Thalidomide-O-amido-C4-NH2 hydrochloride

Cat. No.: HY-107438A

CAS No.: 2245697-86-1

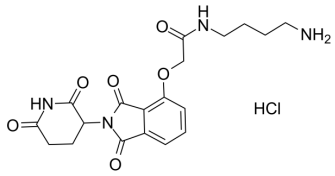
Molecular Formula: $C_{19}H_{23}ClN_4O_6$

Molecular Weight: 438.86

Target: E3 Ligase Ligand-Linker Conjugates

Pathway: PROTAC

Storage: -20°C, stored under nitrogen, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (569.66 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2786 mL	11.3932 mL	22.7863 mL
	5 mM	0.4557 mL	2.2786 mL	4.5573 mL
	10 mM	0.2279 mL	1.1393 mL	2.2786 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: ≥ 2.08 mg/mL (4.74 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.74 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.74 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Thalidomide-O-amido-C4-NH2 hydrochloride, a synthesized E3 ligase ligand-linker conjugate that incorporates the Thalidomide based cereblon ligand and a linker, can be used in the synthesis of PROTACs[1].

IC_{50} & Target

Cereblon

In Vitro

Thalidomide-O-amido-C4-NH2 is an amine intermediate (Compound 41), which can be used as is a heterobifunctional PROTAC BET degrader. The bromodomain and extra-terminal (BET) family proteins, consisting of BRD2, BRD3, BRD4, and testis-specific BRDT members, are epigenetic “readers” and play a key role in the regulation of gene transcription. BET

proteins are considered to be attractive therapeutic targets for cancer and other human diseases. Recently, heterobifunctional small-molecule BET degraders have been designed based upon the proteolysis targeting chimera (PROTAC) concept to induce BET protein degradation[1]. Thalidomide-O-amido-C4-NH2 is a degron-linker (refer to Compound DL6-TL). Degron-linker-targeting ligand, wherein the linker is covalently bound lo at least one degron and at least one targeting ligand, the degron is a compound capable of binding to an ubiquitin ligase such as an E3 ubiquitin ligase (e g, cereblon), and the targeting ligand is capable of binding to the targeted protein (s)[2].

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

REFERENCES

[1]. Zhou B, et al. Discovery of a Small-Molecule Degrader of Bromodomain and Extra-Terminal (BET) Proteins withPicomolar Cellular Potencies and Capable of Achieving Tumor Regression.J Med Chem. 2018 Jan 25;61(2):462-481.

[2]. James Bradner, et al. Methods to induce targeted protein degradation through bifunctional molecules. WO 2017024317 A2.

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