产品名称：
3-Hydroxy-5,6,7,8-tetrahydro-10-oxa-8-aza-benzo[a]azulen-9-one
产品别名：**CID755673**

生物活性：

Description

CID755673 is a potent PKD inhibitor with IC_{50}s of 182 nM, 280 nM and 227 nM for PKD1, PKD2 and PKD3, respectively.

IC_{50} & Target

PKD1	PKD3	PKD2
182 nM (IC_{50})	227 nM (IC_{50})	280 nM (IC_{50})

In Vitro

CID755673 blocks phorbol ester-induced endogenous PKD1 activation in LNCaP cells in a concentration-dependent manner. CID755673 inhibits the known biological actions of PKD1 including phorbol ester-induced class IIa histone deacetylase 5 nuclear exclusion, vesicular stomatitis virus glycoprotein transport from the Golgi to the plasma membrane, and the ilimaquinone-induced Golgi fragmentation. CID755673 inhibits prostate cancer cell proliferation, cell migration, and invasion[1].

In Vivo

Acute administration of the PKD inhibitor CID755673 to normal mice reduces both PKD1 and 2 phosphorylation in a time and dose-dependent manner. Chronic CID755673 administration to T2D db/db mice for two weeks reduces expression of the gene expression signature of PKD activation, enhances indices of both diastolic and systolic left ventricular function and is associated with reduced heart weight[2].

Solvent&Solubility

In Vitro:

DMSO : 100 mg/mL (**460.36 mM**; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	4.6036 mL	23.0181 mL	46.0363 mL
5 mM	0.9207 mL	4.6036 mL	9.2073 mL
10 mM	0.4604 mL	2.3018 mL	4.6036 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (11.51 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (11.51 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)

Solubility: ≥ 2.5 mg/mL (11.51 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (11.51 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (11.51 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (11.51 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Sharlow ER, et al. Potent and selective disruption of protein kinase D functionality by a benzoxoloazepinolone. J Biol Chem. 2008 Nov 28;283(48):33516-26. [2]. Venardos K, et al. The PKD inhibitor CID755673 enhances cardiac function in diabetic db/db mice. PLoS One. 2015 Mar 23;10(3):e0120934.

实验参考：

Cell Assay	The wound-induced migration is triggered by scraping the cells with a plastic pipette tip, and the wound is imaged immediately. The DU145 cells are then are treated with or without CID755673 at different concentrations. The wound is imaged immediately (0 h) and at different intervals with an inverted phase-contrast microscope with a ×10 objective. At the end of the assay, cells are fixed with methanol and stained with crystal violet for a final image[1].
Animal Administration	Mice: For acute inhibitor studies, C57BL6 mice are administered a single dose of vehicle (5% DMSO in PBS, pH 7.4), or the selective PKD inhibitor CID755673 at 1 or 10mg/kg body weight. Mice are killed one or four hr later and heart collected for later analysis. For chronic inhibitor experiments, 8-week old db/db mice receives vehicle or CID755673 at 1 or 10mg/kg bodyweight for 16 days, by daily intraperitoneal (i.p.) injection[2].
Kinase Assay	The radiometric kinase assay is carried out by coincubating 0.5 μCi of [γ-^{32}P]ATP, 20 μM ATP, 50 ng of purified recombinant human PKD (PKD1, PKD2, and PKD3) or CAMKIIα proteins, and 2.5 μg of Syntide-2 in 50 μL of kinase buffer that contains 50 mM Tris-HCl, pH 7.5, 4 mM $MgCl_2$, 10 mM β-mercaptoethanol. The reaction is carried out under conditions that the initial rate is within the linear kinetic range [1].
References	[1]. Sharlow ER, et al. Potent and selective disruption of protein kinase D functionality by a benzoxoloazepinolone. J Biol Chem. 2008 Nov 28;283(48):33516-26. [2]. Venardos K, et al. The PKD inhibitor CID755673 enhances cardiac function in diabetic db/db mice. PLoS One. 2015 Mar 23;10(3):e0120934.