

Product Data Sheet

Product Name: CAY10603

Cat. No.: GC12971

Chemical Properties

Cas. No. 1045792-66-2

Chemical Name tert-butyl N-[4-[3-[[7-(hydroxyamino)-7-oxoheptyl]carbamoyl]-1,2-oxazol-5-yl]phenyl]carbamate

SMILES CC(C)(C)OC(=O)NC1=CC=C(C=C1)C2=CC(=NO2)C(=O)NCCCCCCC(=O)NO

Formula $C_{22}H_{30}N_4O_6$

M.Wt 446.5

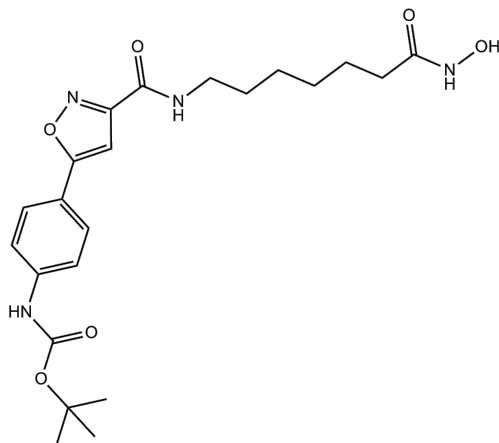
Solubility $\geq 22.35\text{mg/mL}$ in DMSO

Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1-4]:

Cell lines Pancreatic cancer cell lines, A549 and H460 cells, non-small cell lung cancer cells

Caution: Product has not been fully validated for medical applications. For research use only.

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Preparation method The solubility of this compound in DMSO is >22.4mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reacting condition 0.1 µM, 6 h

Applications CAY10603 showed potent antiproliferative activity against pancreatic cancer cell lines with IC₅₀ of <1 µM. CAY10603 was active against both the Mia Paca-2 and Panc04.03 cell lines at the 100 nM level and at the 200–300 nM level against HupT3. CAY10603 (0.1 µM, 6 h) blocked TNF-α-induced caspase-3 activation in endothelial cells. In HPAECs, pre-treated with CAY10603 (CAY, 0.1 µM) for 6 h inhibited TNF-α-induced endothelial permeability. CAY10603 (0.05 µM) significantly decreased the cell viability of NSCLC cells. In A549 and H460 cells, CAY10603 (0.01-0.16 µM) dose-dependently decreased total EGFR levels and the phosphorylation of EGFR, AKT, and ERK. In two human lung adenocarcinoma cell lines: A549 and HCC827, CAY10603 treatment dose-dependently (0.02-0.32 µM) decreased cell proliferation. CAY10603 decreased clone numbers of the lung adenocarcinoma cell lines. CAY10603 clearly induced apoptosis in the lung adenocarcinoma cell line A549. Combination of CAY10603 (0.01 µM) and gefitinib (1 µM) for 48h remarkably inhibited the clono-genic survival of the A549 cells.

Animal experiment [2]:

Animal models C57BL/6 mouse model of endotoxemia

Dosage form Intraperitoneal injection, 5 mg/kg, 2 h

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Application	In a C57BL/6 mouse model of endotoxemia, pre-treatment with CAY10603 significantly inhibited endotoxin-induced caspase-3 activation and attenuated endotoxin-induced lung edema formation in the lung tissues.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

- [1]. Kozikowski, A. P., Tapadar, S., Luchini, D. N., Kim, K. H., & Billadeau, D. D. (2008). Use of the nitrile oxide cycloaddition (NOC) reaction for molecular probe generation: a new class of enzyme selective histone deacetylase inhibitors (HDACIs) showing picomolar activity at HDAC6. *Journal of medicinal chemistry*, 51(15), 4370-4373.
- [2]. Yu, J., Ma, M., Ma, Z., & Fu, J. (2016). HDAC6 inhibition prevents TNF- α -induced caspase 3 activation in lung endothelial cell and maintains cell-cell junctions. *Oncotarget*, 7(34), 54714.
- [3]. Wang, Z., Hu, P., Tang, F., & Xie, C. (2016). HDAC6-mediated EGFR stabilization and activation restrict cell response to sorafenib in non-small cell lung cancer cells. *Medical Oncology*, 33(5), 50.
- [4]. Wang, Z., Tang, F., Hu, P., Wang, Y., Gong, J., Sun, S., & Xie, C. (2016). HDAC6 promotes cell proliferation and confers resistance to gefitinib in lung adenocarcinoma. *Oncology reports*, 36(1), 589-597.

Background

CAY10603 (BML-281) is a potent and selective HDAC6 inhibitor, with an IC₅₀ of 2 pM; CAY10603 (BML-281) also inhibits HDAC1, HDAC2, HDAC3, HDAC8, HDAC10, with IC₅₀s of 271, 252, 0.42, 6851, 90.7 nM.

CAY10603 (Compound 7) shows potent inhibitory activities against pancreatic cancer cell lines, with IC₅₀s of 1, 0.3, 0.1, 0.1, 0.6, <1, 0.5 μ M for BxPC-3, HupT3, Mia Paca-2, Panc 04.03, SU.86.86, HMEC, HPDE6c7, respectively. CAY10603 (100 nM, 200-300 nM) is active against both the Mia

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Paca-2 and Panc04.03 cell lines[1]. CAY10603 inhibits HDAC6 deacetylase activity, and suppresses the proliferation of lung adenocarcinoma cells. CAY10603 also induces apoptosis of lung adenocarcinoma cells. Furthermore, CAY10603 synergizes with gefitinib to induce apoptosis in lung adenocarcinoma cell lines, partly through the destabilization of EGFR and inactivation of the EGFR pathway[2].

[1]. Kozikowski AP, et al. Use of the nitrile oxide cycloaddition (NOC) reaction for molecular probe generation: a new class of enzyme selective histone deacetylase inhibitors (HDACIs) showing picomolar activity at HDAC6. J Med Chem. 2008 Aug 14;51(15):4370-3.

[2]. Wang Z, et al. HDAC6 promotes cell proliferation and confers resistance to gefitinib in lung adenocarcinoma. Oncol Rep. 2016 Jul;36(1):589-97.

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