

Product Data Sheet

Product Name: CCG215022

Cat. No.: GC19090

Chemical Properties

Cas. No. 1813527-81-9

SMILES CC(N1)=C(C(NC2=CC=C(NN=C3)C3=C2)=O)C(C4=CC(C(NCC5=CC=CC=N5)=O)=C(F)C=C4)NC1=O

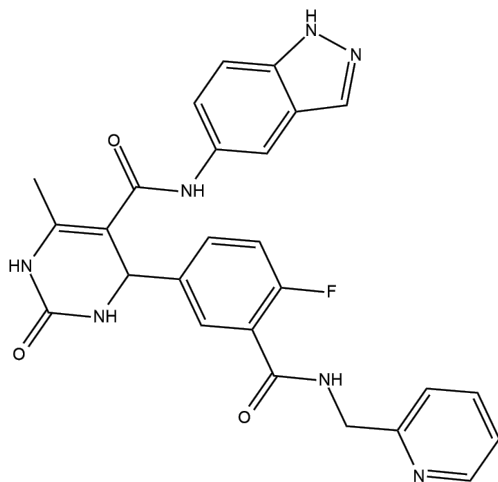
Formula $C_{26}H_{22}FN_7O_3$ M.Wt 499.5

Solubility DMSO : ≥ 28 mg/mL (56.06 mM) 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:**

GRK5 and urea-washed bovine rod outer segments (ROS) are mixed in the dark in buffer containing 20 mM HEPES, pH 7.5, 4 mM MgCl₂, and 2 mM EDTA and incubated for 35 min at room temperature. The reaction mixtures are exposed to ambient fluorescent light for 1 min prior to initiation of the reaction by addition of ATP (with [γ -³²P]ATP) to a final concentration of 1 mM. Final concentration of GRK5 is 100 nM and ROS is between 0.75 and 24 μ M. Reactions are initiated at room temperature, and samples are taken at 2-5 min and then quenched with SDS-PAGE loading dye. Proteins are separated using SDS-PAGE, gel is dried, and the incorporation of γ -³²P is detected using a phosphor storage screen. Rates at 0 min are plotted against the ROS concentration, and V_{max} and K_m values are determined using the Michaelis-Menten equation. V_{max} of each curve is normalized to the V_{max} of GRK5561 run in parallel. Melting point determinations in response to 200 μ M CCG215022 are performed in 20 mM HEPES, pH 7.0, 5 mM MgCl₂, 2 mM DTT, 1 mM CHAPS at a final GRK5 concentration of 0.2 mg/mL and 100 μ M anilinonaphthalene-8-sulfonic acid using a ThermoFluor plate reader. Melting points of GRK5 variants are assayed in a buffer containing 20 mM HEPES, pH 8.0, 200 mM NaCl, 2 mM DTT, 2.5 mM MgCl₂, and 0.1 mM anilinonaphthalene-8-sulfonic acid with or without 5 mM ATP. Final GRK5 concentration for these assays is 0.1 mg/mL[1].

References:

[1]. Homan KT, et al. Crystal Structure of G Protein-coupled Receptor Kinase 5 in Complex with a Rationally Designed Inhibitor. J Biol Chem. 2015 Aug 21;290(34):20649-59.

Background

CCG215022 is a G protein-coupled receptor kinases (GRKs) inhibitor with IC₅₀s of 0.15 $\pm$ 0.07 μ M, 0.38 $\pm$ 0.06 μ M and 3.9 $\pm$ 1 μ M for GRK2, GRK5 and GRK1, respectively.

CCG215022 has nanomolar potency against both GRK2 and GRK5 and is at least 20-fold more potent than Paroxetine. In the course of a GRK2 structure-based drug design campaign, CCG215022 exhibits nanomolar IC₅₀ values against both GRK2 and GRK5 and good selectivity against other

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closely related kinases such as GRK1 and PKA. Treatment of murine cardiomyocytes with CCG215022 results in significantly increases contractility at 20-fold lower concentrations than Paroxetine, an inhibitor with more modest selectivity for GRK2[1].

References:

[1]. Homan KT, et al. Crystal Structure of G Protein-coupled Receptor Kinase 5 in Complex with a Rationally Designed Inhibitor. J Biol Chem. 2015 Aug 21;290(34):20649-59.

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