

Product Data Sheet

Product Name: RIPA-56
Cat. No.: GC31652

Chemical Properties

Cas. No. 1956370-21-0

SMILES CCC(C)(C)C(N(CC1=CC=CC=C1)O)=O

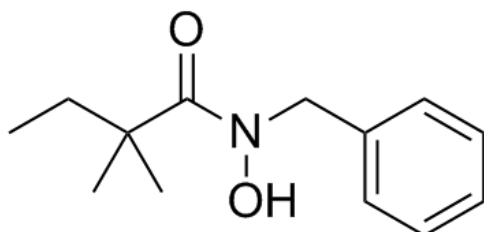
Formula $C_{13}H_{19}NO_2$ M.Wt 221.3

Solubility DMSO : ≥ 100 mg/mL (451.88 mM) Storage Store at $-20^{\circ}C$

General tips For obtaining a higher solubility , please warm the tube at $37^{\circ}C$ and shake it in the ultrasonic bath for a while. Stock solution can be stored below $-20^{\circ}C$ 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



Protocol

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

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Cell experiment: Cell necrosis assay is performed in 96-well cell culture plate. 3,000 cells are plated in each well and cultured at 37°C overnight. HT-29 cells are treated with 20 ng/mL TNF α /100 nM Smac Mimetics/20 μ M z-VAD-FMK and RIPA-56 for 24 h. L929 cells are treated with 20 ng/mL TNF α /20 μ M z-VAD-FMK and RIPA-56 for 6 h. The cell survival ratio is determined using the Cell Titer-Glo Luminescent Cell Viability Assay kit[1].

Animal experiment: Mice: Following intravenous (IV), intraperitoneal (IP), or oral administration (PO) of RIPA-56 to C57BL/6 mice (n=3), blood is sampled through eye puncture at various time points. Compound concentrations in the plasma samples are analyzed by LCMS/MS. Pharmacokinetic parameters are determined from individual animal data using noncompartmental analysis in phoenix 64[1].

References:

[1]. Ren Y, et al. Discovery of a Highly Potent, Selective, and Metabolically Stable Inhibitor of Receptor-Interacting Protein 1 (RIP1) for the Treatment of Systemic Inflammatory Response Syndrome. J Med Chem. 2017 Feb 9;60(3):972-986.

Background

RIPA-56 is a highly potent, selective, and metabolically stable inhibitor of receptor-interacting protein 1 (RIP1) with an IC₅₀ of 13 nM.

RIPA-56 has a half-life of 128 min in human liver microsomal stability assays and an EC₅₀ of 28 nM in TSZ-induced HT-29 necrosis assay. RIPA-56 also demonstrates potency in protection of murine L929 cells from TZ-induced necrosis (EC₅₀=27 nM). RIPA-56 shows efficient inhibition of RIP1 kinase activity, with an IC₅₀ of 13 nM and no inhibition of RIP3 kinase activity at a 10 μ M concentration. RIPA-56 could form tight hydrophobic interactions with RIP1 through both the phenyl group and the 2,2-dimethylbutyl group, and form two important hydrogen bonds[1].

In the SIRS mice disease model, RIPA-56 efficiently reduces tumor necrosis factor alpha (TNF α)-induced mortality and multi-organ damage. Compared to known RIP1 inhibitors, RIPA-56 is potent in

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both human and murine cells, is much more stable in vivo, and is efficacious in animal model studies. RIPA-56 has an impressive PK profile in mice with a 3.1 h half-life, 22% oral bioavailability (P.O.), and 100% bioavailability from intraperitoneal injection (I.P.)[1].

[1]. Ren Y, et al. Discovery of a Highly Potent, Selective, and Metabolically Stable Inhibitor of Receptor-Interacting Protein 1 (RIP1) for the Treatment of Systemic Inflammatory Response Syndrome. J Med Chem. 2017 Feb 9;60(3):972-986.

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