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产品名称：(S)-6-[(3,5-二甲基-1H-吡唑-4-基)甲基]-5-[(4-羟基异唑烷-2-基)羰基]-1-异丁基-3-甲基噻吩并[2,3-D]嘧啶-2,4(1H,3H)-二酮
产品别名：AR-C155858

生物活性：

Description	AR-C155858 is a selective monocarboxylate transporter MCT1 and MCT2 inhibitor with K_is of 2.3 nM and 10 nM, respectively.
IC_{50} & Target	Ki: 2.3 nM (MCT1), 10 nM (MCT2)
In Vitro	AR-C155858 (10 nM-100 nM) inhibits MCT1/MCT2 C-terminal chimaeras[1]. AR-C155858 inhibits MCT2, and the 70% inhibition seen at 10 nM is followed by a gradually increasing inhibition which can only be explained by a Ki value of significantly less than 10 nM. AR-C155858 inhibits MCT1 expressed in Xenopus oocytes in a time- and concentration-dependent manner[2].

Solvent&Solubility

In Vitro:

DMSO : ≥ 50 mg/mL (108.34 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1667 mL	10.8335 mL	21.6671 mL
	5 mM	0.4333 mL	2.1667 mL	4.3334 mL
	10 mM	0.2167 mL	1.0834 mL	2.1667 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: ≥ 2.75 mg/mL (5.96 mM); Clear solution

此方案可获得 ≥ 2.75 mg/mL (5.96 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 27.5 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: ≥ 2.75 mg/mL (5.96 mM); Clear solution

此方案可获得 ≥ 2.75 mg/mL (5.96 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 27.5 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。

References	[1]. Ovens MJ, et al. The inhibition of monocarboxylate transporter 2 (MCT2) by AR-C155858 is modulated by the associated ancillary protein. Biochem J. 2010 Oct 15;431(2):217-25. [2]. Ovens MJ, et al. AR-C155858 is a potent inhibitor of monocarboxylate transporters MCT1 and MCT2 that binds to an intracellular site involving transmembrane helices 7-10. Biochem J. 2010 Jan 15;425(3):523-30. [3]. Vijay N, et al. A Novel Monocarboxylate Transporter Inhibitor as a Potential Treatment Strategy for γ-Hydroxybutyric Acid Overdose. Pharm Res. 2015 Jun;32(6):1894-906.
实验参考：	
Cell Assay	The erythrocytes (5% haematocrit) are pre-incubated for 1 h at room temperature (22°C) with or without AR-C155858 at the required concentration before assaying transport of l-lactate (10 mM) at 6°C. Initial rates of transport are calculated by first-order regression analysis of the time course of pH change and converted into nmol of H^+/min by determining the pH change induced by small additions of standardized NaOH. [1]
Kinase Assay	MCT kinetic assays are performed by monitoring intracellular pH with H^+-sensitive dye BCECF or by determining the uptake of l-[^{14}C]lactate (7.4 MBq/mL). The uptake buffer contains 75 mM NaCl, 2 mM KCl, 0.82 mM $MgCl_2$, 1 mM $CaCl_2$ and 20 mM Tris/Hepes (pH 7.4). AR-C155858 inhibitor titrations are performed at pH 6 with oocytes preincubated for 45 min in a different uptake buffer (75 mM NaCl, 2 mM KCl, 0.82 mM $MgCl_2$, 1 mM $CaCl_2$ and 20 mM Mes, pH 6) containing the required concentration of AR-C155858 prior to measuring the uptake of l-[^{14}C]lactate (0.5 mM). Unless stated otherwise, uptake is determined over 2.5 min for all MCT constructs except for MCT2trn with or without embigin and MCT2/1 with or without embigin, where 5 and 10 min are used respectively. [1]
References	[1]. Ovens MJ, et al. The inhibition of monocarboxylate transporter 2 (MCT2) by AR-C155858 is modulated by the associated ancillary protein. Biochem J. 2010 Oct 15;431(2):217-25. [2]. Ovens MJ, et al. AR-C155858 is a potent inhibitor of monocarboxylate transporters MCT1 and MCT2 that binds to an intracellular site involving transmembrane helices 7-10. Biochem J. 2010 Jan 15;425(3):523-30. [3]. Vijay N, et al. A Novel Monocarboxylate Transporter Inhibitor as a Potential Treatment Strategy for γ-Hydroxybutyric Acid Overdose. Pharm Res. 2015 Jun;32(6):1894-906.