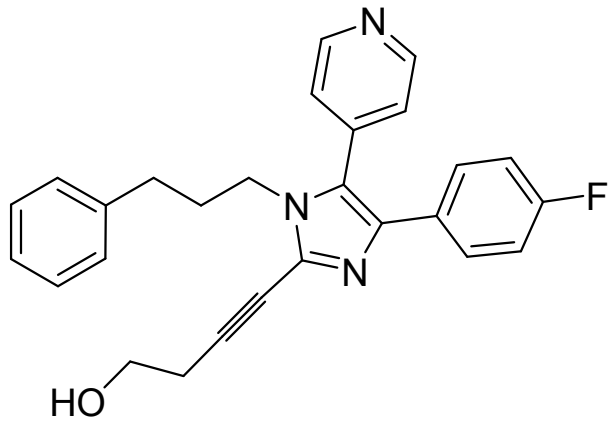
RWJ-67657

SYN-1072



4-(4-(4-fluorophenyl)-1-(3-phenylpropyl)-5-(pyridin-4-yl)-1H-imidazol-2-yl)but-3-yn-1-ol

CAS Registry No.: 215303-72-3

Smiles String:
c1ccc(cc1)CCCn2c(nc(c2c3ccncc3)c4ccc(cc4)F)C#CCCO

Molecular Weight: 425.5

Molecular Formula: C27H24FN3O

Lot Number: Refer to vial

1H-NMR: Available on request

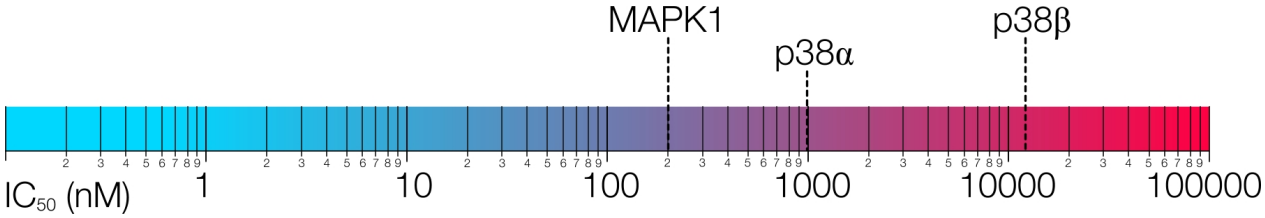
HPLC (Purity): > 95.0% @ 254 nm

ES-MS: Available on request

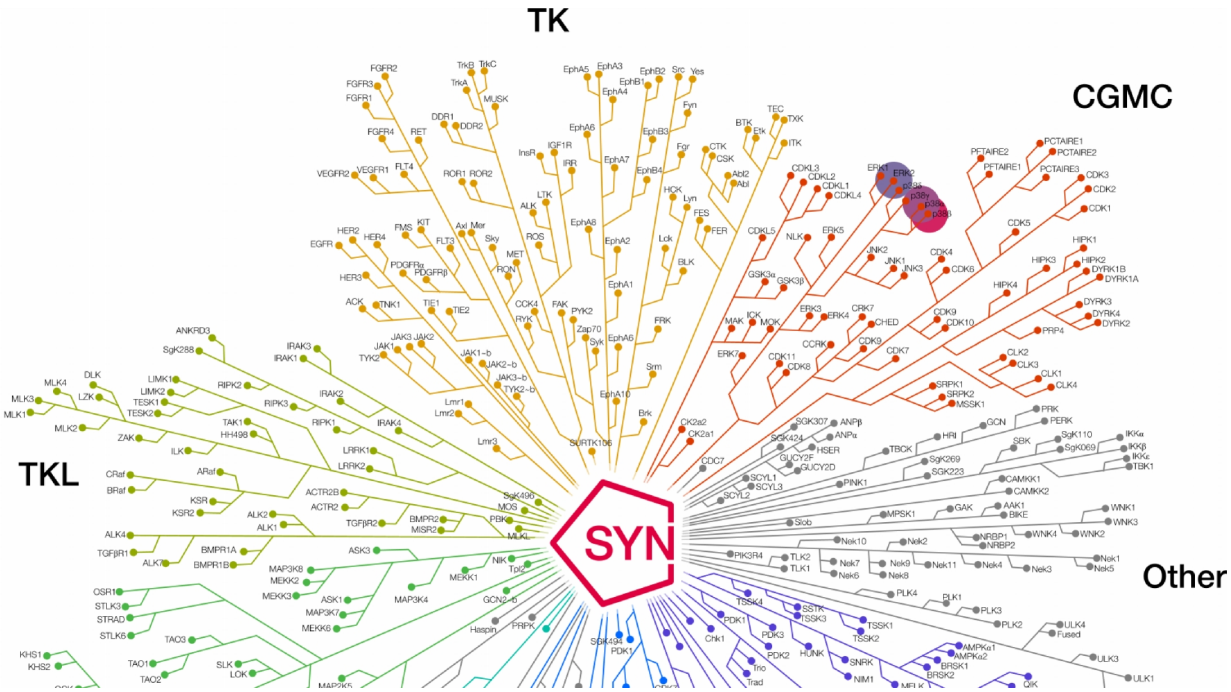
Description:

The cytokine Tumor necrosis factor-alpha (TNF-alpha) is secreted by activated monocytes/macrophages and T lymphocytes and has been implicated in several disease states, including rheumatoid arthritis, inflammatory bowel disease, septic shock, and osteoporosis. Monocyte/macrophage production of TNF-alpha is dependent on the mitogen-activated protein kinase p38. The compound RWJ 67657 is a potent, orally active inhibitor of MAPK and it inhibited the release of TNF-alpha from LPA stimulated human mononuclear cells with an IC(50) of 3 nM, as well as the release of TNF-alpha from peripheral blood mononuclear cells treated with the T cell stimulator and superantigen staphylococcal enterotoxin B with an IC(50) value of 13 nM. Also RWJ 67657 was approximately 10-fold more potent than the literature standard p38 kinase inhibitor SB 203580 in all p38 dependent in vitro systems tested and is much more specific than SB 203580 for p38 kinase. RWJ 67657 inhibited the enzymatic activity of recombinant p38alpha and beta, with in vitro IC50 values of 1 and 11 μM respectively, but not gamma or delta, and in further in vitro test across a panel of other enzymes RWJ 67657 demonstrated no other significant activity.

Biological Activity



Kinome Mapping



Shipping and Storage Temperature

Shipping:
Ambient

Storage:
2 years -20C, Powder 1 month, -4C in DMSO, More than one month -80C in DMSO

Solubility

DMSO 45mg/mL, Ethanol 4mg/mL

Preparing Stock Solutions

Stock Solution (1ml DMSO)	1mM	10mM	20mM	50mM
Mass(mg)	0.4255	4.2550	8.5100	21.2750

References

1. Wadsworth SA, Cavender DE, Beers SA, Lalan P, Schafer PH, Malloy EA, Wu W, Fahmy B, Olini GC, Davis JE, Pellegrino-Gensey JL, Wachter MP, Siekierka JJ. RWJ 67657, a potent, orally active inhibitor of p38 mitogen-activated protein kinase. J Pharmacol Exp Ther. 1999 Nov;291(2):680-7.

2. Wei S, Daniel BJ, Brumlik MJ, Burow ME, Zou W, Khan IA, Wadsworth S, Siekierka J, Curiel TJ. Drugs designed to inhibit human p38 mitogen-activated protein kinase activation treat Toxoplasma gondii and Encephalitozoon cuniculi infection. Antimicrob Agents Chemother. 2007 Dec;51(12):4324-8. Epub 2007 Oct 8.

Ordering Information

To order more of this or any other SYNkinase compound, go to synkinase.com, Call us Toll Free (US Only) at 1- 877-854-6273 or email orders@synkinase.com.