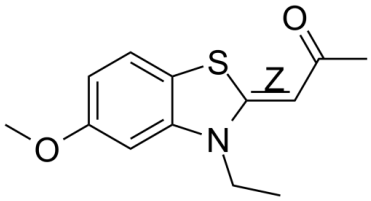
Data Sheet

Product Name:	TG003
Cat. No.:	CS-2036
CAS No.:	719277-26-6
Molecular Formula:	C13H15NO2S
Molecular Weight:	249.33
Target:	Others
Pathway:	Others
Solubility:	DMSO : ≥ 31 mg/mL (124.33 mM)



BIOLOGICAL ACTIVITY:

TG003 is a potent inhibitor of **Clk1/Sty**; inhibits Clk1 and Clk4 with **IC_{50}** values of 20 and 15 nM, respectively. IC50 & Target: IC50: 20 nM (Clk1), 200 nM (Clk2), >10 μM (Clk3), 15 nM (Clk4)[1] **In Vitro:** TG003, shows the most potent effect on Clk1/Sty and Clk4 (IC_{50}, 15–20 nM) and lesser on Clk2 (200 nM). TG003 inhibits SF2/ASF-dependent splicing of β-globin pre-mRNA in vitro by suppression of Clk-mediated phosphorylation. It suppresses serine/arginine-rich protein phosphorylation, dissociation of nuclear speckles, and Clk1/Sty-dependent alternative splicing in mammalian cells[1]. The small drug TG003 increases endogenous expression of p53β and p53γ protein isoforms by modulation of TP53 intron 9 alternative splicing[2]. **In Vivo:** Intrathecal injection of either TG003 (1-100 pM) or IC261 (0.1-1 nM) dose-dependently decreases mechanical allodynia and thermal hyperalgesia induced by carrageenan or CFA[3].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [1]Kinase activity of Clks and SRPKs is assayed in a reaction mixture, containing 200 mM Tris-HCl (pH 7.5), 12.5 mM $MgCl_2$, 8 mM dithiothreitol, 4 mM EGTA, 1–20 μM ATP, 1 μCi of [γ-^{32}P]ATP, 1 μg of synthetic peptide of SF2/ASF RS domain and 0.1-1 μg of purified kinases in a final volume of 40 μL. The final concentration of Me_2SO is adjusted to 1% regardless of inhibitor concentration. The reaction mixture is incubated at 30 or 25 °C for mammalian or Xenopus recombinant proteins, respectively, for 10 min, and a half-portion is spotted on P81 phosphocellulose membrane. The kinase assay conditions, including the incubation period and concentration of kinases and substrates, are optimized to maintain the linearity during incubation. The membrane is washed with 5% phosphoric acid solution or 5% trichloroacetic solution at least over 15 min. The radioactivity is measured using a liquid scintillation counter[1]. **Cell Assay:** [1]2×10^5 HeLa cells or 1.5×10^5 COS-7 cells re-suspended in 2 mL of medium are plated on 6-well dishes, and 2 μL of 10 mM TG003 dissolved in Me_2SO (final concentration at 10 mM), or 2 μL of Me_2SO, is added to some wells. Cells are trypsinized, and the density is counted every 24 h for 3 days. Cells are then fixed with 1 mL of ice-cold 70% ethanol, washed with PBS, incubated in 1 mL of PBS containing 1 μg/mL DNase-free RNase A and 50 μg/mL propidium iodide for 20 min at 37 °C, and proceeded to cell cycle analysis[1].

References:

[1]. Muraki M, et al. Manipulation of alternative splicing by a newly developed inhibitor of Clks. J Biol Chem. 2004 Jun 4;279(23):24246-54.

[2]. Marcel V, et al. Modulation of p53β and p53γ expression by regulating the alternative splicing of TP53 gene modifies cellular response. Cell Death Differ. 2014 Sep;21(9):1377-87.

[3]. Kurihara T, et al. Alleviation of behavioral hypersensitivity in mouse models of inflammatory pain with two structurally different casein kinase 1 (CK1) inhibitors. Mol Pain. 2014 Mar 10;10:17.

CAIndexNames:

2-Propanone, 1-(3-ethyl-5-methoxy-2(3H)-benzothiazolylidene)-, (1Z)-

SMILES:

CC(/C=C1SC2=CC=C(C=C2N\1CC)OC)=O.[Z]

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

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