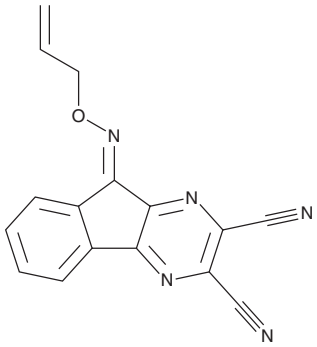
PRODUCT INFORMATION

DUB-IN-3

Item No. 41594

CAS Registry No.:	924296-17-3
Formal Name:	9-[(2-propen-1-yloxy)imino]-9H-indeno[1,2-b]pyrazine-2,3-dicarbonitrile
Synonyms:	Deubiquitinase-IN-3, Deubiquitinase Inhibitor 3, DUBs-IN-3, DUBs Inhibitor 3, HBX 90397
MF:	C16H9N5O
FW:	287.3
Purity:	≥98%
Supplied as:	A solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

DUB-IN-3 is supplied as a solid. A stock solution may be made by dissolving the DUB-IN-3 in the solvent of choice, which should be purged with an inert gas. DUB-IN-3 is soluble (≥10 mg/ml) in DMSO.

Description

DUB-IN-3 is an inhibitor of ubiquitin-specific protease 8 (USP8; IC_{50} = 0.56 µM).[1] It is selective for USP8 over USP7 (IC_{50} = >100 µM). DUB-IN-3 is also an inhibitor of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) papain-like protease (PL^{pro}) when Z-LRGG-AMC is used as a substrate (IC_{50} = 12.5 µM) but not when the larger substrate Ub-AMC is used (IC_{50} = >10 µM).[2] It reduces glutathione (GSH) levels and cystine uptake, as well as increases ferrous iron and reactive oxygen species (ROS) levels, in HCCLM3 cells when used at concentrations of 0.2 or 0.5 µM.[3] It decreases the viability of HCCLM3 cells when used in combination with the ferroptosis inducer RSL3 (Item No. 19288), an effect that can be blocked by the ferroptosis inhibitor ferrostatin-1 (Item No. 17729). DUB-IN-3 (0.1 and 0.2 µM) reduces the proliferation, migration, and oncosphere formation ability of HCCLM3 and Hep3B hepatocellular carcinoma cells. It also reduces tumor growth and metastasis in HCCLM3 and Hep3B mouse models of metastatic lung cancer when administered at a dose of 5 mg/kg per day.

References

1. Colombo, M., Vallese, S., Peretto, I., *et al.* Synthesis and biological evaluation of 9-oxo-9H-indeno[1,2-b]pyrazine-2,3-dicarbonitrile analogues as potential inhibitors of deubiquitinating enzymes. *ChemMedChem* **5(4)**, 552-558 (2010).
2. Cho, C.-C., Li, S.G., Lalonde, T.J., *et al.* Drug repurposing for the SARS-CoV-2 papain-like protease. *ChemMedChem* **17(1)**, e202100455 (2022).
3. Tang, J., Long, G., Ku, K.-H., *et al.* Targeting USP8 inhibits O-GlcNAcylation of SLC7A11 to promote ferroptosis of hepatocellular carcinoma via stabilization of OGT. *Adv. Sci. (Weinh)* **10(33)**, e2302953 (2023).

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