

Product Data Sheet

Product Name: SB590885

Cat. No.: GC11890

Chemical Properties

Cas. No. 405554-55-4

Chemical Name N,N-dimethyl-2-[4-[(4Z)-4-(1-nitroso-2,3-dihydroinden-5-ylidene)-5-(1H-pyridin-4-ylidene)-1H-imidazol-2-yl]phenoxy]ethanamine

SMILES CN(C)CCOC1=CC=C(C=C1)C2=NC(=C3C=CC4=C(CCC4=C3)N=O)C(=C5C=CNC=C5)N2

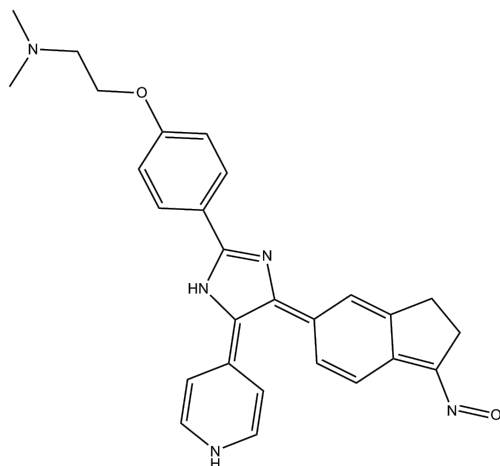
Formula C₂₇H₂₇N₅O₂ M.Wt 453.55

Solubility ≥ 4.54mg/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

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

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Cell experiment: For proliferation assays, cells are treated with compounds in 0.1% DMSO and incubated for 72 hours at 37°C, 5% CO₂. Viable cells are quantified using CellTiter-Glo reagent and luminescence detection on a Victor 2V plate reader. Cells are prepared for cell cycle analysis on a Becton Dickinson FACScan, according to the manufacturer's instructions. Data is acquired and analyzed using CellQuest v3.3 software. Anchorage-independent growth assays are done as described elsewhere, with inhibitors or DMSO vehicle included in the agar layer. Cultures are re-fed with media and inhibitor or DMSO every 5 to 7 days for a total of 28 days. Colonies are visualized and photographed by conventional light microscopy and quantified by counting on a grid in triplicate.

Animal experiment: The pharmacokinetic properties and safety of SB-590885, following i.p. injection, are determined and 50 mg/kg daily injections are found to give therapeutic levels with minimal body weight changes. Tumors are initiated in 8- to 12-week-old female nude mice by s.c. injection of 5×10⁶ A375P cells in Matrigel suspension, and 3 weeks after tumor induction when the tumors had reached a volume of 150 to 250 mm³, mice are randomized into groups of eight prior to treatment. Animals are treated with vehicle [2% N,N-dimethylacetamide, 2% Cremophor EL, and 96% acidified water (pH 4-5)], or vehicle containing 50 mg/kg of SB-590885 daily for 21 days. A cohort of mice treated with SB-590885 are then observed an additional 14 days following cessation of treatment. Tumor volume is measured for 55 days by calipers twice weekly.

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References:

- [1]. King AJ, et al. Demonstration of a genetic therapeutic index for tumors expressing oncogenic BRAF by the kinase inhibitor SB-590885. *Cancer Res*, 2006, 66(23), 11100-11105.
- [2]. Takle AK, et al. The identification of potent and selective imidazole-based inhibitors of B-Raf kinase. *Bioorg Med Chem Lett*, 2006, 16(2), 378-381.
- [3]. Smalley KS, et al. Increased cyclin D1 expression can mediate BRAF inhibitor resistance in BRAF V600E-mutated melanomas. *Mol Cancer Ther*, 2008, 7(9), 2876-2883.

Background

SB590885 is a potent and selective inhibitor of B-Raf kinase with K_i value of 0.16nM [1].

SB590885 is a potent inhibitor of oncogenic B-Raf protein kinase with K_i value of 0.16nM. It is more potent to inhibit B-Raf than C-Raf. The K_i value of SB590885 for C-Raf is 1.72nM. SB590885 is a quite selective inhibitor. It shows no activity against 48 other human kinases such as Abl, AMPK, CK1, CK2 and ERK2. It is found that SB590885 binds to B-Raf within the ATP-binding pocket and stabilizes the active conformation of B-Raf. SB590885 decreases the phosphorylation of ERK and shows anti-proliferation only in tumor cells expressing oncogenic B-Raf V600E. The normal cells and tumor cells not expressing mutant B-Raf have no sensitivity towards SB590885 except the normal melanocytes and primary melanoma cells expressing wild-type B-Raf. Moreover, SB590885 is also found to decrease the transformed and tumorigenic properties of malignant cells expressing mutant B-Raf [1].

References:

- [1] King A J, Patrick D R, Batorsky R S, et al. Demonstration of a genetic therapeutic index for tumors expressing oncogenic BRAF by the kinase inhibitor SB-590885. *Cancer research*, 2006, 66(23): 11100-11105.

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