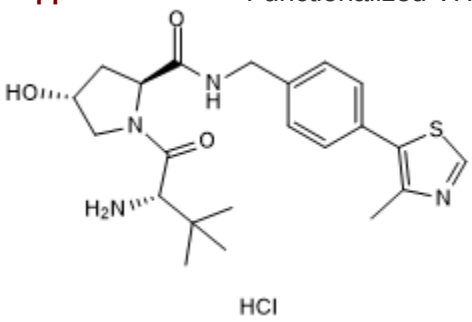
VH 032, amine hydrochloride

Cat. # PC-1007

Background: Small molecule-induced protein degradation is an attractive strategy for the development of chemical probes. Protein degraders have the power to abrogate all of the functions of a drug target at once, including scaffolding functions which are difficult to target with small molecule inhibitors. A novel class of PROTACs that incorporate small molecule VHL ligands to successfully degrade HaloTag7 fusion proteins is developed. HaloPROTACs will inspire the development of future PROTACs with more drug-like properties. In HEK 293 cells stably expressing GFP-HaloTag7, 24 hour treatment with HaloPROTAC1 leads to less than 20% degradation, the longer HaloPROTAC2 leads to nearly 70% degradation of GFP-Halotag7 at 2.5 µM. HaloPROTACs containing protein degrader 1 leads to nearly 70% degradation of GFP-HaloTag7, when sufficiently long linkers are used. Derivative of the von Hippel-Lindau (VHL) ligand, VH 032, commonly used as a precursor to PROTACs that hijack VHL as the E3 ubiquitin ligase component. Supplied with a primary amine functional handle at a position known not to significantly affect binding to VHL, for ready conjugation to a linker/target protein ligand.

Application: Functionalized VHL ligand for PROTACs



Product Information

Purity:	>98%
MW:	467.02
Formula:	$C_{22}H_{31}ClN_4O_3S$
CAS No.	1448189-80-7
Physical State:	Lyophilized white powder
Quantity:	5 mg; 10 mg; 25 mg
Solubility:	40 mg/mL in DMSO
Storage:	Store desiccated as supplied at -20°C for up to 3 years. Store solutions at -80°C for up to 6 months or -20°C for up to 1 month.

References

1. **Buckley DL** et al. HaloPROTACS: Use of Small Molecule PROTACs to Induce Degradation of HaloTag Fusion Proteins. ACS Chem Biol. 2015 Aug 21;10(8):1831-7.
2. **Zengerle** *et al* (2015) Selective small molecule induced degradation of the BET bromodomain protein BRD4. ACS Chem.Biol. ***10*** 1770 PMID: 26035625
3. **Galdeano** *et al* (2014) Structure-guided design and optimization of small molecules targeting the protein-protein interaction between the von Hippel-Lindau (VHL) E3 ubiquitin ligase and the hypoxia inducible factor (HIF) alpha subunit with *in vitro* nanomolar affinities. J.Med.Chem. ***57*** 8657