

Product Data Sheet

Product Name: PI-1840
Cat. No.: GC15802

Chemical Properties

Cas. No. 1401223-22-0

Chemical Name N-isopropyl-2-(4-propylphenoxy)-N-((3-(pyridin-3-yl)-1,2,4-oxadiazol-5-yl)methyl)acetamide

SMILES CCCC1=CC=C(C(=C1)OCC(=O)N(C(C)C)CC2=NC(C3=CC=CC=C3N=N3)=O)C=C

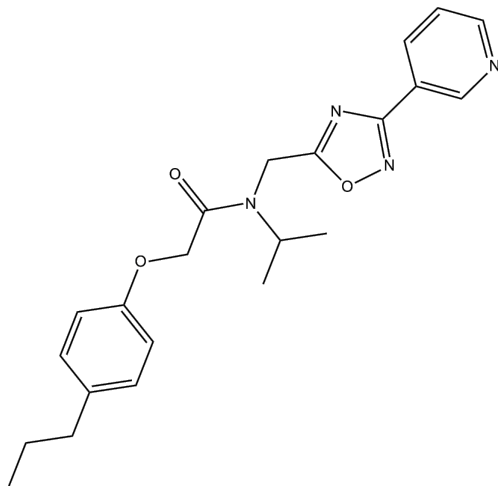
Formula $C_{22}H_{26}N_4O_3$ M.Wt 394.47

Solubility $\geq 70.7\text{mg/mL}$ in DMSO Storage Desiccate at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Background

PI-1840 is a potent and selective inhibitor of proteasome with IC_{50} value of 27 nM for chymotrypsinlike (CT-L) activity [1].

The 26S proteasome consists of a 19S regulatory particle (RP) and a 20S core particle. The 26S proteasome have three main catalytic activities: chymotrypsin-like (CT-L), peptidylglutamyl peptide

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

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hydrolyzing-like (PGPH-L) and trypsin-like (T-L) activities. CT-L activity plays an important role in the degradation of tumor suppressor and apoptotic proteins [1].

PI-1840 is a rapidly reversible and non-covalent proteasome CT-L inhibitor. PI-1840 exhibited excellent selectivity for CT-L over PGPH-L and T-L activities. In MDA-MB-468 human breast cancer cells, PI-1840 inhibited the CT-L activity with IC₅₀ value of 0.37 μ M and inhibited cell survival/proliferation [1]. Also, PI-1840 exhibited 121-fold selectivity for the constitutive 20 S proteasome over the immunoproteasome with IC₅₀ values of 18 and 2170 nM, respectively. In MDA-MB-468 cells, PI-1840 caused the accumulation of CT-L substrates I κ B- α , p27 and Bax. Also, PI-1840 reduced the levels of survivin, p-Akt and Ser(P)-6 and induced apoptosis through poly(ADP-ribose) polymerase cleavage and caspase-3 activation [2].

In nude mice bearing human breast tumor, PI-1840 (150 mg/kg/day, i.p, daily) inhibited tumor growth by 85% [2].

References:

- [1]. Ozcan S, Kazi A, Marsilio F, et al. Oxadiazole-isopropylamides as potent and noncovalent proteasome inhibitors. J Med Chem, 2013, 56(10): 3783-3805.
- [2]. Kazi A, Ozcan S, Tecleab A, et al. Discovery of PI-1840, a novel noncovalent and rapidly reversible proteasome inhibitor with anti-tumor activity. J Biol Chem, 2014, 289(17): 11906-11915.

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