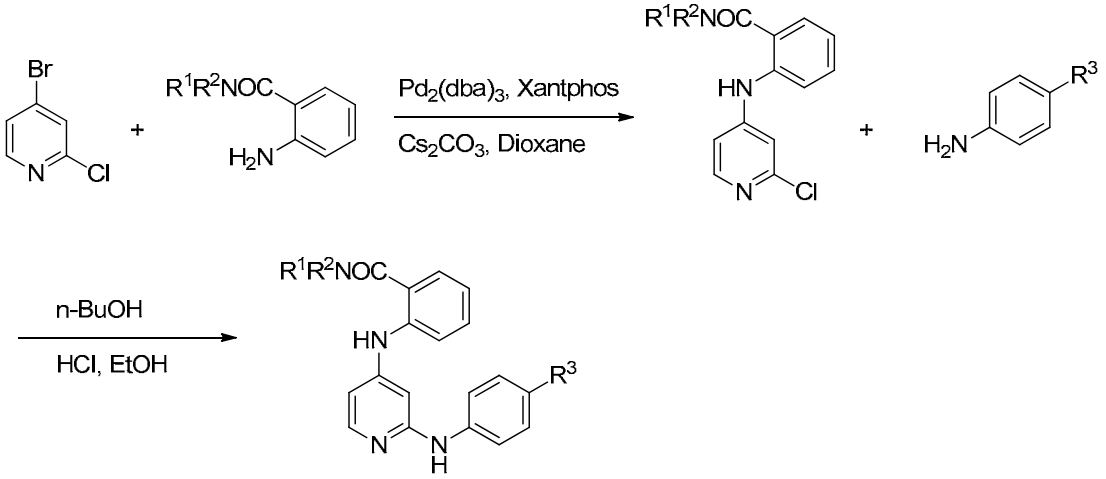
For the synthesis of Compounds **1**, **10-23**, **39** see WO2008/115369 The Scripps Research Institute; Liang, Chris; Koenig, Marcel; He, Yuanjun; Holmberg, Par.

For the synthesis of compound **41**, see WO2004/080980 Novartis A.-G., Switz.; Garcia-Echeverria, Carlos; Kanazawa, Takanori; Kawahara, Eiji; Masuya, Keiichi; Matsuura, Naoko; Miyake, Takahiro; Ohmori, Osamu; Umemura, Ichiro.

The HPLC/MS data for each individual compound is represented by 4 analyses. The first shows the molecular ion. The second shows the total ion count (TIC). The third is the HPLC trace (PDA mode, 200-400nM), and the fourth is the HPLC trace at 254nM. There is a slight time delay between TIC and the peak on the HPLC given that the injected material travels down the HPLC column and is then injected into the mass spec. UV absorbing peaks within the first minute of the HPLC trace are often DMSO or DMAC used to dissolve the sample.

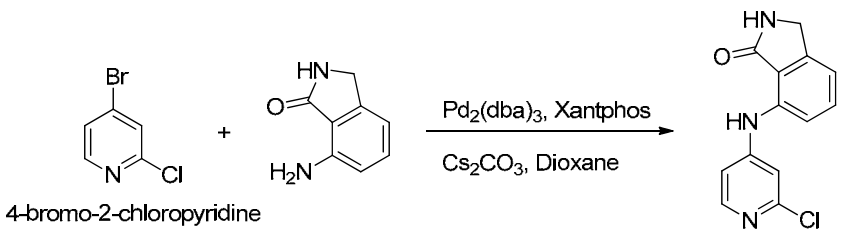
General Synthesis Scheme used to synthesize analogs **24-38, 40**.



Example of the synthesis of Compound **40**

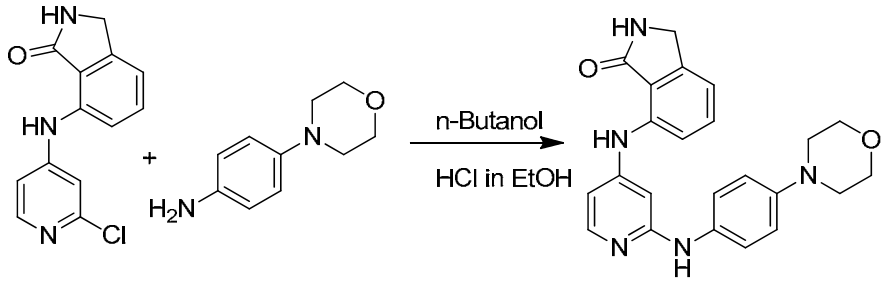
7-((2-((4-morpholinophenyl)amino)pyridin-4-yl)amino)isoindolin-1-one

Step 1: 7-((2-chloropyridin-4-yl)amino)isoindolin-1-one



A mixture of 4-bromo-2-chloropyridine (76 µl, 0.69 mmol), 7-aminoisoindolin-1-one (102 mg, 0.69 mmol), tris(dibenzylideneacetone)dipalladium(0) (59 mg, 0.064 mmol) 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (72 mg, 0.12 mmol) and cesium carbonate (455 mg, 1.40 mmol) in dioxane (12 ml) were heated at 100 °C for 15 h. It was purified by silica gel chromatography.

Step 2: 7-((2-((4-morpholinophenyl)amino)pyridin-4-yl)amino)isoindolin-1-one



A mixture of 7-((2-chloropyridin-4-yl)amino)isoindolin-1-one (28 mg, 0.11 mmol), 4-morpholinoaniline (28 mg, 0.16 mmol) and HCl in Ethanol, 1.25 M, (90 µl, 0.11 mmol) in n-butanol in a pressure vial was heated at 160 °C for 16 h. The solvent was removed and the residue was purified by preparative HPLC to yield the title compound. . LC/MS (M+H) 402.3.

Compounds **25** and **29-38** were prepared following the same general protocol as described for compound **40**, using 2-aminobenzamide and 4-bromo-2-chloropyridine in the first step, followed by the appropriate aniline in the second step (see Table 4).

Compounds **26-28** were prepared following the same general protocol as described for compound **40**, using the appropriate aniline and 4-bromo-2-chloropyridine in the first step (see Table 3), followed by 4-morpholinoaniline in the second step.

Compound **35**: ESI-MS (m/z): 349.0 $[M+H]^+$; ^{1}H-NMR (400 MHz, MeOH-D4) δ 7.75 (dd, 1H), 7.6 (d, 1H), 7.55 (dt, 1H), 7.5 (dd, 1H), 7.3 (dt, 1H), 6.85-6.9 (m, 2H), 6.78 (dd, 1H), 6.55 (dd, 1H), 6.35 (d, 1H), 6.0 (s, 2H).

Compound **36**: ESI-MS (m/z): 355.0 $[M]^+$; ^{1}H-NMR (400 MHz, MeOH-D4) δ 7.95 (s, 1H), 7.88 (d, 1H), 7.7-7.8 (dt, 4H), 7.55 (d, 1H), 7.4-7.5 (m, 3H), 7.35 (t, 1H), 7.1 (t, 1H), 6.65 (s, 1H), 6.55 (d, 1H).

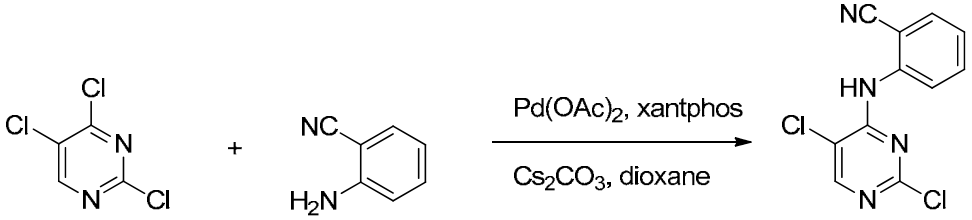
Compound **37**: ESI-MS (m/z): 395.1 $[M+H]^+$; ^{1}H-NMR (400 MHz, MeOH-D4) δ 7.7 (d, 1H), 7.6 (dd, 1H), 7.4 (dd, 1H), 7.35 (dt, 1H), 6.95 (dt, 1H), 6.6 (s, 2H), 6.4 (d, 1H), 6.38 (dd, 1H), 3.7 (s, 6H), 3.6 (s, 3H).

Compound **38**: ESI-MS (m/z): 404.2 $[M]^+$; ^{1}H-NMR (400 MHz, MeOH-D4) δ 7.75 (d, 2H), 7.7 (d, 2H), 7.5 (m, 2H), 7.15-7.0 (m, 4H), 6.5 (d, 1H), 6.4 (s, 1H), 3.8-3.9 (m, 4H), 2.85-2.95 (m, 4H), 2.33 (s, 3H).

Example of the synthesis of Compound **42**

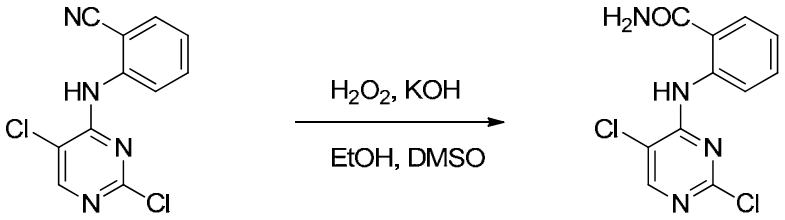
2-((5-chloro-2-((2-methoxy-4-morpholinophenyl)amino)pyrimidin-4-yl)amino)benzamide

Step 1: 2-((2,5-dichloropyrimidin-4-yl)amino)benzonitrile



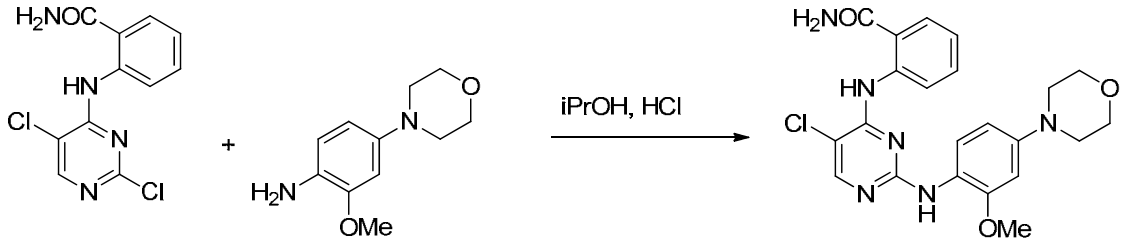
To a solution of 2,4,5-trichloropyrimidine (0.58g) and 2-aminobenzonitrile (0.35g) in dioxane (10mL) was added $Pd(OAc)_2$ (70 mg), xantphos (260 mg) and Cs_2CO_3 (1.95g). The tube was sealed and placed in a microwave reactor and heated at 70°C for 30 min. The crude reaction mixture was filtered through a short pad of silica gel (EtOAc) and concentrated to give a brown solid. Purification on silica gel (EtOAc/hexanes) provided the title compound as a greenish yellow solid (650 mg, 82% yield).

Step 2: 2-((2,5-dichloropyrimidin-4-yl)amino)benzamide



A mixture of the benzonitrile (530 mg) and KOH (560 mg) in EtOH/DMSO (10 mL, 9:1 v/v) was stirred at room temperature for 5 minutes until all of the solids dissolved. A solution of aqueous 30% H_2O_2 (2mL) was added and the reaction was stirred for 1.5h. The reaction was diluted with H_2O (80mL) and stirred for 20 minutes. The resulting yellow precipitate (433 mg, 76% yield) was filtered and washed with H_2O, and dried in air, to afford the title compound >95% pure by analytical HPLC analysis. LC/MS $(M)^+$ 282.98.

Step 3: 2-((5-chloro-2-((2-methoxy-4-morpholinophenyl)amino)pyrimidin-4-yl)amino)benzamide



To a mixture of the pyrimidine (57 mg) and morpholinoaniline (50 mg) in iPrOH (1mL) was added one drop of 12M HCl. The reaction vial was sealed and heated at 95°C for 17h and at 130°C for 2h. After cooling, the resulting suspension was diluted with iPrOH, filtered and washed with iPrOH, E_2tO, and dried in air to give the title compound (92mg, 94% yield). LC/MS $(M)^+$ 455.07; ^{1}H-NMR (400 MHz, DMSO-d6) δ 12.7 (br s, 1H), 9.5 (br s, 1H), 8.6 (br s, 1H), 8.45 (s, 1H), 7.9 (s, 1H), 7.87 (s, 1H), 7.5-7.4 (m, 2H), 7.25 (t, 1H), 6.8 (s, 1H), 6.6 (d, 1H), 3.8 (s, 7H), 3.2 (s, 4H).

Compounds **44-53** were synthesized following the same general protocol as described for compound **42**, using the correct aniline (see Table 5).

Compound **47**: ESI-MS (m/z): 455.1 $[M]^+$; ^{1}H-NMR (400 MHz, DMSO-d6) δ 12.2 (br s, 1H), 9.8 (br s, 1H), 8.7 (d, 1H), 8.4 (s, 1H), 8.3 (s, 1H), 7.86 (d, 1H), 7.81 (s, 1H), 7.3-7.6 (m, 3H), 7.2 (t, 1H), 3.9 (br s, 4H), 3.8 (s, 3H), 3.4 (br s, 4H).

Compound **51**: ESI-MS (m/z): 365.0 $[M]^+$; ^{1}H-NMR (400 MHz, DMSO-d6) δ 11.9 (s, 1H), 10.0 (s, 1H), 8.7 (d, 1H), 8.3 (s, 2H), 7.92 (d, 2H), 7.85 (d, 1H), 7.77 (br s, 1H), 7.7 (d, 2H), 7.6 (t, 1H), 7.2 (t, 1H).

Compound **52**: ESI-MS (m/z): 374.0 $[M]^+$; ^{1}H-NMR (400 MHz, DMSO-d6) δ 11.9 (s, 1H), 9.7 (s, 1H), 8.7 (d, 1H), 8.35 (s, 1H), 8.3 (s, 1H), 7.85 (d, 1H), 7.8 (s, 1H), 7.7 (d, 2H), 7.5 (t, 1H), 7.3 (d, 2H), 7.15 (t, 1H).