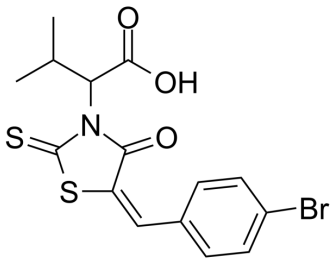
BH3I-1

Cat. No.:	HY-100383
CAS No.:	300817-68-9
Molecular Formula:	$C_{15}H_{14}BrNO_3S_2$
Molecular Weight:	400.31
Target:	Bcl-2 Family; MDM-2/p53; E1/E2/E3 Enzyme
Pathway:	Apoptosis; Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (249.81 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4981 mL	12.4903 mL	24.9806 mL
	5 mM	0.4996 mL	2.4981 mL	4.9961 mL
	10 mM	0.2498 mL	1.2490 mL	2.4981 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.25 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.25 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BH3I-1 is a Bcl-2 family antagonist, which inhibits the binding of the Bak BH3 peptide to Bcl-xL with a K_i of 2.4±0.2 μM in FP assay. BH3I-1 has a K_d of 5.3 μM against the p53/MDM2 pair.

IC_{50} & Target

Bcl-2	Bcl-xL	Bak	Bim

p53/mDM2
5.3 μM (Kd)

In Vitro

BH3I-1, while inhibiting its reported target Bcl-2/Bim and Bcl-xL/Bim, shows significant inhibition of both the p53/hDM2 and p300/Hif-1α interactions. This surprising promiscuity, displays by a well studied compound leads to further interrogate the

p53/hDM2 interaction utilizing a standard fluorescence polarization (FP) assay with purified protein. The results from the FP assay validates the split-luciferase screen and demonstrates that BH3I-1 has a K_d=5.3 μM against the p53/mDM2 pair, which is comparable to its low micromolar potency reported for the BH3 family of receptors[2]. BH3I-1 inhibits interaction between the BH3 domain and Bcl-xL. NMR analyses reveal that BH3I-1 targets the BH3-binding pocket of Bcl-xL with a K_i of 7.8±0.9 μM [3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [3]

Jurkat cells overexpressing Bcl-xL, FL 5.12 and FL 5.12/Bcl-xL cells (5×10^4 cells per well) are seeded into white 96-well plates and treated with various concentrations of the compounds (e.g., BH3I-1; 30 μM and 90 μM)for 48 h. For zVAD-FMK protection experiments, cells are preincubated with 100 μM zVAD-FMK for 1 h before the addition of chemicals. Cell viability is determined with an MTS assay with a Victor plate reader. For PI staining experiments, cells are grown in 24-well plates and then incubated with 2 μg/mL PI. Cell death is determined by FACS analysis in a FACSCalibur machine[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Wang L, et al. Development of dimeric modulators for anti-apoptotic Bcl-2 proteins. Bioorg Med Chem Lett. 2008 Jan 1;18(1):236-40.

[2]. Porter JR, et al. Profiling small molecule inhibitors against helix-receptor interactions: the Bcl-2 family inhibitor BH3I-1 potently inhibits p53/hDM2. Chem Commun (Camb). 2010 Nov 14;46(42):8020-2.

[3]. Degterev A, et al. Identification of small-molecule inhibitors of interaction between the BH3 domain and Bcl-xL. Nat Cell Biol. 2001 Feb;3(2):173-82.

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