

Product Data Sheet

Product Name: CAY10441

Cat. No.: GC18318

Chemical Properties

Cas. No. 221529-58-4

Chemical Name 4,5-dihydro-N-[4-[[4-(1-methylethoxy)phenyl]methyl]phenyl]-1H-imadazol-2-amine

SMILES CC(C)Oc1ccc(cc1)Cc1ccc(cc1)NC1=NCCN1

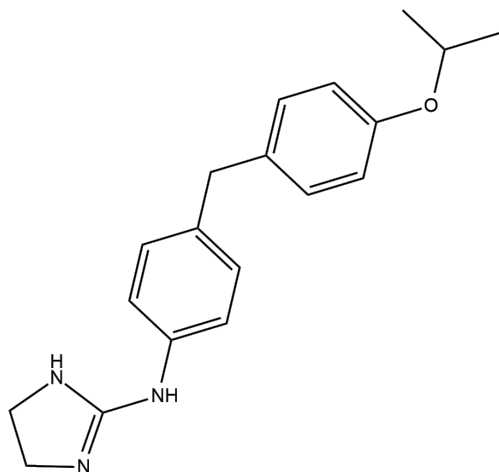
Formula $C_{19}H_{23}N_3O$ M.Wt 309.4

Solubility DMF: 30 mg/ml, DMF:PBS (pH 7.2) (1:10): .05 mg/ml, DMSO: 20 mg/ml, Ethanol: 20 mg/ml 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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- Kinase experiment:** Selectivity is determined by the ability of CAY10441 (10 μ M) to displace specific binding of standard radioligands at 51 receptors. When significant displacement of radioligand is observed (>70% for CAY10441), complete concentration-dependent displacement curves (in triplicate) are constructed to generate IC₅₀ values. Displacement binding at the EP3 receptor is performed. Enzyme inhibition assays are also conducted. CAY10441 is evaluated at 10 μ M in triplicate for inhibition of COX isoforms: COX-1 (ram seminal vesicle), COX-2 (sheep placenta and human umbilical vein). Arachidonic acid is used as a substrate and PGE2 accumulation is detected[1].
- Cell experiment:** BEAS-2B cells are incubated for 30 min at 37°C in supplement-free keratinocyte serum-free medium (KSFM) in the absence and presence of 100 nM CAY10441. Cells are washed with supplement-free KSFM, incubated in the same medium for defined periods, and exposed to 1 μ M Taprostene. Four hours later, cells are harvested in reporter lysis buffer, and luciferase activity is measured. The viability HAECs and BEAS-2B cells is determined colorimetrically by measuring the reduction of the tetrazolium salt MTT to formazan, by mitochondrial dehydrogenases[2].
- Animal experiment:** Rats[1]Male Sprague-Dawley rats (n=3) are administered CAY10441 (5 mg/kg, i.v.). At various times after dose administration, the rats are anesthetized by halothane (5%), blood is collected by orbital bleed into a heparinized syringe and a plasma fraction is obtained by centrifugation of the blood at 2600 $\times$ g for 5 min in a clinical centrifuge. The level of CAY10441 in each sample is determined by high-performance liquid chromatography with detection by mass spectrometry[1].

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- [1]. Bley KR, et al. CAY10441 and RO3244794: characterization of structurally distinct, potent and selective IP (prostacyclin) receptor antagonists. Br J Pharmacol. 2006 Feb;147(3):335-45.
- [2]. Ayer LM, et al. 4,5-Dihydro-1H-imidazol-2-yl)-[4-(4-isopropoxy-benzyl)-phenyl]-amine (CAY10441) is a selective, pseudo-irreversible orthosteric antagonist at the prostacyclin (IP)-receptor expressed by human airway epithelial cells: IP-receptor-mediated inhibition of CXCL9 and CXCL10 release. J Pharmacol Exp Ther. 2008 Feb;324(2):815-26.

Background

CAY10441 (RO1138452) is a potent and selective IP (prostacyclin) receptor antagonist. CAY10441 displays high affinity for IP receptors. In human platelets, pKi is 9.3 ± 0.1 ; in a recombinant IP receptor system, pKi is 8.7 ± 0.06 .

CAY10441 is IP receptor antagonist. The pIC₅₀ values of CAY10441 in attenuating cAMP accumulation is 7.0 ± 0.07 . Functional antagonism of CAY10441 is studied by measuring inhibition of carbaprostacyclin-induced cAMP accumulation in CHO-K1 cells stably expressing the human IP receptor. The antagonist affinity (pKi) of CAY10441 is 9.0 ± 0.06 . Selectivity profiles for CAY10441 are determined via a panel of receptor binding and enzyme assays. CAY10441 displays affinity at imidazoline₂ (I₂) (8.3) and platelet activating factor (PAF) (7.9) receptors[1]. CAY10441 (10 pM-10 μ M) added to cells concurrently with a fixed concentration of Taprostene (1 μ M) prevents, in a concentration-dependent manner, the inhibition of CXCL9 and CXCL10 release, with p[A]₅₀ (molar) values of -8.73 ± 0.11 and -8.47 ± 0.16 ($p > 0.05$), respectively[2].

CAY10441 is a potent and selective antagonist for both human and rat IP receptors and that is possesses analgesic and anti-inflammatory potential. CAY10441 (1-10 mg/kg, i.v.) significantly reduces acetic acid-induced abdominal constrictions. CAY10441 (3-100 mg/kg, p.o.) significantly reduces carrageenan-induced mechanical hyperalgesia and edema formation. One hour after administration of CAY10441 (5 mg/kg, i.v.) to rats, the total plasma concentration is 0.189 μ g/mL, whereas the free plasma concentrations is calculated to be 0.009 μ g/mL (28 nM)[1].

References:

- [1]. Bley KR, et al. RO1138452 and RO3244794: characterization of structurally distinct, potent and selective IP (prostacyclin) receptor antagonists. Br J Pharmacol. 2006 Feb;147(3):335-45.
- [2]. Ayer LM, et al. 4,5-Dihydro-1H-imidazol-2-yl)-[4-(4-isopropoxy-benzyl)-phenyl]-amine

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