

Product Data Sheet

Product Name: TG003
Cat. No.: GC10849

Chemical Properties

Cas. No. 300801-52-9

Chemical Name (1Z)-1-(3-ethyl-5-methoxy-1,3-benzothiazol-2-ylidene)propan-2-one

SMILES CCN1C2=C(C=CC(=C2)OC)SC1=CC(=O)C

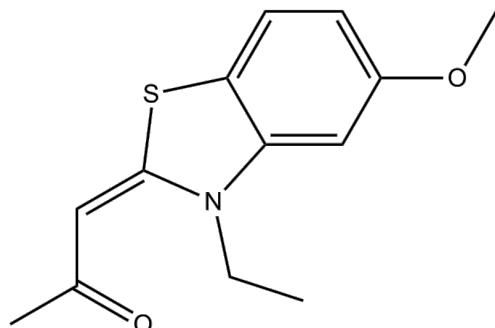
Formula $C_{13}H_{15}NO_2S$ M.Wt 249.33

Solubility $\geq 12.45\text{mg/mL}$ in DMSO 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

Cell experiment [1]:

Cell lines HeLa cells

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

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Soluble in DMSO >12.5mg/mL. General tips for obtaining a higher concentration:
Preparation method 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 2μl of 10 mM TG003 dissolved in Me2SO, final concentration at 10μM, 3 days

Applications TG003 had a potent inhibitory effect on the activity of Clk1 (Cdc2 like kinase1). TG003 inhibited SF2 (Splicing factor2) -dependent splicing of β-globin pre-mRNA in vitro by suppression of Clk-mediated phosphorylation. This drug also suppressed serine/arginine-rich protein phosphorylation, dissociation of nuclear speckles, and Clk1-dependent alternative splicing in cells.

Animal experiment [2]:

Animal models Seven-week-old, male Jcl:TCR mice

Dosage form 30mg/kg TG003 suspended in 5% DMSO, 5% Solutol, 9% Tween-80, and 81% saline, subcutaneously injection

Application TG003, an inhibitor of CLK1 in mice, could act as a splice-modifying compound for exon-skipping therapy. TG003 promoted skipping of dystrophin exon 31 with the c.4303G > T mutation.

Other notes Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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References:

[1]. Muraki M, Ohkawara B, et al. Manipulation of alternative splicing by a newly developed inhibitor of Clks. J Biol Chem, 2004, 279(23): 24246-24254.

[2]. Sako Y1, Ninomiya K1, et al, Development of an orally available inhibitor of CLK1 for skipping a mutated dystrophin exon in Duchenne muscular dystrophy. Sci Rep. 2017 May 30;7:46126. doi: 10.1038/srep46126.

Background

TG003 is a potent and selective inhibitor of Clk-family kinases with IC50 values of 15, 20, 200 nM and >10 μ M for mClk4, 1, 2 and 3, respectively [1]. Also, TG003 is also an inhibitor of casein kinase 1 (CK1) [2].

Cdc2-like kinases (Clks) family consist of Clk1, 2, 3 and 4 and play an important role in mRNA splice site selection. Clks phosphorylate serine/arginine-rich proteins that involved in pre-mRNA processing and release them into the nucleoplasm.

TG003 is a potent and selective Clk-family kinases inhibitor. TG003 competed with ATP with Ki value of 0.01 μ M on Clk1/Sty. In HeLa cytosolic S100 extract, TG003 inhibited Clk1/Sty-mediated phosphorylation of SF2/ASF, which played an important role in alternative splicing. Also, TG003 inhibited the splicing of β -globin pre-mRNA when complemented with rSF2/ASF. In HA-Clk1/Sty-overexpressing HeLa cells, TG003 (10 μ M) reversibly inhibited phosphorylation of SR proteins and caused HA-Clk1/Sty localized in nuclear speckles [1].

In mice, TG003 inhibited the alteration of splicing site selection induced by Clk1/Sty and affected the alternative splicing of endogenous genes. In *X. laevis* embryo, TG003 (10 μ M) rescued the morphological abnormalities in the dorsal ectoderm and mesoderm induced by the overexpression of xClk kinase [1].

References:

[1]. Muraki M, Ohkawara B, Hosoya T, et al. Manipulation of alternative splicing by a newly developed inhibitor of Clks. J Biol Chem, 2004, 279(23): 24246-24254.

[2]. Kurihara T, Sakurai E, Toyomoto M, et al. Alleviation of behavioral hypersensitivity in mouse

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models of inflammatory pain with two structurally different casein kinase 1 (CK1) inhibitors. Mol Pain, 2014, 10: 17.

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