

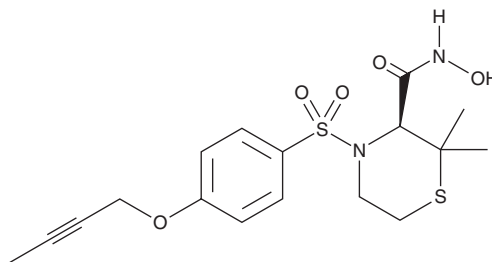
PRODUCT INFORMATION



TMI 1

Item No. 29713

CAS Registry No.: 287403-39-8
Formal Name: (3S)-4-[[4-(2-butyn-1-yloxy)phenyl]sulfonyl]-N-hydroxy-2,2-dimethyl-3-thiomorpholinecarboxamide
MF: C₁₇H₂₂N₂O₅S₂
FW: 398.5
Purity: ≥98%
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

TMI 1 is supplied as a solid. A stock solution may be made by dissolving the TMI 1 in the solvent of choice, which should be purged with an inert gas. TMI 1 is soluble in the organic solvent DMSO at a concentration of approximately 25 mg/ml.

Description

TMI 1 is an inhibitor of disintegrin and metalloproteinase domain-containing protein 17 (ADAM17/TACE; IC₅₀ = 8.4 nM in a cell-free enzyme assay).¹ It inhibits matrix metalloproteinase-1 (MMP-1), -2, -7, -9, -13, and -14, as well as ADAM-TS-4 *in vitro* (IC₅₀s = 6.6, 4.7, 26, 12, 3, 26, and 100 nM, respectively). It also inhibits ADAM8, -10, -12, and -17/TACE in cell-free enzyme assays with K_i values of 21, 16, 1.8, and 0.079 nM, respectively, with slow-binding inhibition of ADAM17/TACE but not the other ADAM enzymes.² TMI 1 inhibits LPS-induced TNF-α secretion in Raw and THP-1 cells (IC₅₀s = 40 and 200 nM, respectively), as well as in isolated human monocytes and whole blood (IC₅₀s = 190 and 300 nM, respectively).¹ It inhibits the production of TNF-α *ex vivo* in synovium isolated from the inflamed joints of patients with rheumatoid arthritis with IC₅₀ values of less than 100 nM without inhibiting TNF-α expression *in vitro*. TMI 1 inhibits LPS-induced TNF-α production in mice (ED₅₀ = 5 mg/kg) and reduces disease severity in mouse models of collagen-induced arthritis. It also decreases cell viability of (ED₅₀s = 1.3-8.1 μM), and induces caspase-3/7 activity in a variety of cancer cell lines and induces tumor apoptosis and reduces tumor growth in an MMTV-ErbB2/neu mouse model of breast cancer when administered at a dose of 100 mg/kg.³

References

1. Zhang, Y., Xu, J., Levin, J., *et al.* Identification and characterization of 4-[[4-(2-butyn-1-yloxy)phenyl]sulfonyl]-N-hydroxy-2,2-dimethyl-(3S)thiomorpholinecarboxamide (TMI-1), a novel dual tumor necrosis factor-α-converting enzyme/matrix metalloprotease inhibitor for the treatment of rheumatoid arthritis. *J. Pharmacol. Exp. Ther.* **309**(1), 348-355 (2004).
2. Moss, M.L. and Rasmussen, F.H. Fluorescent substrates for the proteinases ADAM17, ADAM10, ADAM8, and ADAM12 useful for high-throughput inhibitor screening. *Anal. Biochem.* **366**(2), 144-148 (2007).
3. Mezil, L., Berruyer-Pouyet, C., Cabaud, O., *et al.* Tumor selective cytotoxic action of a thiomorpholin hydroxamate inhibitor (TMI-1) in breast cancer. *PLoS One* **7**(9), e43409 (2012).

WARNING

THIS PRODUCT IS FOR RESEARCH ONLY - NOT FOR HUMAN OR VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

SAFETY DATA

This material should be considered hazardous until further information becomes available. Do not ingest, inhale, get in eyes, on skin, or on clothing. Wash thoroughly after handling. Before use, the user must review the complete Safety Data Sheet, which has been sent via email to your institution.

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