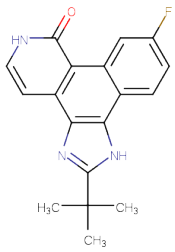
Data Sheet (Cat.No.T3080)

TargetMol
A DRUG SCREENING EXPERT

Pyridone 6

Chemical Properties



CAS No. : 457081-03-7

Formula: C18H16FN3O

Molecular Weight: 309.34

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Pyridone 6 (JAK Inhibitor)(CMP 6) is a potent and selective inhibitor of JAK1 (IC50=15 nM, murine JAK1), JAK2 (IC50=1 nM), JAK3 (Ki=5 nM), and Tyk2 (IC50=1 nM); displaying significantly weaker affinities (130 nM to 10 mM) for other protein tyrosine kinases.
Targets(IC50)	Tyrosine Kinases,JAK
In vitro	Pyridone 6 (P6) is shown to inhibit kinase by interacting within the ATP-binding cleft of each JAK. The IC50 of Pyridone 6 is 3 nM for all of these cytokines; this is comparable to the reported IC50s of Pyridone 6 for JAK2, Tyk2, and JAK3. Pyridone 6 strongly inhibits Th2 and modestly inhibits Th1, whereas it enhances Th17 development when present within a certain range of concentrations. Pyridone 6 reduces IFN-γ and IL-13, whereas it enhances IL-17 and IL-22 expression. Pyridone 6 also inhibits both Th1 and Th2 development, whereas it promotes Th17 differentiation from naive T cells when present within a certain range of concentrations[1]. Pyridone 6 inhibits osteoclast differentiation in mouse bone marrow macrophage (BMM) cultures stimulated by the receptor activator of nuclear factor-k B (NF-k B) ligand (RANKL) and co-cultures of bone marrow cells and osteoblasts. Pyridone 6 suppresses the expression of c-Fos and nuclear factor of activated T cells (NFAT) c1 in BMMs. Pyridone 6 also suppresses I-k B degradation and extracellular signal-regulated kinase (ERK) in mature osteoclasts, suggesting that these are the key molecules that pyridone 6 targets in the inhibition of osteoclast function[2]. Pyridone 6 (P6), is found to inhibit the JAKs in the low nanomolar range (IC50, 1-15 nM) and blocks IL-2-dependent proliferation of CTLL cells. Pyridone 6 is a reversible ATP inhibitor, and when tested against many other kinases, IC50s of >130 nM are required[3].
In vivo	Pyridone 6 (P6) postpones the initiation and diminishes the severity of skin conditions in an AD-like model using NC/Nga mice, effectively mitigating atopic dermatitis (AD) symptoms. Its efficacy is on par with betamethasone ointment, a standard treatment, also serving as a positive control. Conversely, empty PLGA nanoparticles (C-nano) appear ineffective[1].
Kinase Assay	Kinase Assays: Baculovirus-expressed glutathione S-transferase-tagged proteins encoding the intracellular domain of IGF-1R (amino acids 957-1367) and IR (amino acids 979-1382) are used for determinations of IC50s by a homogeneous time-resolved fluorescence assay. A filter binding assay is used for appKi determinations using activated IGF-1R and IR kinases. Expanded kinase-selectivity profiling of GSK1838705A is carried out by screening the compound in the KinaseProfiler panel.

Cell Research	Pyridone 6 (P6) is prepared in DMSO and stored, and then diluted with appropriate medium before use[1]. Naive CD4+ T cells are treated with various concentrations of Pyridone 6 in RPMI 1640 medium 1 h before the appropriate cytokines are added to create each Th-differentiating condition. Immunoblotting is performed using antiphospho-STAT protein Abs or anti-total STAT protein Abs[1].

Solubility Information

Solubility	DMSO: 25 mg/mL, (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	3.2327 mL	16.1634 mL	32.3269 mL
5 mM	0.6465 mL	3.2327 mL	6.4654 mL
10 mM	0.3233 mL	1.6163 mL	3.2327 mL
50 mM	0.0647 mL	0.3233 mL	0.6465 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Li Y, Chen W, Zhu X, et al.Neuronal BST2: A Pruritic Mediator Alongside PAR2 in the Interleukin-27-Driven Itch Pathway.Journal of Investigative Dermatology.2024