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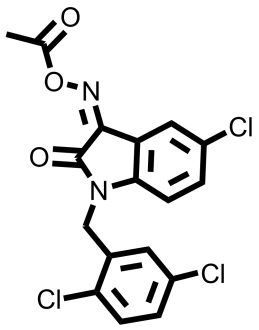
Ubiquitin C-terminal Hydrolase-L1 (UCH-L1) Inhibitor – LDN-57444

Chemical Name: (Z)-3-(acetoxyimino)-5-chloro-1-(2,5-dichlorobenzyl)indolin-2-one



Molecular Weight:	397.64
Formula:	$C_{17}H_{11}Cl_3N_2O_3$
Purity:	≥98%
CAS#:	668467-91-2
Solubility:	DMSO up to 25 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 months -20 °C 1 year

Biological Activity:

LDN-57444 is a novel potent and selective inhibitor of ubiquitin C-terminal hydrolase-L1 (UCH-L1) with IC_{50} ~0.88 μM. It has ~28-fold greater selectivity over UCH-L3 (ubiquitin C-terminal hydrolase L3). LDN-57444 can increase levels of highly ubiquitinated proteins and decreases ubiquitin proteasome activity. It causes cell death through the apoptosis pathway. LDN-57444's activity leads to dramatic alterations in synaptic protein distribution and spine morphology in vivo.

How to Use:

In vitro: LDN-57444 was used at 5-25 μM final concentration in various in vitro assays.

In vivo: LDN-57444 was administered through IP injection at 0.5 mg/kg in a-syn transgenic mice

Reference:

1. Gong B, et al. Ubiquitin hydrolase Uch-L1 rescues beta-amyloid-induced decreases in synaptic function and contextual memory. (2006) Cell. 126(4):775-88.
2. Liu Y, et al. Discovery of inhibitors that elucidate the role of UCH-L1 activity in the H1299 lung cancer cell line. (2003) Chem Biol. 10(9):837-46.
3. Tan YY, et al. Endoplasmic reticulum stress contributes to the cell death induced by UCH-L1 inhibitor. (2008) Mol Cell Biochem. 318(1-2):109-15.
4. Cartier AE, et al. Regulation of synaptic structure by ubiquitin C-terminal hydrolase L1. (2009) J Neurosci. 29(24):7857-68.