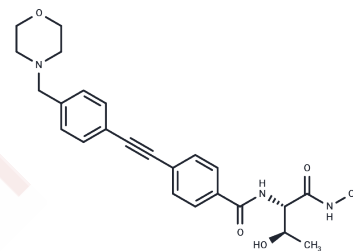


## CHIR-090

## Chemical Properties

CAS No. :	728865-23-4
Formula:	C <sub>24</sub> H <sub>27</sub> N <sub>3</sub> O <sub>5</sub>
Molecular Weight:	437.49
Appearance:	no data available
Storage:	Powder: -20°C for 3 years   In solvent: -80°C for 1 year



## Biological Description

Description	CHIR-090 is a very potent and selective LpxC inhibitor with antibiotic activity.
Targets(IC50)	Antibacterial
In vitro	CHIR-090 is a highly effective, slow, tight-binding inhibitor targeting the LpxC deacetylase from <i>Aquifex aeolicus</i> , displaying significant antibiotic properties against Gram-negative pathogens like <i>P. aeruginosa</i> and <i>E. coli</i> . Its mode of action includes a two-step slow, tight-binding inhibition mechanism against <i>E. coli</i> LpxC, with an inhibition constant ( $K_i$ ) of 4 nM, indicating potent activity at low nanomolar concentrations against LpxC orthologues from a range of Gram-negative bacteria including <i>Pseudomonas aeruginosa</i> , <i>Neisseria meningitidis</i> , and <i>Helicobacter pylori</i> . Contrarily, CHIR-090 exhibits weaker inhibition against LpxC from <i>Rhizobium leguminosarum</i> ( $K_i=340$ nM), demonstrating a reduced efficacy and conventional inhibition pattern without the slow, tight-binding characteristic. This differential inhibition renders <i>E. coli</i> strains with LpxC from <i>R. leguminosarum</i> resistant to CHIR-090, even at concentrations 400 times the minimal inhibitory concentration effective against wild-type <i>E. coli</i> . 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 <i>E. coli</i> antibiotic, demonstrating significant <i>E. coli</i> LpxC inhibition within the low nanomolar (nM) range in vitro. Notably, <i>E. coli</i> 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 <i>E. coli</i> 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 <i>E. coli</i> 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 A <sub>600</sub> of 0.02 and grown with shaking at 30°C. When the A <sub>600</sub> reaches 0.15, parallel cultures are 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: 60 mg/mL (137.15 mM), Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
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### 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.

### 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.

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