

Product Data Sheet

Product Name: 1-NM-PP1

Cat. No.: GC11696

Chemical Properties

Cas. No. 221244-14-0

Chemical Name 1-tert-butyl-3-(naphthalen-1-ylmethyl)pyrazolo[3,4-d]pyrimidin-4-amine

SMILES CC(C)(C)N1C2=C(C(=N1)CC3=CC=CC4=CC=CC=C43)C(=NC=N2)N

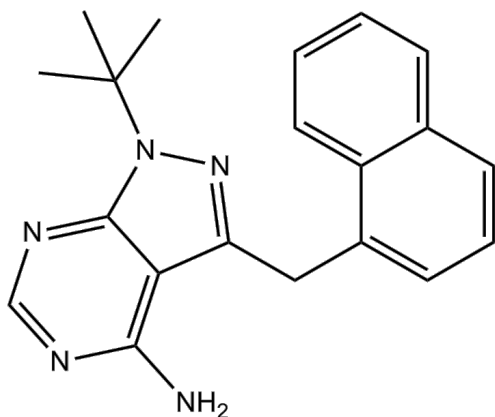
Formula C₂₀H₂₁N₅ M.Wt 331.41

Solubility ≥ 16.55mg/mL in DMSO, ≥ 9.22 mg/mL in EtOH with ultrasonic and 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

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

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Kinase experiment [1]:

In vitro kinase assays

We carried out in vitro kinase assays (except for Cdc28) in the presence of 0.2 $\mu\text{Ci}/\mu\text{l}$ [γ -32P]ATP at low ATP concentration (10 nM) so that IC₅₀ values represent a rough measure of the inhibition constant (K_i). Measurement of inhibitor IC₅₀ values were done as Liu, Y. et al. described. Purified Cdc28–His6 (1 nM) and MBP–Clb2 (3 nM) were incubated for 10 min at 23°C in a 25 μl reaction mixture containing 5 μg histone H1, 1 μCi of [γ -32P]ATP (1 μCi per 10 μM and 1 μCi per 1 mM), and varying concentrations of 1-NM-PP1 in kinase buffer (25mM HEPES-NaOH pH 7.4, 10mM NaCl, 10mM MgCl₂ and 1mM dithiothreitol). Reaction products were analysed by 15% SDS–PAGE followed by autoradiography. For the determination of Cdc28 kinetic constants, varying concentrations of [γ -32P]ATP (1 μCi per 100 μM) were incubated and analysed as above.

Cell experiment [2]:

Cell lines

PDK1^{+/+} ES cells

Preparation method

This compound is soluble in DMSO. 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 24h-72h; or 20 μM for 48h

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Applications

1-NM-PP1 suppressed the phosphorylation of PDK1 targets in PDK1^{+/+} ES cells expressing PDK1 L159G but not WT PDK1. Moreover, 1-NM-PP1 inhibited sorbitol-induced MSK1 S212 T-loop phosphorylation, ERK/p38MAPK phosphorylation sites S581 and ERK/p38 dependent autophosphorylation at S376. 1-NM-PP1 also inhibited IGF1-stimulated PKB/Akt T308 phosphorylation and S6K activity in PDK1^{+/+} +LG ES cells.

References:

1. Bishop, A. C., Ubersax, J. A., Petsch, D. T., Matheos, D. P., Gray, N. S., Blethrow, J., Shimizu, E., Tsien, J. Z., Schultz, P. G., Rose, M. D., Wood, J. L., Morgan, D. O. and Shokat, K. M. (2000) A chemical switch for inhibitor-sensitive alleles of any protein kinase. *Nature*. 407, 395-401
2. Tamguney, T., Zhang, C., Fiedler, D., Shokat, K. and Stokoe, D. (2008) Analysis of 3-phosphoinositide-dependent kinase-1 signaling and function in ES cells. *Exp Cell Res*. 314, 2299-2312

Background

1-NM-PP1 is a C3-modified analog of cell-permeable PP1, acts as a potent and selective inhibitor of protein kinase families [1].

1-NM-PP1 has shown the selective inhibition of protein kinases that have been mutated with the IC₅₀ values of 28 μ M, 1.0 μ M, 3.4 μ M, 29 μ M, 24 μ M, 4.3 nM, 3.2 nM, 120 nM, 5 nM and 8 nM for v-Src, c-Fyn, c-Abl, CDK2, CAMKII, v-Src-as1, c-Fyn-as1, cAbl-as2, CDK2-as1 and CAMKII-as1, respectively. 1-NM-PP1 inhibited each of the five target kinases at low nanomolar concentrations with target-specificities ranging from 85-fold to 400-fold measured against the most inhibitable wild-type kinases. In addition, the in vitro study has also revealed that Cdc28-as1 is highly sensitive to 1-NM-PP1 with ATP kinetic K_m values of 35 μ M and 322 μ M, the K_{cat} values of 132 min⁻¹ and 21.3 min⁻¹, the K_{cat}/K_m values of 3.7 and 0.066, the IC₅₀ values of 22 μ M and 0.002 μ M for Cdc28/Clb2 and Cdc28-as1/Clb2, respectively [1].

References:

- [1] Bishop AC1, Ubersax JA, Petsch DT, Matheos DP, Gray NS, Blethrow J, Shimizu E, Tsien JZ,

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Schultz PG, Rose MD, Wood JL, Morgan DO, Shokat KM. A chemical switch for inhibitor-sensitive alleles of any protein kinase. Nature. 2000 Sep 21; 407(6802):395-401.

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