-$, or $-CON(R^6)-$, and R is an optionally substituted group selected from C_{1-6} aliphatic or phenyl, or R^2 and $R^{2'}$ are taken together with their intervening atoms to form a substituted or unsubstituted benzo, pyrido, pyrimido, or partially unsaturated 6-membered carbocyclo ring.

4. The compound according to claim 2, wherein said compound has one or more features selected from the group consisting of:

(a) Ring D is an optionally substituted ring selected from phenyl, pyridinyl, piperidinyl, piperazinyl, pyrrolidinyl, morpholinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, 2,3-dihydro-1*H*-isoindolyl, 2,3-dihydro-1*H*-indolyl, isoquinolinyl, quinolinyl, or naphthyl;

(b) R^x and R^Y are taken together with their intervening atoms to form a 5-7 membered unsaturated or partially unsaturated carbocyclic ring optionally substituted with -R, oxo, halo, -OR, -C(=O)R, $-CO_2R$, -COCOR, $-NO_2$, -CN, -S(O)R, $-SO_2R$, -SR, $-N(R^4)_2$, $-CON(R^4)_2$, $-SO_2N(R^4)_2$, $-OC(=O)R$, $-N(R^4)COR$, $-N(R^4)CO_2$(optionally substituted C_{1-6} aliphatic), $-N(R^4)N(R^4)_2$, $-C=NN(R^4)_2$, -C=N-OR, $-N(R^4)CON(R^4)_2$, $-N(R^4)SO_2N(R^4)_2$, $-N(R^4)SO_2R$, or $-OC(=O)N(R^4)_2$; and

(c) each R^5 is independently selected from halo, oxo, CN, NO_2, $-N(R^4)_2$, $-CO_2R$, $-CONH(R^4)$, $-N(R^4)COR$, $-SO_2N(R^4)_2$, $-N(R^4)SO_2R$, -SR, -OR, -C(O)R, or a substituted or unsubstituted group selected from 5-6 membered heterocyclyl, C_{6-10} aryl, or C_{1-6} aliphatic.

5. The compound according to claim 4, wherein:

(a) Ring D is an optionally substituted ring selected from phenyl, pyridinyl, piperidinyl, piperazinyl, pyrrolidinyl, morpholinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, 2,3-dihydro-1*H*-isoindolyl, 2,3-dihydro-1*H*-indolyl, isoquinolinyl, quinolinyl, or naphthyl;

(b) R^x and R^Y are taken together with their intervening atoms to form a 5-7 membered unsaturated or partially unsaturated carbocyclic ring optionally substituted with -R, oxo, halo, -OR, -C(=O)R, $-CO_2R$, -COCOR, $-NO_2$, -CN, -S(O)R, $-SO_2R$, -SR, $-N(R^4)_2$, $-CON(R^4)_2$, $-SO_2N(R^4)_2$, $-OC(=O)R$, $-N(R^4)COR$, $-N(R^4)CO_2$(optionally substituted C_{1-6} aliphatic), $-N(R^4)N(R^4)_2$, $-C=NN(R^4)_2$, -C=N-OR, $-N(R^4)CON(R^4)_2$, $-N(R^4)SO_2N(R^4)_2$, $-N(R^4)SO_2R$, or $-OC(=O)N(R^4)_2$; and

(c) each R^5 is independently selected from halo, oxo, CN, NO_2, $-N(R^4)_2$, $-CO_2R$, $-CONH(R^4)$, $-N(R^4)COR$, $-SO_2N(R^4)_2$, $-N(R^4)SO_2R$, -SR, -OR, -C(O)R, or a substituted or

unsubstituted group selected from 5-6 membered heterocyclyl, C_{6-10} aryl, or C_{1-6} aliphatic.

6. The compound according to claim 4, wherein said compound has one or more features selected from the group consisting of:

(a) R^x and R^y are taken together with their intervening atoms to form a 6-membered unsaturated or partially unsaturated carbocyclic ring optionally substituted with halo, CN, oxo, C_{1-6} alkyl, C_{1-6} alkoxy, (C_{1-6} alkyl)carbonyl, (C_{1-6} alkyl)sulfonyl, mono- or dialkylamino, mono- or dialkylaminocarbonyl, mono- or dialkylaminocarbonyloxy, or 5-6 membered heteroaryl;

(b) each R^5 is independently selected from -halo, -CN, -oxo, -SR, -OR, $-N(R^4)_2$, -C(O)R, or a substituted or unsubstituted group selected from 5-6 membered heterocyclyl, C_{6-10} aryl, or C_{1-6} aliphatic; and

(c) $R^{2'}$ is hydrogen and R^2 is selected from $R^{2'}$ is hydrogen or methyl and R^2 is T-W-R^6 or R, wherein W is $-C(R^6)_2O-$, $-C(R^6)_2N(R^6)-$, -CO-, $-CO_2-$, $-C(R^6)OC(O)-$, $-C(R^6)_2N(R^6)CO-$, or $-CON(R^6)-$, and R is an optionally substituted group selected from C_{1-6} aliphatic or phenyl, or R^2 and $R^{2'}$ are taken together with their intervening atoms to form a substituted or unsubstituted benzo, pyrido, or partially unsaturated 6-membered carbocyclic ring optionally substituted with -halo, $-N(R^4)_2$, $-C_{1-4}$ alkyl, $-C_{1-4}$ haloalkyl, $-NO_2$, $-O(C_{1-4}$ alkyl), $-CO_2(C_{1-4}$ alkyl), -CN, $-SO_2(C_{1-4}$ alkyl), $-SO_2NH_2$, $-OC(O)NH_2$, $-NH_2SO_2(C_{1-4}$ alkyl), $-NHC(O)(C_{1-4}$ alkyl), $-C(O)NH_2$, or $-CO(C_{1-4}$ alkyl), wherein the (C_{1-4} alkyl) is a straight, branched, or cyclic alkyl group.

7. The compound according to claim 6, wherein:

(a) R^x and R^y are taken together with their intervening atoms to form a 6-membered unsaturated or partially unsaturated carbocyclic ring optionally substituted with halo, CN, oxo, C_{1-6} alkyl, C_{1-6} alkoxy, (C_{1-6} alkyl)carbonyl, (C_{1-6} alkyl)sulfonyl, mono- or dialkylamino, mono- or dialkylaminocarbonyl, mono- or dialkylaminocarbonyloxy, or 5-6 membered heteroaryl;

(b) each R^5 is independently selected from -halo, -CN, -oxo, -SR, -OR, $-N(R^4)_2$, -C(O)R, or a substituted or unsubstituted group selected from 5-6 membered heterocyclyl, C_{6-10} aryl, or C_{1-6} aliphatic; and

(c) $R^{2'}$ is hydrogen and R^2 is selected from $R^{2'}$ is hydrogen or methyl and R^2 is T-W-R^6 or R, wherein W is $-C(R^6)_2O-$, $-C(R^6)_2N(R^6)-$, -CO-, $-CO_2-$, $-C(R^6)OC(O)-$, $-C(R^6)_2N(R^6)CO-$, or $-CON(R^6)-$, and R is an optionally substituted group selected from C_{1-6} aliphatic or phenyl, or R^2 and $R^{2'}$ are taken together with their intervening atoms to form a substituted or unsubstituted benzo, pyrido, or partially unsaturated 6-membered carbocyclic ring optionally substituted with -halo, $-N(R^4)_2$, $-C_{1-4}$ alkyl, $-C_{1-4}$ haloalkyl, $-NO_2$, $-O(C_{1-4}$ alkyl), $-CO_2(C_{1-4}$ alkyl), -CN, $-SO_2(C_{1-4}$ alkyl), $-SO_2NH_2$, $-OC(O)NH_2$, $-NH_2SO_2(C_{1-4}$ alkyl), $-NHC(O)(C_{1-4}$ alkyl), $-C(O)NH_2$, or $-CO(C_{1-4}$ alkyl), wherein the (C_{1-4} alkyl) is a straight, branched, or cyclic alkyl group.

8. The compound according to claim 1, wherein said compound is selected from Table 2.

9. A composition comprising a compound according to any of claims 1-8 and a pharmaceutically acceptable carrier.

10. The composition according to claim 9, further comprising a second therapeutic agent.

11. A method of inhibiting GSK-3, Aurora, or Src activity in a patient comprising the step of administering to said patient a therapeutically effective amount of the composition according to claim 9.

12. The method according to claim 11, wherein said method inhibits GSK-3 activity in a patient.

13. A method of inhibiting GSK-3, Aurora, or Src activity in a biological sample comprising contacting said biological sample with the compound according to claim 1.

14. A method of treating a disease that is alleviated by treatment with an GSK-3 inhibitor, said method comprising the step of administering to a patient in need of such a treatment a therapeutically effective amount of the composition according to claim 9.

15. The method according to claim 14, further comprising the step of administering to said patient a second therapeutic agent.

16. The method according to claim 14, wherein said disease is diabetes.

17. The method according to claim 14, wherein said disease is Alzheimer's disease.

18. The method according to claim 14, wherein said disease is schizophrenia.

19. A method of enhancing glycogen synthesis in a patient in need thereof, which method comprises the step of administering to said patient a therapeutically effective amount of the composition according to claim 9.

20. A method of lowering blood levels of glucose in a patient in need thereof, which method comprises the step of administering to said patient a therapeutically effective amount of the composition according to claim 9.

21. A method of inhibiting the production of hyperphosphorylated Tau protein in a patient in need thereof, which method comprises the step of administering to said patient a therapeutically effective amount of the composition according to claim 9.

22. A method of inhibiting the phosphorylation of β-catenin in a patient in need thereof, which method comprises the step of administering to said patient a therapeutically effective amount of the composition according to claim 9.

23. A method of treating a disease that is alleviated by treatment with an aurora inhibitor, which method comprises the step of administering to a patient in need of such a treatment a therapeutically effective amount of the composition according to claim 9.

24. The method according to claim 23, further comprising the step of administering to said patient a second therapeutic agent.

25. The method according to claim 23, wherein said disease is cancer.

26. A method of treating a disease that is alleviated by treatment with a Src inhibitor, which method comprises the step of administering to a patient in need of such a treatment a therapeutically effective amount of the composition according to claim 9.

27. The method according to claim 26, further comprising the step of administering to said patient a second therapeutic agent.

28. The method according to claim 26, wherein said disease is selected from hypercalcemia, osteoporosis, osteoarthritis, or symptomatic treatment of bone metastasis.

29. The method according to claim 26, wherein said disease is cancer.

30. A method of inhibiting ERK activity in a patient comprising the step of administering to said patient a therapeutically effective amount of a composition comprising a pharmaceutically acceptable carrier and the compound according to claim 1 wherein $R^{2'}$ is hydrogen and R^x and R^y are taken together with their intervening atoms to form a benzo ring.

31. A method of inhibiting ERK activity in a biological sample comprising contacting said biological with the compound according to claim 1 wherein $R^{2'}$ is hydrogen and R^x and R^y are taken together with their intervening atoms to form a benzo ring.

32. A method of treating a disease that is alleviated by treatment with an ERK inhibitor, said method comprising the step of administering to a patient in need of such a treatment a therapeutically effective amount of a composition comprising a pharmaceutically acceptable carrier and the compound according to claim 1 wherein $R^{2'}$ is hydrogen and R^X and R^Y are taken together with their intervening atoms to form a benzo ring.

33. The method according to claim 32, further comprising the step of administering to said patient a second therapeutic agent.

34. The method according to claim 32, wherein said disease is selected from cancer, stroke, diabetes, hepatomegaly, cardiovascular disease, Alzheimer's disease, cystic fibrosis, viral disease, autoimmune diseases, atherosclerosis, restenosis, psoriasis, allergic disorders, inflammation, and neurological disorders.

35. The method according to claim 34, wherein said disease is cancer.

36. The method according to claim 34, wherein said disease is restenosis.