Product Data Sheet

Product Name: (2R,4R)-APDC
Cat. No.: GC11379

Chemical Properties

Cas. No.	169209-63-6		
Chemical Name	(2R,4R)-4-aminopyrrolidine-2,4-dicarboxylic acid		
SMILES	OC([C@]1(C[C@H](C(O)=O)NC1)N)=O		
Formula	$C_6H_{10}N_2O_4$	M.Wt	174.16
Solubility	Soluble to 100 mM in Water	Storage	Desiccate at RT
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	(2R,4R)-APDC		

Protocol

Kinase experiment [1]:

Binding assays	Radioligand binding to NMDA, AMPA, kainate, and metabotropic glutamate receptors was performed utilizing [3H]CGS19755, [3H]AMPA, [3H]kainate, and [3H]glutamate as the radioligands, respectively. Measure the cyclic adenosine monophosphate (cAMP) and tritiated inositol monophosphates ([3H]IP) levels in rat cerebral cortical slices.

Cell experiment [2]:

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Cell lines	Human mGluR2 expressing CHO cell
Preparation method	The solubility of this compound is up to 100 mM in sterile water. General tips for obtaining a higher concentration: Please warm the tube at 37℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.
Reacting condition	(2R,4R)-APDC were added and incubated for 20 min at 37°C.
Applications	2R,4R-APDC inhibited forskolin-stimulated CAMP formation in human mGluR2 expressing cells with greater potency than lS,3R-ACPD, but unlike lS,3R-ACPD, (2R,4R)-APDC showed no obvious activation of phosphoinostide hydrolysis in human mGluR.lcc expressing cells..

Animal experiment [1]:

Animal models	Female Wistar rats were anesthetized with pentobarbitone Na, and a lumbar laminectomy was performed to allow insertion of a seven-barrel glass microelectrode into the gray matter of the spinal cord. Action potential firing rate of single neurons was recorded continuously in response to timed intermittent ejection of AMPA (10 mM in 200 mM NaCl, pH 7.4) from one barrel of the electrode.

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Dosage form	When consistent submaximal responses were established, (2R,4R)-APDC at 25 mM in 175 mM NaCl, pH 7.4 were ejected on different cells.
Application	(2R,4R)-APDC caused a robust enhancement of AMPA responses on AMPA evoked responses in intact rat spinal cord neurons.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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References:

[1] Monn JA, et al. Synthesis of the four isomers of 4-aminopyrrolidine-2,4-dicarboxylate: identification of a potent, highly selective, and systemically-active agonist for metabotropic glutamate receptors negatively coupled to adenylate cyclase. J Med Chem. 1996 Jul 19;39(15):2990-3000.

[2] Schoepp DD, et al. Selective inhibition of forskolin-stimulated cyclic AMP formation in rat hippocampus by a novel mGluR agonist, 2R,4R-4-aminopyrrolidine-2,4- dicarboxylate. Neuropharmacology. 1995 Aug;34(8):843-50.

Background

EC50: 0.4 μM

2R,4R-APDC is a highly selective and relatively potent group II metabotropic glutamate receptor agonist for human mGlu2. L-Glutamate (Glu) is EAA neurotransmitter in the mammalian CNS. Its effects are mediated by a variety of presynaptic and postsynaptic neuronal receptors.

In vitro: 2R,4R-APDC blocked forskolin-stimulated cAMP with none of the other activities of lS,3R-ACPD. forskolin-stimulated cAMP formation in human mGluR2 expressing cells with about three-fold greater potency than lS,3R-ACPD were also inhibited by 2R,4R-APDC, which, unlike lS,3R-ACPD, exhibited no appreciable activation of phosphoinostide hydrolysis in human mGluR. Thus, 2R,4R-APDC should be a useful pharmacological tool to explore the functions of mGluRs coupled to inhibition of adenylate cyclase [1]. The

effects of four isomers of APDC were investigated at glutamate receptors in vitro. (2R,4R)-APDC, an aza analog of the nonselective mGluR agonist (1S,3R)-ACPD possessed relatively high affinity for metabotropic glutamate receptors (mGluRs) with no effects on radioligand binding to NMDA, AMPA, or kainate receptors up to 100 íM. None of the other APDC isomers exhibited significant mGluR binding affinity, indicating that this interaction is highly stereospecific [2].

In vivo: Both (1S,3R)-ACPD and (2R,4R)-APDC were effectively attenuating forskolin-stimulated cAMP formation in the adult rat cerebral cortex; however, while (1S,3R)-ACPD was also effectively stimulating basal tritiated inositol monophosphate production of the neonatal rat cerebral cortex, (2R,4R)-APDC was not effectively stimulating phosphoinositide hydrolysis in this tissue preparation. An augmentation of AMPA-induced excitation was produced by microelectrophoretic application of either (1S,3R)-ACPD or (2R,4R)-APDC to intact rat spinal neurons [2].

Clinical trial: Clinical study has been conducted.

References:
[1] Schoepp DD, Johnson BG, Salhoff CR, Valli MJ, Desai MA, Burnett JP, Mayne NG, Monn JA. Selective inhibition of forskolin-stimulated cyclic AMP formation in rat hippocampus by a novel mGluR agonist, 2R,4R-4-aminopyrrolidine-2,4- dicarboxylate. Neuropharmacology. 1995 Aug;34(8):843-50.
[2] Monn JA, Valli MJ, Johnson BG, Salhoff CR, Wright RA, Howe T, Bond A, Lodge D, Spangle LA, Paschal JW, Campbell JB, Griffey K, Tizzano JP, Schoepp DD. Synthesis of the four isomers of 4-aminopyrrolidine-2,4-dicarboxylate: identification of a potent, highly selective, and systemically-active agonist for metabotropic glutamate receptors negatively coupled to adenylate cyclase. J Med Chem. 1996 Jul 19; 39 (15):2990-3000.

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