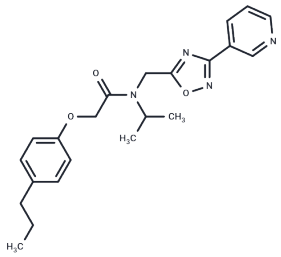
Data Sheet (Cat.No.T6941)

TargetMol

PI-1840

Chemical Properties



CAS No. : 1401223-22-0

Formula: C22H26N4O3

Molecular Weight: 394.47

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	PI-1840(IC50 = 27 nM)is a reversible and selective chymotrypsin-like (CT-L) inhibitor, with little proteasome proteolytic effects on trypsin-like (T-L) and postglutamyl-peptide-hydrolysis-like (PGPH-L).
Targets(IC50)	Apoptosis,Bcl-2 Family,NF-κB,Proteasome,Caspase,Autophagy,PARP
In vitro	PI-1840 potently inhibits proteasomal CT-L activity with IC50 of 0.37 μM in intact human MDA-MB-468 cancer cells, and inhibits proliferation/survival of human MDA-MB-468 cells. [1] In intact cancer cells, PI-1840 inhibits CT-L activity, induces the accumulation of proteasome substrates p27, Bax, and IκB-α, inhibits survival pathways and viability, and induces apoptosis. [2]
In vivo	PI-1840 (150 mg/kg i.p.) inhibits the tumor growth in mice of MDA-MB-231 breast tumors. [2]
Kinase Assay	CT-L, T-L, PGPH-L proteolytic activity assays: In the high-throughput screen, fluorogenic peptides are used as substrates to assay (at 10 μM) the 50,000 compounds library from ChemBridge for inhibitory activity against the CT-L proteolytic activity of the purified rabbit 20S proteasome. To test for selectivity for CT-L over T-L and PGPH-L the corresponding fluorogenic peptides are used. Briefly, 1 nM of purified 20S rabbit proteasome is incubated with 20 μM Suc-Leu-Leu-Val-Tyr-AMC for the CT-L activity, Bz-Val-Gly-Arg-AMC for the T-L activity, and benzyloxycarbonyl Z-Leu-Leu-Glu-AMC for the PGPH-L activity for 1 h at 37 °C in 100 μL of assay buffer (50 mM Tris-HCl, pH 7.6) with or without compound. After incubation, production of hydrolyzed 7-amido-4-methyl-coumarin (AMC) groups is measured using a WALLAC Victor2 1420 Multilabel Counter with an excitation filter of 355 nm and an emission filter of 460 nm. The amount of AMC released is within the linear range. Bortezomib is used as a positive control for IC50 determinations. To determine proteasome activity in whole cell, extracts (5 μg) from cultured cell lysate is used instead of 20S rabbit proteasome, and followed the same assay mentioned above.
Cell Research	Cells are plated in 96-well plates in 100 μL medium and allowed to attach overnight. Cells are then incubated for 120 h with varying concentrations of inhibitors. Media is aspirated and replaced with 100 μL complete media containing 1 mg/ml MTT and incubated for three hours at 37 °C in 5% CO2 humidified incubator. Media is then aspirated and DMSO is added. Cells are incubated for 10 min at room temperature while shaking, and the absorbance is determined at 540 nm using a μQuant

Cell Research	spectrophotometric plate reader. The IC50 values are determined using equation under CT-L, T-L, PGPH-L proteolytic activity assays.(Only for Reference)

Solubility Information

Solubility	Ethanol: 31 mg/mL (78.59 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 72 mg/mL (182.52 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (5.07 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.535 mL	12.6752 mL	25.3505 mL
5 mM	0.507 mL	2.535 mL	5.0701 mL
10 mM	0.2535 mL	1.2675 mL	2.535 mL
50 mM	0.0507 mL	0.2535 mL	0.507 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Ozcan S, et al. J Med Chem. 2013, 56(10), 3783-3805.
Lü Z, Li X, Li K, et al. Nitazoxanide and related thiazolides induce cell death in cancer cells by targeting the 20S proteasome with novel binding modes. Biochemical Pharmacology. 2022: 114913.
Kazi A, J Biol Chem. 2014, 289(17), 11906-11915.