

Product Data Sheet

Product Name: WZ4003

Cat. No.: GC16549

Chemical Properties

Cas. No. 1214265-58-3

Chemical Name N-[3-[5-chloro-2-[2-methoxy-4-(4-methylpiperazin-1-yl)anilino]pyrimidin-4-yl]oxyphenyl]propanamide

SMILES CCC(=O)NC1=CC(=CC=C1)OC2=NC(=NC=C2Cl)NC3=C(C=C(C=C3)N4CCN(CC4)C)OC

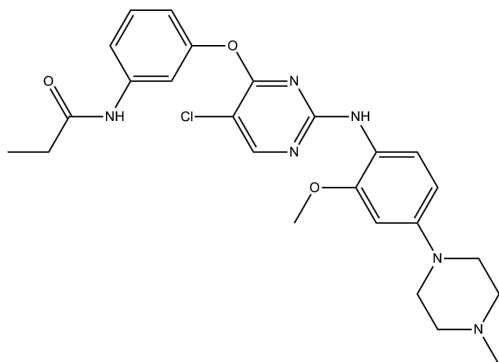
Formula $C_{25}H_{29}ClN_6O_3$ M.Wt 496.99

Solubility $\geq 7.85\text{mg/mL}$ in DMSO with gentle warming 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

Kinase experiment [1]:

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

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Kinase assays

In vitro activities of purified GST–NUAK1 were measured using Cerenkov counting of incorporation of radioactive ^{32}P from $[\gamma\text{-}^{32}\text{P}]\text{ATP}$ into Sakamototide substrate peptide. Reactions were carried out in a 50 μl reaction volume for 30 min at 30°C and reactions were terminated by spotting 40 μl of the reaction mix on to P81 paper and immediately immersing in 50 mM orthophosphoric acid. Samples were washed three times in 50 mM orthophosphoric acid followed by a single acetone rinse and air drying. The kinase-mediated incorporation of $[\gamma\text{-}^{32}\text{P}]\text{ATP}$ into Sakamototide was quantified by Cerenkov counting.

Cell experiment [2]:

Cell lines U2OS cell lines

Preparation method The solubility of this compound in DMSO is $>7.85\text{mg/mL}$. General tips for obtaining a higher concentration: Please warm the tube at 37°C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reacting condition 10 μM for 16h

Applications WZ4003 impaired the invasive potential of U2OS cells in a 3D cell invasion assay to the same extent as NUAK1 knockdown, which indicates that WZ4003 will serve as useful chemical probes to delineate the biological roles of the NUAK kinases.

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References:

[1] Banerjee S, Buhrlage SJ, Huang HT, et al. Characterization of WZ4003 and HTH-01-015 as selective inhibitors of the LKB1-tumour-suppressor-activated NIAK kinases. *Biochem J*, 2014, 457(1): 215-225.

Background

WZ4003 is a potent and selective inhibitor of NIAK1 and NIAK2 with IC₅₀ values of 20 and 100 nM, respectively [1].

NIAK family SNF1-like kinase-1 (NIAK1) and the related NIAK2 belong to the AMP-activated protein kinase (AMPK) family and are activated by liver kinase B1 (LKB1) tumour suppressor protein kinase [1].

WZ4003 is a potent and selective NIAK1/2 inhibitor. In HEK-293 cells, WZ4003 inhibited the phosphorylation of myosin phosphate-targeting subunit 1 (MYPT1), which was phosphorylated by NIAK1 at Ser445. In HEK-293 cells overexpressing inhibitor-resistant NIAK1[A195T], WZ4003 didn't inhibit the phosphorylation of MYPT1 at Ser445. In mouse embryonic fibroblasts (MEFs), WZ4003 significantly inhibited migration in a wound-healing assay and inhibited MEFs proliferation. In a cell invasion assay, WZ4003 inhibited the invasive potential of U2OS cells [1]. In U2OS cells, WZ4003 (10 µM) inhibited phosphorylation of MYPT1 and reduced the cells in S-phase by 50%. Also, WZ4003 prevented cells from entering into mitosis [2].

References:

[1]. Banerjee S, Buhrlage SJ, Huang HT, et al. Characterization of WZ4003 and HTH-01-015 as selective inhibitors of the LKB1-tumour-suppressor-activated NIAK kinases. *Biochem J*, 2014, 457(1): 215-225.

[2]. Banerjee S, Zagórska A, Deak M, et al. Interplay between Polo kinase, LKB1-activated NIAK1 kinase, PP1βMYPT1 phosphatase complex and the SCFβTrCP E3 ubiquitin ligase. *Biochem J*, 2014, 461(2): 233-245.

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