

Product Data Sheet

Product Name: GW843682X

Cat. No.: GC11621

Chemical Properties

Cas. No. 660868-91-7

Chemical Name 5-(5,6-dimethoxybenzimidazol-1-yl)-3-[[2-(trifluoromethyl)phenyl]methoxy]thiophene-2-carboxamide

SMILES COC1=C(C=C2C(=C1)N=CN2C3=CC(=C(S3)C(=O)N)OCC4=CC=CC=C4C(F)(F)F)OC

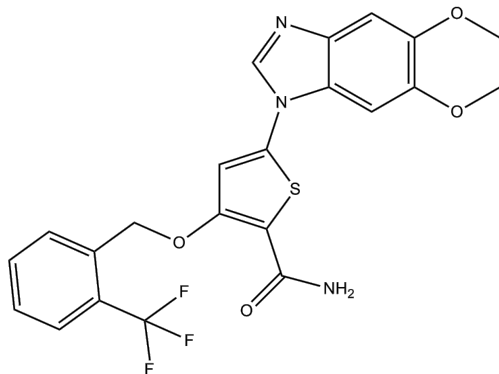
Formula $C_{22}H_{18}F_3N_3O_4S$ M.Wt 477.46

Solubility DMSO: 40 mg/ml, Ethanol: 4 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:**

PLK1 and PLK3 proteins are prepared from baculovirus-infected *Trichoplusia ni* cells. Enzyme activity for PLK1 and PLK3 is determined as follows. All measurements are obtained under conditions where signal production increased linearly with time and enzyme. Test compounds are added to white 384-well assay plates (0.1 μ L for 10 μ L and some 20 μ L assays, 1 μ L for some 20 μ L assays) at variable known concentrations in 100% DMSO. DMSO (1-5% final) and EDTA (65 mM) are used as controls. Reaction Mix contains the following components at 22°C: 25 mM HEPES (pH 7.2); 15 mM MgCl₂; 1 μ M ATP; 0.05 μ Ci/well [γ -33P]ATP (10 Ci/mmol); 1 μ M substrate peptide (Biotin-Ahx-SFNDTLDFD); 0.15 mg/mL bovine serum albumin; 1 mM DTT; and 2 nM PLK1 kinase domain or 5 nM full-length PLK3. Reaction Mix (10 or 20 μ L) is quickly added to each well immediately following addition of enzyme via automated liquid handlers and incubated for 1 to 1.5 h at 22°C. The 20 μ L enzymatic reactions are stopped with 50 μ L of stop mix [50 mM EDTA, 4.0 mg/mL streptavidin SPA beads in Dulbecco's PBS (without Mg²⁺ and Ca²⁺), 50 μ M ATP] per well. The 10 μ L reactions are stopped with 10 μ L of stop mix [50 mM EDTA, 3.0 mg/mL streptavidin-coupled SPA Imaging Beads in Dulbecco's PBS (without Mg²⁺ and Ca²⁺), 50 μ M ATP] per well. Plates are sealed, spun at 500 $\times$ g for 1 min or settled overnight, and counted in Packard TopCount for 30 s/well or imaged with a Viewlux imager. Signal above background (EDTA controls) is converted to percent inhibition relative to that obtained in control (DMSO-only) wells[1].

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Cell experiment: Assays are carried out and data analyzed. In these assays, H460 cells are plated at a density of 2,000 per well, HDF cells are plated at 5,000 per well, and the drug-resistant cell line MES-SA/DX5 and its sensitive parent line MES-SA are plated at 7,000 and 6,000 per well, respectively, in a 96-well plate. These densities allowed vehicle controls to grow logarithmically during the course of the 3-day assay. All cells are exposed to 3-fold dilutions of the compound (30-0.00152 μM) in low-glucose DMEM containing 5% FBS, 50 $\mu\text{g/mL}$ gentamicin, and 0.3% (v/v) DMSO (HDF cells); RPMI 1640 containing 5% FBS, 50 $\mu\text{g/mL}$ gentamicin, and 0.3% (v/v) DMSO (H460); or McCoy's 5A containing 5% FBS, 50 $\mu\text{g/mL}$ gentamicin, and 0.3% (v/v) DMSO (MES-SA and MES-SA/DX5)[1].

References:

- [1]. Lansing TJ, et al. In vitro biological activity of a novel small-molecule inhibitor of polo-like kinase 1. Mol Cancer Ther. 2007 Feb;6(2):450-9. Epub 2007 Jan 31.
- [2]. Didier C, et al. Evaluation of Polo-like Kinase 1 inhibition on the G2/M checkpoint in Acute Myelocytic Leukaemia. Eur J Pharmacol. 2008 Sep 4;591(1-3):102-5.
- [3]. Ikezoe T, et al. A novel treatment strategy targeting polo-like kinase 1 in hematological malignancies. Leukemia. 2009 Sep;23(9):1564-76.

Background

GW843682X is a selective, ATP-competitive inhibitor of PLK1 and PLK3, with IC₅₀s of 2.2 nM and 9.1 nM, respectively, and is also >100-fold selective against ~30 other kinases. GW843682X (compound 1) is effective on inhibition of growth of tumor cells, with IC₅₀s of 0.41, 0.57, 0.11, 0.38, and 0.70 μM for A549, BT474, HeLa, H460 and HCT116 cell lines. GW843682X dose-dependently inhibits PLK1 phosphorylation of Ser15-p53, with an IC₅₀ of 0.14 μM . GW843682X (3 μM) causes a strong G2-M arrest in HDF cells and H460 cells after treatment for 24, 48, and 72 h. GW843682X (5 μM) leads to apoptosis in H460 cells instead of HDF cells[1]. GW843682X inhibits proliferation of U937 cells with an EC₅₀ of 120 nM. GW843682X (500 nM) in combination with 5 μM VP-16 suppresses 50% of entry into mitosis in U937 cells[2]. GW843682X (0.06-1 μM) has inhibitory activities against proliferation of acute leukemia cells, and potentiates the anti-proliferative activity of vincristine. Moreover, GW843682X (0.1-1 μM) induces apoptosis of leukemia cells in a dose- and

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time-dependent manner. GW843682X (0.5-1 μ M) dephosphorylates Bcl-xl in leukemia cells[3].

Reference :

- [1]. Lansing TJ, et al. In vitro biological activity of a novel small-molecule inhibitor of polo-like kinase 1. Mol Cancer Ther. 2007 Feb;6(2):450-9. Epub 2007 Jan 31.
- [2]. Didier C, et al. Evaluation of Polo-like Kinase 1 inhibition on the G2/M checkpoint in Acute Myelocytic Leukaemia. Eur J Pharmacol. 2008 Sep 4;591(1-3):102-5.
- [3]. Ikezoe T, et al. A novel treatment strategy targeting polo-like kinase 1 in hematological malignancies. Leukemia. 2009 Sep;23(9):1564-76.

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