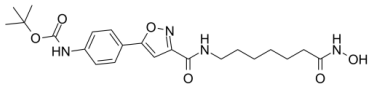
Data Sheet

Product Name:	CAY10603
Cat. No.:	CS-3491
CAS No.:	1045792-66-2
Molecular Formula:	C22H30N4O6
Molecular Weight:	446.50
Target:	HDAC
Pathway:	Cell Cycle/DNA Damage; Epigenetics
Solubility:	DMSO : ≥ 50 mg/mL (111.98 mM)



BIOLOGICAL ACTIVITY:

CAY10603 (BML-281) is a potent and selective **HDAC6** inhibitor, with an **IC_{50}** of 2 pM; CAY10603 (BML-281) also inhibits HDAC1, HDAC2, HDAC3, HDAC8, HDAC10, with **IC_{50}**s of 271, 252, 0.42, 6851, 90.7 nM. IC50 & Target: IC50: 2 pM (HDAC6), 0.42 nM (HDAC3), 90.7 nM (HDAC10), 252 nM (HDAC2), 271 nM (HDAC1), 6851 nM (HDAC8)[1] **In Vitro:** CAY10603 (Compound 7) shows potent inhibitory activities against pancreatic cancer cell lines, with IC_{50}s of 1, 0.3, 0.1, 0.1, 0.6, <1, 0.5 μM 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 Paca-2 and Panc04.03 cell lines[1]. CAY10603 inhibits HDAC6 deacetylase activity, and supresses 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].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [1]Purified HDACs are incubated with 1 mm carboxyfluorescein (FAM)-labeled acetylated peptide substrate and test compound for 17 h at 25°C in HDAC assay buffer containing 100 mm HEPES (pH 7.5), 25 mm KCl, 0.1% BSA, and 0.01% Triton X-100. Reactions are terminated by the addition of buffer containing 0.078% SDS for a final SDS concentration of 0.05%. Substrate and product are separated electrophoretically using a Caliper LabChip 3000 system with blue laser excitation and green fluorescence detection (CCD2). The fluorescence intensity in the substrate and product peaks is determined using the Well Analyzer software on the Caliper system. The reactions are performed in duplicate for each sample. IC_{50} values are automatically calculated using the IDBS XLFit version 4.2.1 plug-in for Microsoft Excel and the XLFit 4-Parameter Logistic Model (sigmoidal dose-response model): ((A+((B_A)/1+((C/x)D)))), in which x is compound concentration, A and B are respectively the estimated minimum and maximum of percent inhibition, C is the inflection point, and D is the Hill slope of the sigmoidal curve. **Cell Assay:** CAY10603 is dissolved in DMSO.[1]The pancreatic cancer cell lines BxPc-3, HupT3, Mia Paca-2, Panc 04.03, and SU 86.86 are obtained from ATCC and are grown in medium (DMEM or RPMI) containing 10% fetal calf serum and l-glutamine. Pancreatic cancer cells are plated out in duplicate into 6 wells of a 96-well microtiter plate at 2.5-4P103 cells per well. Four hours post plating, individual wells are treated with diluent (DMSO) or varying concentrations of SAHA or the indicated HDACIs from a concentration of 1 nm to 50 mm. Cytotoxicity is measured at time “0”, and 72 h post treatment using the colorimetric MTT assay. The IC_{50} values are calculated using XLfit.

References:

[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.

CAIndexNames:

Carbamic acid, N-[4-[3-[[[7-(hydroxyamino)-7-oxoheptyl]amino]carbonyl]-5-isoxazolyl]phenyl]-, 1,1-dimethylethyl ester

SMILES:

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

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