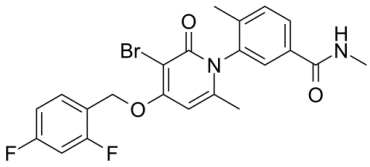
Data Sheet

Product Name:	PH-797804
Cat. No.:	CS-0465
CAS No.:	586379-66-0
Molecular Formula:	C22H19BrF2N2O3
Molecular Weight:	477.30
Target:	Autophagy; p38 MAPK
Pathway:	Autophagy; MAPK/ERK Pathway
Solubility:	DMSO : 50 mg/mL (104.76 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

PH-797804 is a ATP-competitive, selective **p38α/p38β** inhibitor (**IC_{50}**=26 nM and **K_i**=5.8 nM for p38α; **K_i**=40 nM for p38β) and does not inhibit JNK2. IC50 & Target: IC50: 26 nM (p38α)[1]

Ki: 5.8 nM (p38α), 40 nM (p38β)[2] **In Vitro:** PH-797804 blocks LPS-induced TNF-α production and p38 kinase activity in the human monocytic U937 cell line, with comparable IC_{50} of 5.9 nM and 1.1 nM. PH-797804 has no inhibitory effect on either the JNK pathway (c-Jun phosphorylation) or ERK pathway (ERK phosphorylation) in U937 cells at concentrations up to 1 μM. PH-797804 inhibits RANKL- and M-CSF-induced osteoclast formation in a concentration-dependent manner, with IC50 of 3 nM in primary rat bone marrow cells[1].

IC_{50} values for PH-797804 against the following targets have been determined to be greater than 200 μM (unless specified): CDK2, ERK2, IKK1, IKK2, IKKi, MAPKAP2, MAPKAP3, MKK7 (>100 μM), MNK, MSK (>164 μM), PRAK, RSK2, and TBK1, which means the activity of PH-797804 is specific[2]. **In Vivo:** Orally dosing of PH-797804 effectively inhibits acute inflammatory responses induced by systemically administered endotoxin in both rat and cynomolgus monkeys. PH-797804 treatment for 10 days demonstrates robust anti-inflammatory activity in chronic disease models, significantly reducing both joint inflammation and associated bone loss in streptococcal cell wall-induced arthritis in rats and mouse collagen-induced arthritis. Dose-response analysis resulted in ED50 values of 0.07 mg/kg and 0.095 mg/kg in rat and cynomolgus monkeys, respectively. PH-797804 inhibits LPS-induced TNF-α, IL-6, and MK-2 activity in a dose- and concentration-dependent manner in a human endotoxin challenge model[1].

References:

[1]. Hope HR, et al. Anti-inflammatory properties of a novel N-phenyl pyridinone inhibitor of p38 mitogen-activated protein kinase: preclinical-to-clinical translation. J Pharmacol Exp Ther, 2009, 331(3), 882-895.

[2]. Xing L, et al. Structural bioinformatics-based prediction of exceptional selectivity of p38 MAP kinase inhibitor PH-797804. Biochemistry, 2009, 48(27), 6402-6411.

CAIndexNames:

Benzamide, 3-[3-bromo-4-[(2,4-difluorophenyl)methoxy]-6-methyl-2-oxo-1(2H)-pyridinyl]-N,4-dimethyl-

SMILES:

O=C(C1=CC=C(C(N2C(C)=CC(OCC3=CC=C(C=C3F)F)=C(C2=O)Br)=C1)C)NC

Caution: Product has not been fully validated for medical applications. For research use only.

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