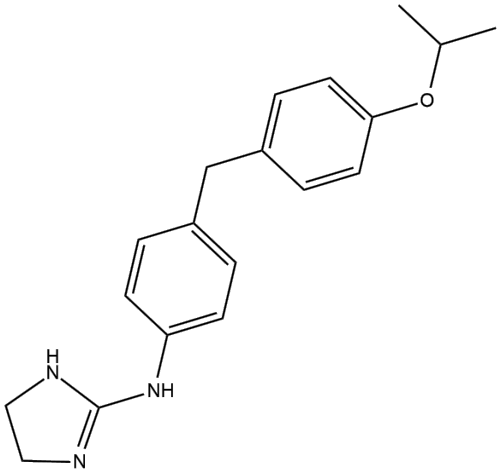
Product Data Sheet

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

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Kinase experiment: Selectivity is determined by the ability of CAY10441 (10μM) 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 μM 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 μM 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× 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].

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

[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 μM) added to cells concurrently with a fixed concentration of Taprostene (1 μM) 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 μg/mL, whereas the free plasma concentrations is calculated to be 0.009 μg/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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