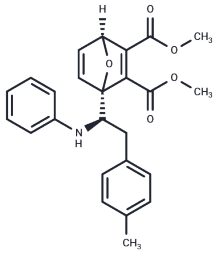
Data Sheet (Cat.No.T5199)

TargetMol

COH000

Chemical Properties



CAS No. : 1534358-79-6

Formula: C25H25NO5

Molecular Weight: 419.47

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	COH000 is a covalent and irreversible inhibitor of small ubiquitin-like modifier (SUMO)-activating enzyme and inhibited SUMOylation (IC50: ~ 0.2 μM in vitro).
Targets(IC50)	E1/E2/E3 Enzyme
In vitro	COH000 inhibited SUMOylation with an average IC50 of approximately 0.2 μM in vitro but did not inhibit ubiquitylation in a Ubc13-mediated poly-ubiquitylation assay tested under the same condition at concentrations up to 100 μM. COH000 treatment induced apoptosis in HCT-116 cells. The level of apoptosis was reduced when SAE2 was overexpressed by transfection and was increased when SAE2 was knocked down in HCT116 cells.
In vivo	Once the tumor became palpable, the tumor-bearing Es1e/SCID mice were treated with COH000 or vehicle for 14 days. COH000 significantly inhibited tumor growth. In addition, COH000 significantly reduced SAE2 levels in tumor tissues.
Kinase Assay	Briefly, SAE, Ubc9, GST-SUMO and His6-RanGap-1 proteins were expressed and purified as described previously.Assay buffer contained 50 mMTris-HCl pH 7.4, 0.3 mM DTT, 10 mM MgCl2, and 0.005% Tween-20. The assays were conducted using 1536-well, white plates. 2 μL of Mixture 1, containing 12.5 nM SAE and 100 nM His6-RanGap-1 in the assay buffer was mixed with 70 nl of 2 mM compounds dissolved in DMSO. Then 2 μL of Mixture 2, containing 20 mM ATP, 12.5 nM E2 and 30 nM GST-SUMO in assay buffer, was added. After incubation for 90 min at room temperature, 1 μl of pre-mixed Ni acceptor beads and Glutathione Donor beads, at 10 μg/ml each, was added. After incubation for 60 min at room temperature, readings were made on a BMG LabtechPheraStar in an AlphaScreen mode (Ex: 680 nm; Em: 570 nm).
Cell Research	Cell proliferation was measured using a CellTiter 96 AQueous One Solution Cell Proliferation Assay (MTS-based) after COH000 or its analog (54 or 55) treatment at the indicated concentrations and the time points. Briefly, cells were incubated with 20 mL of CellTiter 96 AQueous reagentafter the treatment and incubated at 37C until color development. Absorbance measurements were performed using a SpectraMax M5 reader. For assays measuring anti-proliferation effects, all values were normalized to the vehicle treatment. All values are represented graphically as mean ± standard deviation (STDEV) from three independent samples (n=3).

Animal Research	Mice were housed in a controlled environment (12-h light/12-h dark cycle) with access to waterand fed a standard diet generally from 6 to 8 weeks of age. Body weight was measured weekly and food intake was monitored. For colorectal cancer xenograft with COH000 treatment, HCT116 cells were s.c. injected into a plasma esterase-deficient SCID mouse strain (Es1e/SCID), male, 8-10 weeks. When the tumors became palpable, COH000 was administered subcutaneously peritumoral injection once a day at a dose of 10 mg per kilogram of body weight. Mice in the control group received equal volumes of vehicle (5% DMSO, 30% solutol in PBS). Tumor volume was measured until the endpoint was reached. Mice were euthanized using CO2 inhalation and tumors were excised.

Solubility Information

Solubility	H2O: < 0.1 mg/mL (insoluble), DMSO: 35.71 mg/mL (85.13 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.384 mL	11.9198 mL	23.8396 mL
5 mM	0.4768 mL	2.384 mL	4.7679 mL
10 mM	0.2384 mL	1.192 mL	2.384 mL
50 mM	0.0477 mL	0.2384 mL	0.4768 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

Li YJ, et al. Allosteric Inhibition of Ubiquitin-like Modifications by a Class of Inhibitor of SUMO-Activating Enzyme. Cell Chem Biol. 2018 Dec 5. pii: S2451-9456(18)30386-6.

Sun B, Wu H, Lu J, et al. Irisin reduces bone fracture by facilitating osteogenesis and antagonizing TGF-β/Smad signaling in a growing mouse model of osteogenesis imperfecta. Journal of Orthopaedic Translation. 2023, 38: 175-189.