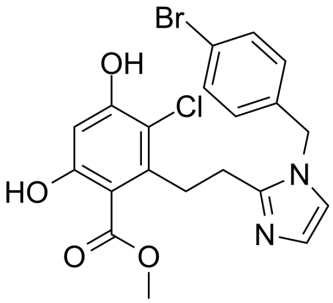
4-Br-Bnlm

Cat. No.:	HY-121845
CAS No.:	1654775-71-9
Molecular Formula:	$C_{20}H_{18}BrClN_2O_4$
Molecular Weight:	465.72
Target:	Others
Pathway:	Others
Storage:	4°C, sealed storage, away from moisture and light * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 33.33 mg/mL (71.57 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1472 mL	10.7361 mL	21.4721 mL
	5 mM	0.4294 mL	2.1472 mL	4.2944 mL
	10 mM	0.2147 mL	1.0736 mL	2.1472 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 (5.37 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.37 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

4-Br-Bnlm is a selective inhibitor of glucose-regulated protein 94 (Grp94) with an EC_{50} value of 0.96 μM. 4-Br-Bnlm reduces the levels of mutant myocilin proteins as well as wild-type myocilin misfold in cells. 4-Br-Bnlm promotes the clearance of toxic formsof myocilin and reduces myocilin toxicity[1][2].

IC_{50} & Target

EC50: 0.96 μM (glucose-regulated protein 94, Grp94)[1][2]

In Vitro

4-Br-Bnlm (0-100 μM; 24 h) inhibits 1477N mutant myocilin in human embryonic kidney (HEK) cells expression[1].
4-Br-Bnlm (30 μM; 24 h) reduces mutant myocilin levels and toxicity in primary human trabecular meshwork (HTM) cells[1].
4-Br-Bnlm (3, 10 and 30 μM; 24 h) inhibits myocilin secretion with dose-dependent manner in myocilin cell[1].
4-Br-Bnlm (30 μM and 100 μM; 24 h) doesn't induces a heat shock response in the HTM cells[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	Primary human HTM cells.
Concentration:	30 μM.
Incubation Time:	24 h.
Result:	Significantly reduced the level of Y437H mutant myocilin without affecting WT myocilin and the RFP vector in HEK cells.

Western Blot Analysis[1]

Cell Line:	HEK cells.
Concentration:	0, 1, 3, 10, 30 and 100 μM.
Incubation Time:	24 h.
Result:	Significantly decreased 1477N mutant myocilin in HEK cells expression without causing the degradation of other Hsp90-dependent clients Akt and Ras.

In Vivo

4-Br-Bnlm (300 μM; eye drops; once daily for 12 weeks) clears the mutant myocilin within trabecular meshwork (TM) cells and decreases intraocular pressure (IOP) in Tg-MYOC^{Y437H} mice model. 4-Br-Bnlm improves photopic negative response (PhNR) deficits[2].

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

Animal Model:	Tg-MYOC^{Y437H} mice[2].
Dosage:	300 μM.
Administration:	Eye drops; once daily for 12 weeks.
Result:	Inhibited mutant myocilin expression and restored the PhNR deficits.

REFERENCES

[1]. Stothert AR, et al, Fontaine SN, Crowley VM, Mishra S, Blagg BS, Lieberman RL, Dickey CA. Exploiting the interaction between Grp94 and aggregated myocilin to treat glaucoma. Hum Mol Genet. 2014 Dec 15;23(24):6470-80.

[2]. Stothert AR, et al. Isoform-selective Hsp90 inhibition rescues model of hereditary open-angle glaucoma. Sci Rep. 2017 Dec 20;7(1):17951.

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