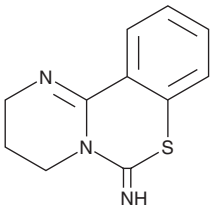
PRODUCT INFORMATION

PD 404182

Item No. 34396

CAS Registry No.:	72596-74-8
Formal Name:	3,4-dihydro-2H,6H-pyrimido[1,2-c][1,3]benzothiazin-6-imine
MF:	$C_{11}H_{11}N_3S$
FW:	217.3
Purity:	≥98%
UV/Vis.:	λ_{max}: 225 nm
Supplied as:	A solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

PD 404182 is supplied as a solid. A stock solution may be made by dissolving the PD 404182 in the solvent of choice, which should be purged with an inert gas. PD 404182 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of PD 404182 in these solvents is approximately 20, 25, and 30 mg/ml, respectively.

PD 404182 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, PD 404182 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. PD 404182 has a solubility of approximately 0.09 mg/ml in a 1:10 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

PD 404182 is an antiviral agent.[1,2] It inhibits the activity of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) main protease (M^{pro}), also known as 3C-like protease ($3CL^{pro}$; IC_{50} = 0.081 µM), and prevents herpes simplex virus 1 (HSV-1) and HSV-2 infection in Vero cells when used at a concentration of 0.2 µM. PD 404182 also inhibits dimethylarginine dimethylaminohydrolase 1 (DDAH-1) and histone deacetylase 8 (HDAC8; IC_{50}s = 9 and 0.011 µM for the human enzymes, respectively), as well as bacterial KDO 8-P synthase (K_i = 0.026 µM), an enzyme important for LPS biosynthesis.[3-5] It reduces endothelial tube formation and LPS-induced nitric oxide (NO) production in primary human dermal microvascular endothelial cells.[3]

References

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2. Chamoun-Emanuelli, A.M., Bobart, M., Moncla, B., *et al.* Evaluation of PD 404,182 as an anti-HIV and anti-herpes simplex virus microbicide. *Antimicrob. Agents Chemother.* **58(2)**, 687-697 (2014).
3. Ghebremariam, Y.T., Erlanson, D.A., and Cooke, J.P. A novel and potent inhibitor of dimethylarginine dimethylaminohydrolase: a modulator of cardiovascular nitric oxide. *J. Pharmacol. Exp. Ther.* **348(1)**, 69-76 (2014).
4. Kleinschek, A., Meyners, C., Digiorgio, E., *et al.* Potent and selective non-hydroxamate histone deacetylase 8 inhibitors. *ChemMedChem* **11(23)**, 2598-2606 (2016).
5. Birck, M.R., Holler, T.P., and Woodard, R.W. Identification of a slow tight-binding inhibitor of 3-deoxy-d-*manno*-octulosonic acid 8-phosphate synthase. *J. Am. Chem. Soc.* **122**, 9334-9335 (2000).

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