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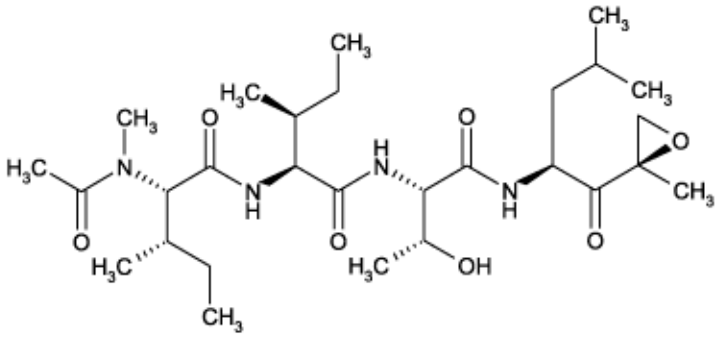
ProductInformation

EPOXOMICIN

Product Number **E 3652**
Storage Temperature: –20 °C

CAS#: 134381-21-8
Synonyms: L-Threoninamide, N-acetyl-N-methyl-L-isoleucyl -L-isoleucyl-N-[(1S)-3-methyl-1-[[(2R)-2-methyloxiranyl] carbonyl]butyl]; BU 4061T



Product Description
Molecular Weight: 554.7
Molecular Formula: $C_{28}H_{50}N_4O_7$

Epoxomicin, a natural product isolated from an *Actinomycetes* species, is an α^1, β^1-epoxy-ketone tetrapeptide proteasome inhibitor. It is a cell-permeable, potent, selective and irreversible proteasome inhibitor. It covalently binds to the catalytic β subunits of proteasome IFN-γ- inducible subunits LMP7 and MECL1 and their housekeeping respective counterparts X (MEB-1) and Z subunits.[1]

Epoxomicin inhibits primarily chymotrypsin-like, but also trypsin-like, and peptidylglutamyl peptide-hydrolyzing (PGPH) activities of the proteasome.[1,4] Epoxomicin is a more potent inhibitor of chymotrypsin-like activity of the proteasome than lactacystin, inhibiting the activity 80-fold faster than lactacystin.[1] Epoxomicin does not inhibit non-proteasomal proteases like calpain, chymotrypsin, trypsin, cathepsin B, or papain at concentrations of up to 50 µM, unlike some peptide aldehyde proteasome inhibitors .[1,4]

As a result of its selective and unique activity, it inhibits NFκB activation *in vitro* and potently blocks *in vivo* inflammation in the murine ear edema assay.[1] Because NFκ is a key regulator of inflammation, Epoxomicin would be an attractive agent for antiinflammatory therapeutic intervention.

In addition, its proteasome inhibition results in modulation of antigen presentation with potential applications for treatment of autoimmune diseases and prevention of transplant rejection.[2] Expoxomicin also demonstrates anitumor activity.[3]

Precautions and Disclaimer
This product is for laboratory research use only. Please consult the Material Safety Data Sheet for handling recommendations before working with this material.

Preparation instructions
Epoxomicin is soluble in DMSO (10 mg/ml) and insoluble in water. Solutions can be stored at –20 °C for up to 3 months.

References

1. Meng, L., et al., Epoxomicin, a potent and selective proteasome inhibitor, exhibits *in vivo* antiinflammatory activity. Proc. Natl. Acad. Sci. USA, **96,** 10403-08 (1999).
2. Schwartz, K., et al., The selective proteasome inhibitors Lactacytin and Epoxomicin can be used to either up- or down-regulate antigen presentation in nontoxic doses. J. Immunol., **164**, 6147-57 (2000).
3. Sin, N. et al., Total synthesis of the potent proteasome inhibitor Epoxomicin: a useful tool for understanding proteasome biology. Bioorganic & Medicinal Chemistry Letters, **9**, 2283-88 (1999).
4. Princiotta, M. F., et al., Proc. Natl. Acad. Sci. USA, **98**, 513 (2001).

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