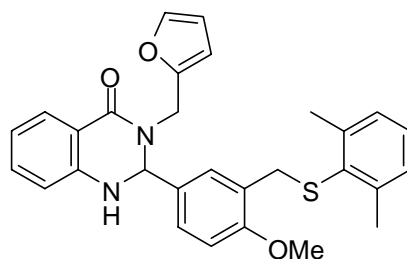


Thyrotropin Receptor Stimulates Internalization-independent Persistent
Phosphoinositide Signaling

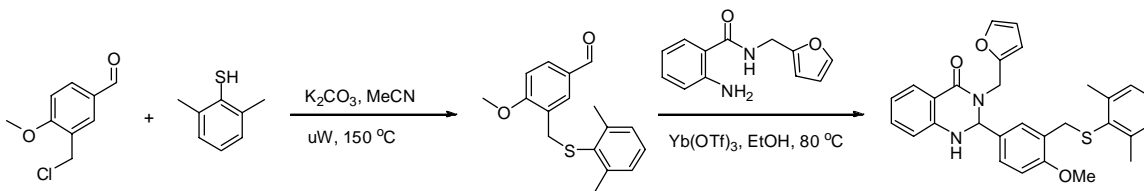
Alisa Boutin, Michael D. Allen, Elizabeth Geras-Raaka, Wenwei Huang, Susanne
Neumann and Marvin C. Gershengorn

Molecular Pharmacology

Name: 2-(3-((2,6-dimethylphenylthio)methyl)-4-methoxyphenyl)-3-(furan-2-ylmethyl)-2,3-dihydroquinazolin-4(1H)-one



Synthesis of 2-(3-((2,6-dimethylphenylthio)methyl)-4-methoxyphenyl)-3-(furan-2-ylmethyl)-2,3-dihydroquinazolin-4(1H)-one (WWH07-084)



To a solution of 3-(chloromethyl)-4-methoxybenzaldehyde (91.0 mg, 0.5 mmol, 1.0 equiv) and 2,6-dimethylbenzenethiol (68.4 mg, 0.5 mmol, 1.0 equiv) in 4 mL

acetonitrile was added potassium carbonate (0.55 g, 4.0 mmol, 8.0 equiv). The mixture was heated to 150 °C in the microwave for 10 min. After filtered off the solid and removed the solvent, 2-amino-*N*-(furan-2-ylmethyl)benzamide (107 mg, 0.5 mmol, 1.0 equiv) in 5 mL of EtOH was added followed by addition of Ytterbium trifluoromethanesulfonate (62 mg, 0.1 mmol, 0.2 equiv). The mixture was heated at 80 °C for 2 hours. Upon completion, the mixture was dried down and chromatographed on silica gel with 10-60% EtOAc/Hexanes gradient elution to give 2-(3-((2,6-dimethylphenylthio)methyl)-4-methoxyphenyl)-3-(furan-2-ylmethyl)-2,3-dihydroquinazolin-4(1H)-one (101.4 mg, 42%) as a white solid after triturating with diethyl ether. ¹HNMR (400 MHz, DMSO-*d*₆) δ ppm 2.26 (s, 6 H), 3.56 (d, *J*=15.7 Hz, 1 H), 3.66 (s, 3 H), 3.72 (d, 1 H), 3.79 (d, 1 H), 5.12 (d, *J*=15.7 Hz, 1 H), 5.55 (d, *J*=2.2 Hz, 1 H), 6.25 (d, *J*=3.1 Hz, 1 H), 6.41 (dd, *J*=3.0, 1.9 Hz, 1 H), 6.59 (d, *J*=8.0 Hz, 1 H), 6.66 (t, *J*=7.5 Hz, 1 H), 6.78 - 6.94 (m, 2 H), 7.00 - 7.28 (m, 6 H), 7.59-7.66 (m, 2 H); LCMS: (electrospray + ve), *m/z* 485.2 (MH)⁺, *t*_R = 7.16 min, UV₂₅₄ = 98%.