

Product Data Sheet

Product Name: TC-G-1008

Cat. No.: GC19349

Chemical Properties

Cas. No. 1621175-65-2

SMILES CS(=O)(NC1=CC=C(CNC2=NC(NC)=NC(C3=NC=CC=C3)=C2)C(Cl)=C1)=O

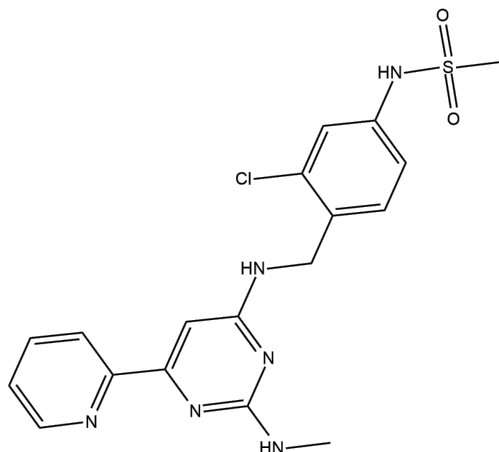
Formula $C_{18}H_{19}ClN_6O_2S$ M.Wt 418.9

Solubility DMSO : ≥ 100 mg/mL (238.72 mM) Storage Store at $-20^{\circ}C$

General tips For obtaining a higher solubility , please warm the tube at $37^{\circ}C$ and shake it in the ultrasonic bath for a while. Stock solution can be stored below $-20^{\circ}C$ 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: HEK293-GPR39 cells are plated and cultured in poly-d-lysine-coated, white, 384-well plates (4000 cells/well) in the growth medium overnight at 37°C in the presence of 5% CO₂. For pretreatment of the cells with GPR39 ligands (TC-G-1008) or vehicle control (DMSO), the culture medium is removed and the cells are stimulated with GPR39 ligands in assay buffer for the indicated time at 37°C. Then, the compound solution is removed and washed twice with PBS containing 0.1% BSA. For measurement of intracellular cAMP, the cells are stimulated with drugs in stimulation buffer for 30 min at 37°C. The intracellular cAMP level is determined by using HTRF cAMP dynamic 2 kit[2].

Animal experiment: Mice: Mice are given single oral doses of 10, 30, and 100 mg/kg of TC-G-1008[1].

References:

- [1]. Peukert S, et al. Discovery of 2-Pyridylpyrimidines as the First Orally Bioavailable GPR39 Agonists. ACS Med Chem Lett. 2014 Aug 4;5(10):1114-8.
[2]. Shimizu Y, et al. Rho kinase-dependent desensitization of GPR39; a unique mechanism of GPCR downregulation. Biochem Pharmacol. 2017 Sep 15;140:105-114.

Background

TC-G-1008 (GPR39-C3) is a potent and orally available GPR39 agonist with EC₅₀ values of 0.4 and 0.8 nM for rat and human receptors respectively.

TC-G-1008 shows selectivity over a panel of kinases (IC₅₀s > 10 μM) and does not exhibit relevant binding affinity for the related ghrelin and neurotensin-1 receptors (IC₅₀s > 30 μM)[1]. In HEK293-GPR39 cells, GPR39-C3, which is a positive allosteric modulator, activates cAMP production (downstream of G_s), IP₁ accumulation (downstream of G_q), SRF-RE-dependent transcription (downstream of G_{12/13}), and β-arrestin recruitment. GPR39-C3 induces dose- and time-dependent loss of response in cAMP production by second challenge of the compound[2].

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Rat and mouse plasma protein binding for TC-G-1008 is measured as 99.3% and 99.1%, respectively. TC-G-1008 is orally bioavailable in mice and robustly induces acute GLP-1 levels. Upon single oral doses of 10, 30, and 100 mg/kg of aqueous suspensions in 0.5% methylcellulose/0.1% Tween 80, TC-G-1008 achieves, between 1 and 1.5 h, maximal exposures of 1.4, 6.1, and 25.3 μ M, respectively[1].

References:

- [1]. Peukert S, et al. Discovery of 2-Pyridylpyrimidines as the First Orally Bioavailable GPR39 Agonists. ACS Med Chem Lett. 2014 Aug 4;5(10):1114-8.
- [2]. Shimizu Y, et al. Rho kinase-dependent desensitization of GPR39; a unique mechanism of GPCR downregulation. Biochem Pharmacol. 2017 Sep 15;140:105-114.

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