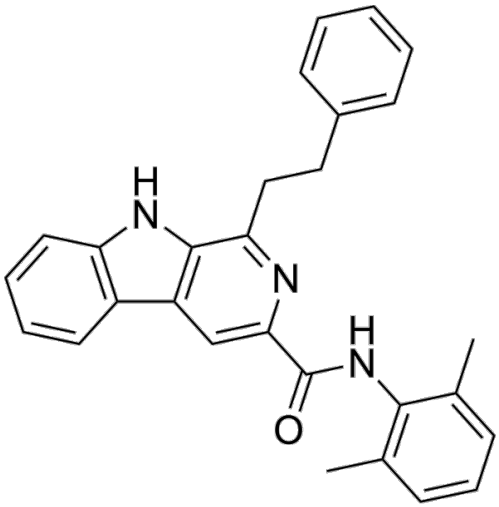
Product Data Sheet

Product Name: Y1693
Cat. No.: GC81612

Chemical Properties

Cas. No.	2812381-74-9		
Formula	$C_{28}H_{25}N_3O$	M.Wt	419.52
Solubility	DMSO: 25 mg/mL (59.59 mM; Need ultrasonic)	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



Background

Y1693 is an orally active RANKL inhibitor with a K d of 5.03 μM for hRANKL. Y1693 inhibits the activation of the downstream c-fos/NFATc1 signaling pathway by blocking its interaction with RANK. Y1693 significantly inhibits RANKL-induced osteoclast differentiation, F-actin ring formation and bone resorptive activity, while downregulating the mRNA and protein expressions of TRAP, cathepsin K, c-fos and NFATc1. Y1693 shows no obvious cytotoxicity to bone marrow-derived macrophages and osteoclast precursor cells, and exhibits favorable ADME properties. Y1693 improves ovariectomy-induced osteoporosis in mice and reverses ligation-induced periodontal alveolar bone loss. Y1693 is

applicable to research related to osteoporosis and periodontal diseases [1] [2].

In Vivo, Y1693 (20-60 mg/kg; p.o.; once daily 5×/week; 28 days) produces a 23.4% recovery of bone mineral density and ameliorates bone loss in ovariectomized mice with osteoporosis[1]. Y1693 (20 mg/kg; i.p.; daily; 28 days) increases alveolar bone mass by 60.7%, bone volume by 51.9%, while ameliorating ligature-induced periodontal bone loss in mice[1].

In Vitro, Y1693 (0.1-10 μM; 5-6 day) potently inhibits RANKL-induced osteoclastogenesis in BMMs with an IC_{50} of 0.52 μM, achieving 89.3% inhibition at 1 μM and 45.9% inhibition at 0.1 μM [1]. Y1693 (1-10 μM; 3 day) is non-cytotoxic to BMMs at concentrations up to 10 μM[1]. Y1693 (0.1-5 μM; 5-6 day) inhibits RANKL-induced F-actin ring formation in BMM-derived osteoclasts in vitro in a dose-dependent manner[1]. Y1693 (0.5-5 μM; 3 day) dose-dependently downregulates the mRNA expression of TRAP, cathepsin K, c-fos, and NFATc1 in RANKL-stimulated BMMs[1]. Y1693 (1-10 μM; 3 day) dose-dependently inhibits the protein expression of c-fos and NFATc1 in RANKL-stimulated BMMs[1]. Y1693 (0.1-5 μM; 2 day) dose-dependently inhibits RANKL-induced bone resorption by mature osteoclasts on bovine femur bone slices, with nearly complete inhibition at 5 μM[1].

References:
[1]. Yang K, et al. Development of an Orally Active Small-Molecule Inhibitor of Receptor Activator of Nuclear Factor-κB Ligand. J Med Chem. 2022;65(16):10992-11009.
[2]. Zhang Xiaofei, et al. A class of 3-amido-β-carboline compounds, their preparation method and use. CN116332929A. 2021-12-23.