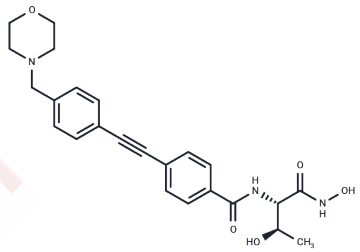
Data Sheet (Cat.No.T3702)

TargetMol

CHIR-090

Chemical Properties



CAS No. : 728865-23-4

Formula: C24H27N3O5

Molecular Weight: 437.49

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	CHIR-090 is a very potent and selective LpxC inhibitor with antibiotic activity.
Targets(IC50)	Antibacterial,Antibiotic
In vitro	CHIR-090 is a highly effective, slow, tight-binding inhibitor targeting the LpxC deacetylase from Aquifex aeolicus, displaying significant antibiotic properties against Gram-negative pathogens like P. aeruginosa and E. coli. Its mode of action includes a two-step slow, tight-binding inhibition mechanism against E. coli LpxC, with an inhibition constant (Ki) of 4 nM, indicating potent activity at low nanomolar concentrations against LpxC orthologues from a range of Gram-negative bacteria including Pseudomonas aeruginosa, Neisseria meningitidis, and Helicobacter pylori. Contrarily, CHIR-090 exhibits weaker inhibition against LpxC from Rhizobium leguminosarum (Ki=340 nM), demonstrating a reduced efficacy and conventional inhibition pattern without the slow, tight-binding characteristic. This differential inhibition renders E. coli strains with LpxC from R. leguminosarum resistant to CHIR-090, even at concentrations 400 times the minimal inhibitory concentration effective against wild-type E. coli. Nevertheless, CHIR-090 showcases outstanding antibiotic efficacy against select pathogens, on par with ciprofloxacin, emphasizing its potential as a therapeutic agent.
In vivo	CHIR-090 is a potent E. coli antibiotic, demonstrating significant E. coli LpxC inhibition within the low nanomolar (nM) range in vitro. Notably, E. coli W3110 colonies resistant to a 1 μg/mL concentration of CHIR-090 do not occur unless subjected to prior chemical mutagenesis. However, a specific strain of E. coli W3110 can grow on LB agar with CHIR-090 concentrations ranging from 1 to 10 μg/mL, which is significantly higher (4 to 40 times) than the minimum inhibitory concentration (MIC) of 0.25 μg/mL identified under our conditions for the wild-type E. coli W3110. The growth rate of W3110RL strain is unaffected by 1 μg/mL CHIR-090, maintaining a doubling time of 40 minutes, identical to that of the wild-type strain without the inhibitor. Conversely, the wild-type strain ceases growth approximately two hours after exposure to 1 μg/mL of CHIR-090[1].
Kinase Assay	Disk diffusion is conducted, except that 10 μg of each antibiotic compound is used per filter. Growth in liquid medium in the presence of CHIR-090 is evaluated as follows: cells from overnight cultures are inoculated into 50 mL portions of LB broth at an A600 of 0.02 and grown with shaking at 30°C. When the A600 reaches 0.15, parallel cultures are

Kinase Assay	treated with either 6 μL of 500 μg/mL CHIR-090 in DMSO or 6 μL of DMSO. To assess cumulative growth, cultures are maintained in log phase growth by 10-fold dilution into pre-warmed medium, containing the same concentrations of DMSO or DMSO/CHIR-090, whenever the A600 reaches 0.4. The minimal inhibitory concentration is defined as the lowest antibiotic concentration at which no measurable bacterial growth is observed in LB medium containing 1% DMSO (v/v), when inoculated at a starting density of A600=0.01. Cultures are incubated with shaking for 24 h at 30°C in the presence of CHIR-090. Experiments are performed in triplicate[1].

Solubility Information

Solubility	DMSO: 12.2 mg/mL (27.89 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween-80+45% Saline: 1 mg/mL (2.29 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2858 mL	11.4288 mL	22.8577 mL
5 mM	0.4572 mL	2.2858 mL	4.5715 mL
10 mM	0.2286 mL	1.1429 mL	2.2858 mL
50 mM	0.0457 mL	0.2286 mL	0.4572 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.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Barb AW, et al. Inhibition of lipid A biosynthesis as the primary mechanism of CHIR-090 antibiotic activity in Escherichia coli. Biochemistry. 2007 Mar 27;46(12):3793-802.

Barb AW, et al. Structure of the deacetylase LpxC bound to the antibiotic CHIR-090: Time-dependent inhibition and specificity in ligand binding. Proc Natl Acad Sci U S A. 2007 Nov 20;104(47):18433-8.