产品名称：8-氯-4-甲基-5H-二苯并[B,E][1,4]二氮哌嗪
产品别名：氯氮平 N-氧化；Clozapine (N-oxide)

生物活性：

Description	Clozapine (N-oxide) is a pharmacologically inert metabolite of Clozapine, an antipsychotic drug. Clozapine (N-oxide) is a agonist for the DREADD (Designer Receptors Exclusively Activated by Designer Drug) system[1][2]. Clozapine is a potent antagonist of dopamine. Clozapine is also a potent and selective agonist at the muscarinic M4 receptor (EC50=11 nM)[3][4].
In Vivo	fter a single intraperitoneal (i.p.) injection of Clozapine N-oxide (1 mg/kg) into mice, Clozapine N-oxide (CNO) plasma levels peak at 15 min and are very low after 2 h. Acutely administered CNO can be metabolically converted to Clozapine in other species such as human and guinea-pig. The metabolites that may form after chronic administration of CNO to DREADD-expressing mice (or other species) have not been studied systematically. However, even if back-transformation to Clozapine occurs after chronic CNO administration, it should be noted that Clozapine is a more potent (by ~10-fold) DREADD agonist than CNO itself. Moreover, confounding biological effects of potential CNO metabolites can be easily identified by including both saline- and CNO-treated WT animals in a particular DREADD study. Despite the short plasma half-life of CNO in mice, the biological effects that have been described after acute treatment of DREADD-expressing experimental animals are usually much longer (6-10 h). One possibility is that CNO tends to accumulate in tissues, although other scenarios are also feasible[1]. Using a general pharmacokinetic model for the interconversion process, the mean total clearances of Clozapine and Clozapine N-oxide (CNO) are 28.45 L/hr and 45.30 L/hr, respectively[2].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 100 mg/mL (291.70 mM)** **Methanol : ≥ 28.6 mg/mL (83.43 mM)** **H_2O : 1 mg/mL (2.92 mM;** Need ultrasonic) * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.9170 mL	14.5849 mL	29.1698 mL
5 mM	0.5834 mL	2.9170 mL	5.8340 mL
10 mM	0.2917 mL	1.4585 mL	2.9170 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 (7.29 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (7.29 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 (7.29 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.29 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。
References	[1]. Wess J, et al. Novel designer receptors to probe GPCR signaling and physiology. Trends Pharmacol Sci. 2013 Jul;34(7):385-92. [2]. Chang WH, et al. Reversible metabolism of clozapine and clozapine N-oxide in schizophrenic patients. Prog Neuropsychopharmacol Biol Psychiatry. 1998 Jul;22(5):723-39. [3]. Silva RR, et al. Evaluation of Functional Selectivity of Haloperidol, Clozapine, and LASSBio-579, an Experimental Compound With Antipsychotic-Like Actions in Rodents, at G Protein and Arrestin Signaling Downstream of the Dopamine D2 Receptor. Front Pharmacol. 2019 Jun 4;10:628. [4]. Zorn SH, et al. Clozapine is a potent and selective muscarinic M4 receptor agonist. Eur J Pharmacol. 1994 Nov 15;269(3):R1-2.