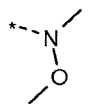
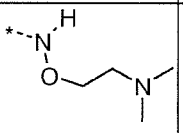
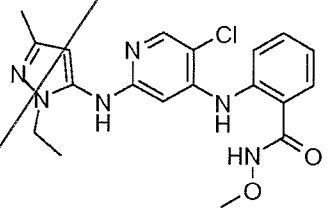
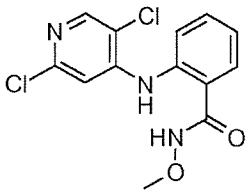
Ex	Name	R_c	Data
37	2-({5-chloro-2-[(1, 3-dimethyl-1H-pyrazol-5-yl) amino]-4-pyridinyl} amino)-*N*-methyl-*N*-(methyloxy)benzamide		LC-MS (ES) m/z = 387 $(M+H)^+$; 1H NMR (400 MHz, MeOD) δ ppm 8.16 (s, 1 H) 7.93 (s, 1 H) 7.50 - 7.66 (m, 2 H) 7.11 - 7.25 (m, 1 H) 6.62(s, 1 H) 5.99 (s, 1 H) 3.80 (s, 3 H) 3.55 - 3.70 (s, 3 H) 2.11 - 2.26 (s, 3 H)
38	2-({5-Chloro-2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-4-pyridinyl}amino)-*N*-{[2-(dimethylamino)ethyl]oxy}benzamide		LC-MS (ES) m/z = 444, 446 $(M+H)^+$; 1H NMR (400 MHz, MeOD) δ ppm 8.50 (s, 1 H) 7.93 (s, 1 H) 7.64 - 7.71 (m, 1 H) 7.51 - 7.61 (m, 2 H) 7.21(ddd, J = 8.0, 6.2, 2.3 Hz, 1 H) 6.58 (s, 1 H) 5.98 (s, 1 H) 4.22 - 4.31 (m, 2 H) 3.61 (s, 3 H) 3.33- - 3.40 (m, 2H) 2.96 (s, 6 H) 2.19 (s, 3 H)

Example 39

2-({5-Chloro-2-[(1-ethyl-3-methyl-1*H*-pyrazol-5-yl)amino]-4-pyridinyl}amino)-*N*-(methyloxy)benzamide



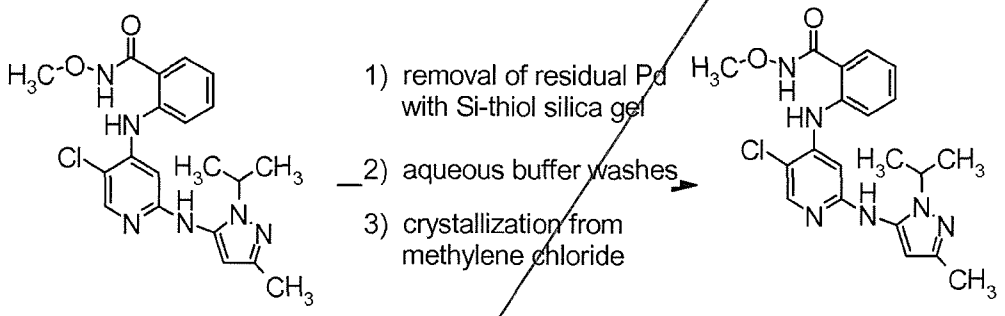
39a) 2-[(2,5-Dichloro-4-pyridinyl)amino]-*N*-(methyloxy)benzamide



A vessel was charged with 3-[(2,5-dichloro-4-pyridinyl)amino]benzoic acid (1.0g, 3.53 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (677 mg, 3.53 mmol) and hydroxybenzotriazole (HOBT) (541 mg, 3.53 mmol) in N,N-dimethylformamide (DMF, 7.0 mL) and was stirred at room temperature for 30 min. To this solution methoxylamine hydrochloride (0.3 g, 3.53 mmol) was added and reaction mixture was stirred for another 10 min. The reaction

The reaction mixture was stirred overnight tat the room temperature. Water (4000 mL) was added and the solution was acidified with acetic acid (20 mL). The solution was extracted 2 x 2 L of ethyl acetate. The organic was washed with water (1 L), brine, and dried over $MgSO_4$, filtered and evaporated. 2-[(5-Chloro-2-{[3-methyl-1-(1-methylethyl)-1H-pyrazol-5-yl]amino}-4-pyridinyl)amino]-N-(methyloxy)benzamide (74 g, 164 mmol, 94 % yield, 92 % pure) was isolated as a yellow foam. 1H NMR (400 MHz, DMSO-d_6) δ ppm 1.27 (d, J=6.57 Hz, 6 H) 2.10 (s, 3 H) 3.71 (s, 3 H) 4.39 (quin, J=6.51 Hz, 1 H) 5.93 (s, 1 H) 6.66 (s, 1 H) 7.08 - 7.19 (m, 1 H) 7.49 - 7.64 (m, 3 H) 7.98 (s, 1 H) 8.50 (s, 1 H) 9.50 (s, 1 H) 11.93 (s, 1 H).; HPLC Rt= 2.13 min, MS (ESI): $[M+H]^+$ = 415.1.

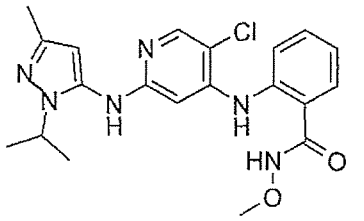
Purification of Example 41a and 41b Products



2-[(5-Chloro-2-{[3-methyl-1-(1-methylethyl)-1H-pyrazol-5-yl]amino}-4-pyridinyl)amino]-N-(methyloxy)benzamide (173.3 g, 63.5% w/w, 265.2 mmoles) was dissolved in ethyl acetate (3.50 L, 20 volumes) and heated to about 50° C. To this solution was added Si-thiol (functionalized silica gel) (87 g, 50% loading). The mixture was held at about 50 °C for 16-20 hours. It was then filtered off the Si-thiol silica gel. The filter cake was rinsed with ethyl acetate (2 x 200 mL each) and filtrates were combined. Then the combined filtrates were washed with 1 M aqueous ammonium formate at pH 9.4 (5 x 1 L each), washed with water, brine, and dried over magnesium sulfate. Dried EtOAC was filtered and stripped to dryness giving a yellow foam. It was dried at 50-55 °C for about 2 hours to a constant weight of 160 g. This material was slurried in methylene chloride (800 mL, 5 volumes), heated to reflux to afford a solution, and filtered. The solution was cooled to 20-25° C. The product crystallized upon cooling. After about 2 hours, the product was collected by filtration and rinsed with methylene chloride. The white solid was dried at 50-55° C for 14-16 hours to a constant weight. 2-[(5-Chloro-2-{[3-methyl-1-(1-methylethyl)-1H-pyrazol-5-yl]amino}-4-pyridinyl)amino]-N-(methyloxy)benzamide (85.0 g, 204.9 mmoles, 77% overall yield) was isolated as a white solid. 1H NMR (400 MHz, DMSO-d_6) δ ppm 1.27 (d, J=6.57 Hz, 6 H) 2.10 (s, 3 H) 3.70 (s, 3 H) 4.39 (quin, J=6.57 Hz, 1 H) 5.92 (s, 1 H)

Claims

1. 2-[(5-Chloro-2-{[3-methyl-1-(1-methylethyl)-1*H*-pyrazol-5-yl]amino}-4-pyridinyl)amino]-*N*-(methyloxy)benzamide, which is a compound of formula



or a salt thereof.

2. A pharmaceutically acceptable salt of 2-[(5-Chloro-2-{[3-methyl-1-(1-methylethyl)-1*H*-pyrazol-5-yl]amino}-4-pyridinyl)amino]-*N*-(methyloxy)benzamide.

3. 2-[(5-Chloro-2-{[3-methyl-1-(1-methylethyl)-1*H*-pyrazol-5-yl]amino}-4-pyridinyl)amino]-*N*-(methyloxy)benzamide.

4. A pharmaceutical composition comprising 2-[(5-Chloro-2-{[3-methyl-1-(1-methylethyl)-1*H*-pyrazol-5-yl]amino}-4-pyridinyl)amino]-*N*-(methyloxy)benzamide or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable excipient.

5. 2-[(5-Chloro-2-{[3-methyl-1-(1-methylethyl)-1*H*-pyrazol-5-yl]amino}-4-pyridinyl)amino]-*N*-(methyloxy)benzamide or a pharmaceutically acceptable salt thereof for use in therapy.

6. 2-[(5-Chloro-2-{[3-methyl-1-(1-methylethyl)-1*H*-pyrazol-5-yl]amino}-4-pyridinyl)amino]-*N*-(methyloxy)benzamide or a pharmaceutically acceptable salt thereof for use in the treatment of cancer.

7. The use of 2-[(5-Chloro-2-{[3-methyl-1-(1-methylethyl)-1*H*-pyrazol-5-yl]amino}-4-pyridinyl)amino]-*N*-(methyloxy)benzamide or a pharmaceutically acceptable salt thereof in the preparation of a medicament for use in the treatment of cancer.

8. A combination of (a) 2-[(5-Chloro-2-{[3-methyl-1-(1-methylethyl)-1*H*-pyrazol-5-yl]amino}-4-pyridinyl)amino]-*N*-(methyloxy)benzamide or a pharmaceutically acceptable salt thereof and (b) at least one anti-neoplastic agent.

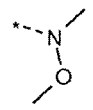
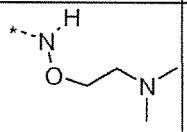
9. A combination as claimed in claim 8 for use in treatment of cancer.

10. The use of a combination as claimed in claim 8 in the preparation of a medicament for use in the treatment of cancer.

11. A compound for use as claimed in claim 6, or a combination for use as claimed in claim 9, or a use as claimed in claim 7 or claim 10 wherein the cancer is mesothelioma.

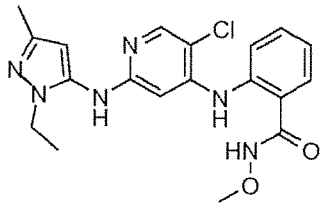
12. A compound for use as claimed in claim 6, or a combination for use as claimed in claim 9, or a use as claimed in claim 7 or claim 10 wherein the cancer is ovarian cancer.

13. A compound for use as claimed in claim 6, or a combination for use as claimed in claim 9, or a use as claimed in claim 7 or claim 10 wherein the cancer is glioblastoma multiform.

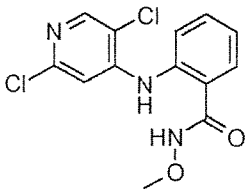
Ex	Name	R_c	Data
37	2-({5-chloro-2-[(1, 3-dimethyl-1H-pyrazol-5-yl) amino]-4-pyridinyl} amino)-*N*-methyl-*N*-(methyloxy)benzamide		LC-MS (ES) m/z = 387 $(M+H)^+$; 1H NMR (400 MHz, MeOD) δ ppm 8.16 (s, 1 H) 7.93 (s, 1 H) 7.50 - 7.66 (m, 2 H) 7.11 - 7.25 (m, 1 H) 6.62(s, 1 H) 5.99 (s, 1 H) 3.80 (s, 3 H) 3.55 - 3.70 (s, 3 H) 2.11 - 2.26 (s, 3 H)
38	2-({5-Chloro-2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-4-pyridinyl}amino)-*N*-{[2-(dimethylamino)ethyl]oxy}benzamide		LC-MS (ES) m/z = 444, 446 $(M+H)^+$; 1H NMR (400 MHz, MeOD) δ ppm 8.50 (s, 1 H) 7.93 (s, 1 H) 7.64 - 7.71 (m, 1 H) 7.51 - 7.61 (m, 2 H) 7.21(ddd, J = 8.0, 6.2, 2.3 Hz, 1 H) 6.58 (s, 1 H) 5.98 (s, 1 H) 4.22 - 4.31 (m, 2 H) 3.61 (s, 3 H) 3.33- - 3.40 (m, 2H) 2.96 (s, 6 H) 2.19 (s, 3 H)

Example 39

2-({5-Chloro-2-[(1-ethyl-3-methyl-1*H*-pyrazol-5-yl)amino]-4-pyridinyl}amino)-*N*-(methyloxy)benzamide



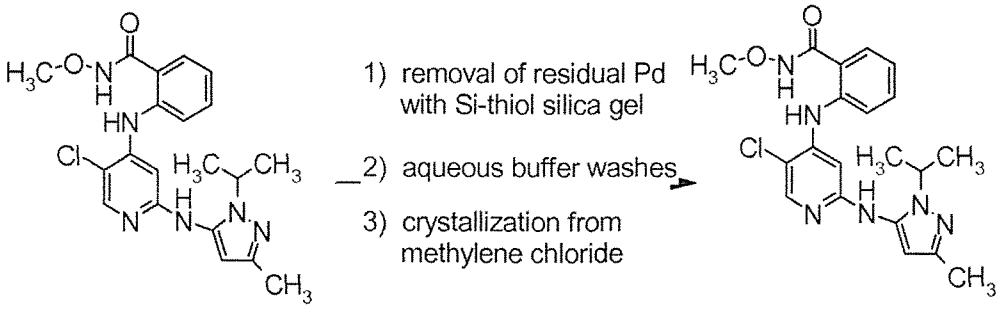
39a) 2-[(2,5-Dichloro-4-pyridinyl)amino]-*N*-(methyloxy)benzamide



A vessel was charged with 2-[(2,5-dichloro-4-pyridinyl)amino]benzoic acid (1.0g, 3.53 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (677 mg, 3.53 mmol) and hydroxybenzotriazole (HOBT) (541 mg, 3.53 mmol) in N,N-dimethylformamide (DMF, 7.0 mL) and was stirred at room temperature for 30 min. To this solution methoxylamine hydrochloride (0.3 g, 3.53 mmol) was added and reaction mixture was stirred for another 10 min. The reaction

The reaction mixture was stirred overnight at room temperature. Water (4000 mL) was added and the solution was acidified with acetic acid (20 mL). The solution was extracted 2 x 2 L of ethyl acetate. The organic was washed with water (1 L), brine, and dried over $MgSO_4$, filtered and evaporated. 2-[(5-Chloro-2-{[3-methyl-1-(1-methylethyl)-1H-pyrazol-5-yl]amino}-4-pyridinyl)amino]-N-(methyloxy)benzamide (74 g, 164 mmol, 94 % yield, 92 % pure) was isolated as a yellow foam. 1H NMR (400 MHz, DMSO-d_6) δ ppm 1.27 (d, *J*=6.57 Hz, 6 H) 2.10 (s, 3 H) 3.71 (s, 3 H) 4.39 (quin, *J*=6.51 Hz, 1 H) 5.93 (s, 1 H) 6.66 (s, 1 H) 7.08 - 7.19 (m, 1 H) 7.49 - 7.64 (m, 3 H) 7.98 (s, 1 H) 8.50 (s, 1 H) 9.50 (s, 1 H) 11.93 (s, 1 H).; HPLC Rt= 2.13 min, MS (ESI): $[M+H]^+$ = 415.1.

Purification of Example 41a and 41b Products



2-[(5-Chloro-2-{[3-methyl-1-(1-methylethyl)-1H-pyrazol-5-yl]amino}-4-pyridinyl)amino]-N-(methyloxy)benzamide (173.3 g, 63.5% w/w, 265.2 mmoles) was dissolved in ethyl acetate (3.50 L, 20 volumes) and heated to about 50° C. To this solution was added Si-thiol (functionalized silica gel) (87 g, 50% loading). The mixture was held at about 50 °C for 16-20 hours. It was then filtered off the Si-thiol silica gel. The filter cake was rinsed with ethyl acetate (2 x 200 mL each) and filtrates were combined. Then the combined filtrates were washed with 1 M aqueous ammonium formate at pH 9.4 (5 x 1 L each), washed with water, brine, and dried over magnesium sulfate. Dried EtOAC was filtered and stripped to dryness giving a yellow foam. It was dried at 50-55 °C for about 2 hours to a constant weight of 160 g. This material was slurried in methylene chloride (800 mL, 5 volumes), heated to reflux to afford a solution, and filtered. The solution was cooled to 20-25° C. The product crystallized upon cooling. After about 2 hours, the product was collected by filtration and rinsed with methylene chloride. The white solid was dried at 50-55° C for 14-16 hours to a constant weight. 2-[(5-Chloro-2-{[3-methyl-1-(1-methylethyl)-1H-pyrazol-5-yl]amino}-4-pyridinyl)amino]-N-(methyloxy)benzamide (85.0 g, 204.9 mmoles, 77% overall yield) was isolated as a white solid. 1H NMR (400 MHz, DMSO-d_6) δ ppm 1.27 (d, *J*=6.57 Hz, 6 H) 2.10 (s, 3 H) 3.70 (s, 3 H) 4.39 (quin, *J*=6.57 Hz, 1 H) 5.92 (s, 1 H)

CLAIMS

1. A compound that is:

2-[(5-Chloro-2-{[3-methyl-1-(1-methylethyl)-1*H*-pyrazol-5-yl]amino}-4-pyridinyl)amino]-*N*-(methyloxy)benzamide;

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1 that is:

2-[(5-Chloro-2-{[3-methyl-1-(1-methylethyl)-1*H*-pyrazol-5-yl]amino}-4-pyridinyl)amino]-*N*-(methyloxy)benzamide.

3. A pharmaceutical composition comprising the compound according to claim 1 and one or more pharmaceutically acceptable carriers, diluents or excipients.

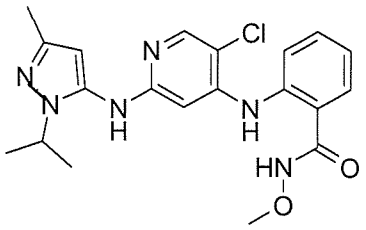
4. A pharmaceutical composition comprising the compound according to claim 2 and one or more pharmaceutically acceptable carriers, diluents or excipients.

5. A process for preparing a pharmaceutical composition containing a pharmaceutically acceptable carrier and the compound of claim 1 which process comprises bringing the compound of claim 1 into association with one or more pharmaceutically acceptable carriers, diluents or excipients.

6. A pharmaceutical composition according to claim 3, wherein the composition is in tablet form.

7. A pharmaceutical composition according to claim 4, wherein the composition is in tablet form.

8. A compound that is:



HCl.

9. A pharmaceutical composition comprising the compound according to claim 8 and one or more pharmaceutically acceptable carriers, diluents or excipients.

10. A pharmaceutical composition according to claim 9, wherein the composition is in tablet form.

11. A process for preparing a pharmaceutical composition containing a pharmaceutically acceptable carrier and the compound of claim 8 which process comprises bringing the compound of claim 8 into association with the pharmaceutically acceptable carrier.