

Product Data Sheet

Product Name: Chroman 1

Cat. No.: GC16097

Chemical Properties

Cas. No. 1273579-40-0

Chemical Name (3S)-N-[2-[2-(dimethylamino)ethoxy]-4-(1H-pyrazol-4-yl)phenyl]-6-methoxy-3,4-dihydro-2H-chromene-3-carboxamide

SMILES CN(C)CCOC1=C(C=CC(=C1)C2=CN=C2)NC(=O)C3CC4=C(C=CC(=C4)OC)OC3

Formula $C_{24}H_{28}N_4O_4$

M.Wt 436.5

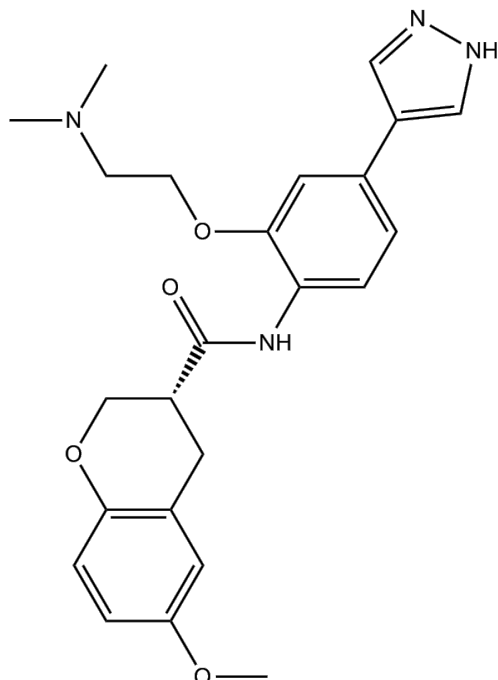
Solubility DMSO: ≥ 40 mg/mL

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.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

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**Kinase
experiment:**

Assays are performed using the HTRF KinEASE STK S2 kit. A 5 μ L mixture of 1 μ M STK2 substrate and 20 μ M ATP in STK-buffer is added to the wells. Inhibitor (including Chroman 1, 20 nL) at various concentrations is then dispensed. Reaction is started by addition of 0.5 nM ROCK-II in STK-buffer (5 μ L). After 4 h at room temperature (rt), the reaction is stopped by addition of 10 μ L mixture of 1 $\times$ STK antibody-Cryptate in detection buffer and 62.5 nM Sa-XL in detection buffer. After 1 h at rt, the plates are read on the Viewlux in HTRF mode[1].

References:

[1]. Yen Ting Chen, et al. Asymmetric synthesis of potent chroman-based Rho kinase (ROCK-II) inhibitors. Med.Chem.Commun., 2011, 2, 73-75.

Background

Chroman 1 is a highly potent ROCK-II inhibitor. ROCK is a member of the AGC kinase family of serine/threonine kinases that is comprised of two highly homologous isoforms, which are ROCK-I and ROCK-II.. As one of the downstream effectors of RhoA, ROCK regulates stress fiber formation and actin cytoskeletal organization via phosphorylation of myosin light chain. Currently, there is plenty of interest in the inhibition of Rho kinase (ROCK) to treat various diseases.

In vitro: Chroman 1 was found to be a sub-nanomolar ROCK-II inhibitor with excellent to moderate selectivity over related kinases studied as a preliminary assessment, such as AKT1, protein kinase A (PKA), and the highly homologous Cdc42-binding kinase. In addition, Chroman 1 also showed good in-vitro activity in the functional cell-based myosin light chain bis-phosphorylation assay [1].

In vivo: Pharmacokinetic evaluation in rats showed that Chroman 1 had moderately improved oral bioavailability (27–35%) relative to its lead compounds, which were benzodioxane and chroman. In addition, Chroman 1 also displayed an unique intriguing pharmacokinetic profile, which was with high systemic exposure through oral delivery [1].

Clinical trial: So far, there is no clinical study reported.

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[1] Chen YT, Bannister TD, Weiser A, Griffin E, Lin L, Ruiz C, Cameron MD, Schürer S, Duckett D, Schrter T, LoGrasso P, Feng Y. Chroman-3-amides as potent Rho kinase inhibitors. Bioorg Med Chem Lett. 2008 Dec 15;18(24):6406-9.

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