产品名称：3-[[4-[6-溴-2-[4-(4-甲基哌嗪-1-基)苯基]-3H-咪唑并[4,5-b]吡啶-7-基]哌嗪-1-基]甲基]-5-甲基异恶唑
产品别名：CCT 137690

生物活性：

Description	CCT 137690 is a potent and orally available aurora kinase inhibitor with IC_{50}s of 15, 25, and 19 nM for aurora A, B and C, respectively.		
IC_{50} & Target	Aurora A	Aurora B	Aurora C
	15 nM (IC_{50})	25 nM (IC_{50})	19 nM (IC_{50})
In Vitro	CCT 137690 displays antiproliferative activity in a range of human tumor cell lines, including SW620 colon carcinoma (GI50=0.30 μM) and A2780 ovarian cancer cell line (GI50=0.14 μM). CCT 137690 inhibits in vitro phosphorylation of histone H3. CCT 137690 is a moderate inhibitor of the hERG ion-channel (IC50=3.0 μM)[1]. CCT137690 efficiently inhibits histone H3 and TACC3 phosphorylation (Aurora B and Aurora A substrates, respectively) in HCT116 and HeLa cells. Continuous exposure of tumour cells to the inhibitor causes multipolar spindle formation, chromosome misalignment, polyploidy and apoptosis[2].		
In Vivo	CCT 137690 slows the growth of the SW620 xenografts with no observed toxicity[1]. CCT 137690 significantly inhibits tumour growth in a transgenic mouse model of neuroblastoma (TH-MYCN) that overexpresses MYCN protein and is predisposed to spontaneous neuroblastoma formation[2].		

Solvent&Solubility

In Vitro:

DMSO : 16.67 mg/mL (**30.23 mM**; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8133 mL	9.0665 mL	18.1330 mL
	5 mM	0.3627 mL	1.8133 mL	3.6266 mL
	10 mM	0.1813 mL	0.9067 mL	1.8133 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: ≥ 1.67 mg/mL (3.03 mM); Clear solution

此方案可获得 ≥ 1.67 mg/mL (3.03 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 16.699999 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: ≥ 1.67 mg/mL (3.03 mM); Clear solution

	此方案可获得 ≥ 1.67 mg/mL (3.03 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 16.699999 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: ≥ 1.67 mg/mL (3.03 mM); Clear solution 此方案可获得 ≥ 1.67 mg/mL (3.03 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 16.699999 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Bavetsias V, et al. Imidazo[4,5-b]pyridine derivatives as inhibitors of Aurora kinases: lead optimization studies toward the identification of an orally bioavailable preclinical development candidate. J Med Chem. 2010 Jul 22;53(14):5213-28. [2]. Faisal A, et al. The aurora kinase inhibitor CCT137690 downregulates MYCN and sensitizes MYCN-amplified neuroblastoma in vivo. Mol Cancer Ther. 2011 Nov;10(11):2115-23.

实验参考：

Cell Assay	Cells are plated in 96-well plates at 3,000 cells per well and are treated with a range of 0 to 25 mol/L of CCT137690 for 72 h. Cell proliferation assays are performed by colorimetric 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT)[2].
Animal Administration	Mice: Animals are randomized into two groups, group 1: treatment with 100 mg/kg CCT137690 n=4 or group 2: vehicle control n=4. Treatment is administered via oral gavage twice daily. Tumour volumes are measured at day 0, 3 (48 hours after treatment started), 7 and 10 using 1H MRI[2].
References	[1]. Bavetsias V, et al. Imidazo[4,5-b]pyridine derivatives as inhibitors of Aurora kinases: lead optimization studies toward the identification of an orally bioavailable preclinical development candidate. J Med Chem. 2010 Jul 22;53(14):5213-28. [2]. Faisal A, et al. The aurora kinase inhibitor CCT137690 downregulates MYCN and sensitizes MYCN-amplified neuroblastoma in vivo. Mol Cancer Ther. 2011 Nov;10(11):2115-23.