

Product Data Sheet

Product Name: CPCCOEt

Cat. No.: GC18134

Chemical Properties

Cas. No. 179067-99-3

Chemical Name (1a*S*,7a*S*,*Z*)-ethyl 7-(hydroxyimino)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate

SMILES O=C([C@]1([C@H]/2C1)OC3=CC=CC=C3C2=N/O)OCC

Formula C₁₃H₁₃NO₄

M.Wt 247.25

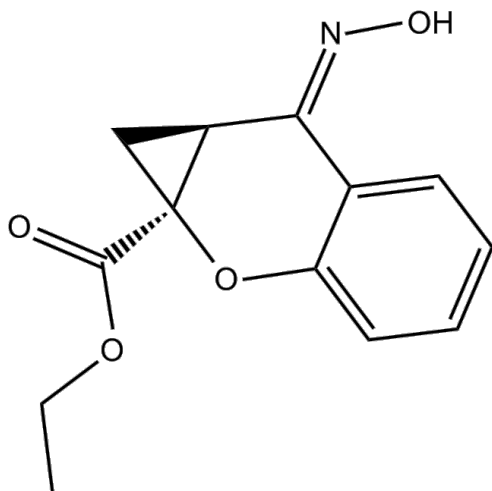
Solubility DMSO: 100 mM

Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Caution: Product has not been fully validated for medical applications. For research use only.

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Cell experiment [1]:

Cell lines	CHO cells expressing the human metabotropic glutamate receptor mGlu1a (CHO-Lac-mGlu1 α)
Preparation Method	CHO cells were seeded into 24-well multidishes in the presence of 1 μ Ci/ml myo-[^{3} H]inositol 48 hours before agonist/antagonist manipulation. During the last 20 hours of culture, 100 μ M isopropyl- β -D-thiogalactoside (IPTG) was added to the culture medium to induce mGlu1a receptor expression. The cell monolayers were washed with Krebs-Henseleit buffer. All experiments were performed in the presence of 3U/ml glutamic-pyruvic transaminase and 3mM pyruvate to prevent receptor activation by endogenous glutamate. CPCCOEt (3 μ M–300 μ M) was added 30 minutes before, and LiCl (10mM) 15 minutes before the addition of the agonist L-quisqualate (10 μ M). Stimulation with the agonist lasted for 30 minutes.
Reaction Conditions	3 μ M–300 μ M; 30min
Applications	CPCCOEt antagonized L-quisqualate-induced phosphoinositide hydrolysis in a non-competitive and reversible manner. CPCCOEt significantly inhibited L-quisqualate-stimulated [^{3} H]InsP accumulation, with complete inhibition of mGlu1a receptor-mediated signalling observed in the presence of 300 μ M CPCCOEt.

Animal experiment [2]:

Animal models	Male Long Evans hooded rats with chronic constriction injury (CCI) of the sciatic nerve or hind paw injection of complete Freund's adjuvant (CFA)
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Preparation Method Rats were implanted with a chronic indwelling intrathecal (i.t.) catheter. For behavioral testing, rats were placed in an observation chamber for a 30-40 minute habituation period. Rats were then lightly anesthetized with isofluorane for an intrathecal injection of CPCCOEt or vehicle, and returned to the chamber. Post-injection measurements began 20 minutes after injection. Sustained nociceptive behaviors were recorded following a subcutaneous (s.c.) injection of 1.0% formalin (for CCI rats) or 0.03% capsaicin (for CFA rats) into the ipsilateral plantar hind paw.

Dosage form 500nmoles; i.t.; single injection

Applications CPCCOEt significantly reduced formalin-induced nociception in CCI rats and capsaicin-induced nociception in CFA rats. CPCCOEt significantly attenuated the formalin-induced increases in spinal glutamate concentrations in CCI rats and the capsaicin-induced increases in spinal glutamate concentrations in CFA rats.

References:

- [1] Hermans E, Nahorski SR, Challiss RA. Reversible and non-competitive antagonist profile of CPCCOEt at the human type 1alpha metabotropic glutamate receptor. *Neuropharmacology*. 1998 Dec;37(12):1645-7.
- [2] Kumar N, Laferriere A, Yu JS, et al. Metabotropic glutamate receptors (mGluRs) regulate noxious stimulus-induced glutamate release in the spinal cord dorsal horn of rats with neuropathic and inflammatory pain. *J Neurochem*. 2010 Jul;114(1):281-90.

Background

CPCCOEt is a non-competitive metabotropic glutamate receptor 1 (mGluR1) antagonist. CPCCOEt inhibits receptor signaling by binding to the transmembrane domain of mGluR1, disrupting the intramolecular interaction between the agonist-bound extracellular domain and the transmembrane domain. CPCCOEt can be used in neuroscience and oncology-related research^[1-4].

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In vitro, Hs683, A172, and U87 glioma cell lines were treated with CPCCOEt (100-350 μ M) for five days. CPCCOEt significantly reduced the viability of these cells in a concentration-dependent manner^[5]. CHO cells expressing the human mGlu1a receptor were pretreated with CPCCOEt (3 μ M–300 μ M) for 30 minutes, followed by stimulation with L-quisqualate (10 μ M) for 30 minutes. CPCCOEt significantly inhibited L-quisqualate-induced phosphoinositide hydrolysis and reduced mGlu1a receptor-mediated signaling^[6].

In vivo, CPCCOEt (500nmol; single treatment) was administered via intrathecal injection to chronic constriction injury rats 20 minutes before formalin stimulation. CPCCOEt significantly reduced formalin-induced nociception in CCI rats, as well as the associated increases in spinal glutamate concentrations^[7]. In male C57BL/6J mice (10-24 weeks old), CPCCOEt (10 and 30mg/kg; single treatment) was administered via intraperitoneal injection 10 minutes before ethanol (4.0g/kg) administration. CPCCOEt did not significantly alter ethanol-induced sedation and hypnotic effects^[8].

References:

- [1] Litschig S, Gasparini F, Rueegg D, et al. CPCCOEt, a noncompetitive metabotropic glutamate receptor 1 antagonist, inhibits receptor signaling without affecting glutamate binding. *Mol Pharmacol*. 1999 Mar;55(3):453-61.
- [2] Bräuner-Osborne H, Jensen AA, Krosgaard-Larsen P. Interaction of CPCCOEt with a chimeric mGlu1b and calcium sensing receptor. *Neuroreport*. 1999 Dec 16;10(18):3923-5.
- [3] Fukunaga I, Yeo CH, Batchelor AM. The mGlu1 antagonist CPCCOEt enhances the climbing fibre response in Purkinje neurones independently of glutamate receptors. *Neuropharmacology*. 2007 Feb;52(2):450-8.
- [4] Haas HS, Pfragner R, Siegl V, et al. The non-competitive metabotropic glutamate receptor-1 antagonist CPCCOEt inhibits the in vitro growth of human melanoma. *Oncol Rep*. 2007 Jun;17(6):1399-404.
- [5] Dalley CB, Wroblewska B, Wolfe BB, et al. The Role of Metabotropic Glutamate Receptor 1 Dependent Signaling in Glioma Viability. *J Pharmacol Exp Ther*. 2018 Oct;367(1):59-70.
- [6] Hermans E, Nahorski SR, Challiss RA. Reversible and non-competitive antagonist profile of CPCCOEt at the human type 1alpha metabotropic glutamate receptor. *Neuropharmacology*. 1998 Dec;37(12):1645-7.
- [7] Kumar N, Laferriere A, Yu JS, et al. Metabotropic glutamate receptors (mGluRs) regulate noxious stimulus-induced glutamate release in the spinal cord dorsal horn of rats with neuropathic and

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inflammatory pain. J Neurochem. 2010 Jul;114(1):281-90.

[8] Sharko AC, Hodge CW. Differential modulation of ethanol-induced sedation and hypnosis by metabotropic glutamate receptor antagonists in C57BL/6J mice. Alcohol Clin Exp Res. 2008 Jan;32(1):67-76.

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