

Product Data Sheet

Product Name: BTZ043
Cat. No.: GC40680

Chemical Properties

Cas. No. 1161233-85-7

SMILES O=C1N=C(N2CCC3(OC[C@H](C)O3)CC2)SC4=C([N+])([O-])=O)C=C(C(F)(F)F)C=C41

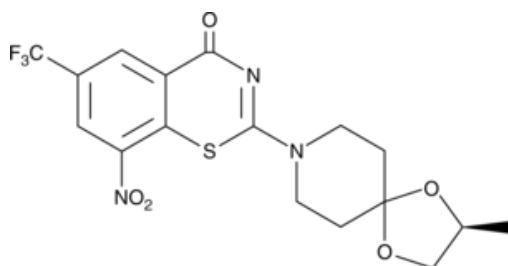
Formula C₁₇H₁₆F₃N₃O₅S M.Wt 431.4

Solubility DMF: 1 mg/ml, DMSO: 1 mg/ml 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 sizes: ship with RT, or blue ice upon request.

Structure



Protocol

Animal experiment:

Mice[2] Animal efficacy is determined in a standard mouse infection model. BALB/c mice are infected with a low bacillary load (~200 CFU) of *M. tuberculosis* H37Rv via aerosol. Treatment started four-weeks post infection. Mice are dosed by gavage with 37.5, or 300 mg of BTZ043, per kg body weight, in carboxymethyl cellulose formulation (0.25%), once daily, six times/week, for four weeks. Control and treated mice are sacrificed, lungs and spleens homogenized and dilutions plated for enumeration of viable bacilli[2].

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

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Address: 10292 Central Ave. #205, Montclair, CA, USA

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References:

- [1]. Vadim Makarov et al. The 8-Pyrrole-Benzothiazinones Are Noncovalent Inhibitors of DprE1 from *Mycobacterium tuberculosis*. *Antimicrob Agents Chemother*, 2015 Aug, 59(8): 4446-4452.
- [2]. Makarov V, et al. Benzothiazinones kill *Mycobacterium tuberculosis* by blocking arabinan synthesis. *Science*. 2009 May 8;324(5928):801-4.
- [3]. Norma Alejandra González-Martínez et al. In Vivo Activity of the Benzothiazinones PBTZ169 and BTZ043 against *Nocardia brasiliensis*. *PLoS Negl Trop Dis*, 2015 Oct, 9(10): e0004022.

Background

BTZ043 is an inhibitor of decaprenyl-phosphoribose-epimerase (DprE1), with MICs of 2.3 nM and 9.2 nM for *M. tuberculosis* H37Rv and *Mycobacterium smegmatis*, respectively.

The MIC of BTZ043 against *M. tuberculosis* H37Rv and *Mycobacterium smegmatis* are 1 ng/mL (2.3 nM) and 4 ng/mL (9.2 nM), respectively[2]. The in vitro activity of BTZ043 against 30 *Nocardia brasiliensis* isolates is also tested. The MIC50 and MIC90 values for BTZ043 are 0.125 and 0.25 µg/mL. The MIC for *N. carnea* ATCC 6847 is 0.003 µg/mL, for *N. transvalensis* ATCC 6865 is 0.003 µg/mL, for *N. brasiliensis* NCTC10300 is 0.03 µg/mL, and for *N. brasiliensis* HUJEG-1 is 0.125 µg/mL. The MIC value for *M. tuberculosis* H37Rv is 0.000976 µg/mL. The MIC value of BTZ-043 is >64 µg/mL for *Escherichia coli* ATCC 25922 and *S. aureus* ATCC 29213[3].

Four weeks of treatment with BTZ043 reduces the bacterial burden in the lungs and spleens by 1 and 2 logs, respectively, at the concentrations used. Additional results suggest that BTZ043 efficacy is time-rather than dose-dependent. Acute (5 g/kg) and chronic (25 and 250 mg/kg) toxicology studies in uninfected mice show that, even at the highest dose tested, there are no adverse anatomical, behavioral, or physiological effects after one month[2].

References:

- [1]. Vadim Makarov et al. The 8-Pyrrole-Benzothiazinones Are Noncovalent Inhibitors of DprE1 from *Mycobacterium tuberculosis*. *Antimicrob Agents Chemother*, 2015 Aug, 59(8): 4446-4452.
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