

Product Data Sheet

Product Name: BRL 50481

Cat. No.: GC15472

Chemical Properties

Cas. No. 433695-36-4

Chemical Name N,N,2-trimethyl-5-nitrobenzenesulfonamide

SMILES CC1=C(S(N(C)C)(=O)=O)C=C(N(=O)=O)C=C1

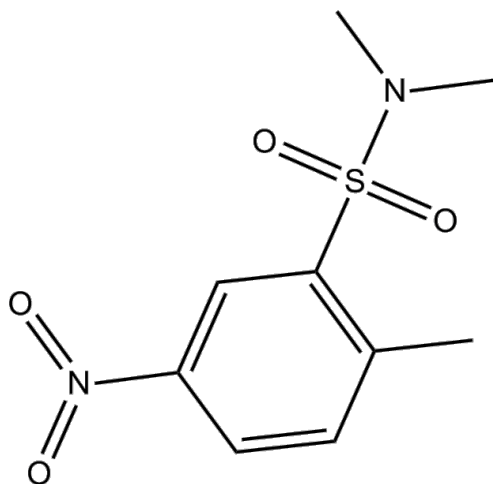
Formula $C_9H_{12}N_2O_4S$ M.Wt 244.27

Solubility DMF: 20 mg/ml, DMF:PBS (pH7.2) (1:40): 0.02 mg/ml, DMSO: 15 mg/ml, Ethanol: 15 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 size: ship with RT, or blue ice upon request.

Structure



Protocol

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

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

Product Data Sheet

Cell experiment: MOLT-4 cells in 96-well plates are treated for 30 min with BRL-50481 as indicated. The cAMP content is then determined by an immunospecific ELISA. Results are expressed as a percentage of the response affected by 100 μ M IBMX[2].

References:

- [1]. Safavi M, et al. New methods for the discovery and synthesis of PDE7 inhibitors as new drugs for neurological and inflammatory disorders. *Expert Opin Drug Discov.* 2013 Jun;8(6):733-51.
- [2]. Smith SJ, et al. Discovery of BRL 50481 [3-(N,N-dimethylsulfonamido)-4-methyl-nitrobenzene], a selective inhibitor of phosphodiesterase 7: in vitro studies in human monocytes, lung macrophages, and CD8+ T-lymphocytes. *Mol Pharmacol.* 2004 Dec;66(6):1679-89.

Background

BRL 50481 is a selective inhibitor of phosphodiesterase (PDE) 7. At substrate concentrations of 50 nM and 1 μ M, the hydrolysis of cAMP by hrPDE7A1 was inhibited by BRL 50481 with IC₅₀ values of 0.26 and 2.4 μ M, respectively [1]. BRL 50481 is a selective and potent inhibitor of human recombinant PDE7A with an IC₅₀ value of 26 nM [2].

PDE7 is of a high affinity as a cAMP-specific PDE. PDE7 could be a good treatment target for T cell related diseases, airway diseases or central nervous system (CNS) disorders [3].

At 1 μ M and 50 nM cAMP, BRL 50481 was a selective inhibitor of hrPDE7A1, with 416 and 1884 times less potencies against PDE3, and 38 and 238 times less potencies against hrPDE4A4, respectively. BRL 50481 did not significantly inhibit PDE1C, PDE1B, PDE5 and PDE2 at concentrations below 100 μ M. BRL 50481 showed a competitive inhibition potency against hrPDE7A1 with a K_i value of 180 $\pm$ 10 nM. But in MOLT-4 T cells, BRL 50481 increased the cAMP content with an EC₅₀ >> 100 μ M. The EC₈₀ value of rolipram is about 10 μ M. When the effect of BRL 50481 at concentrations of 10–300 μ M on cAMP mass was examined in the presence of rolipram at a submaximal concentration, the mean concentration-response curve of BRL 50481 was displaced upwards of a significantly greater magnitude, compared to the sum of the cAMP response affected by BRL 50481 and rolipram alone [1].

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

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

Product Data Sheet

Compared to treatment with A-350619 or BRL 50481 alone, the combination of methylene blue and BRL 50481 significantly delayed the onset of action in received mice for jerky movements and convulsion. The combination of methylene blue and exogenously administered BRL 50481 (2 mg/kg, i.p.) significantly had an anti-convulsant activity [4].

References:

- [1]. Smith SJ, Cieslinski LB, Newton R, et al. Discovery of BRL 50481 [3-(N,N-dimethylsulfonamido)-4-methyl-nitrobenzene], a selective inhibitor of phosphodiesterase 7: in vitro studies in human monocytes, lung macrophages, and CD8+ T-lymphocytes. Mol Pharmacol, 2004, 66(6):1679-89.
- [2]. Gil C, Campillo NE, Perez DI, et al. PDE7 inhibitors as new drugs for neurological and inflammatory disorders. Expert Opin Ther Patents, 2008, 18(10):1127-1139.
- [3]. Castro A, Jerez MJ, Gil C, et al. CODES, a novel procedure for ligand-based virtual screening: PDE7 inhibitors as an application example. Eur J Med Chem, 2008, 43(7):1349-59.
- [4]. Nandhakumar J, Ernest V and Tyagi MG. Evaluation of Seizure Activity After Phosphodiesterase Inhibition (BRL 50481) with Guanylate Cyclase Activation (A-350619) and Inhibition (Methylene blue) in Animal Models of Epilepsy. J Neurol Neurophysiol, 2011, 2:110.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

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