### Chemical Properties

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product Name</strong></td>
<td>Epoxomicin</td>
</tr>
<tr>
<td><strong>Cas No.</strong></td>
<td>134381-21-8</td>
</tr>
<tr>
<td><strong>M.Wt.</strong></td>
<td>554.7</td>
</tr>
<tr>
<td><strong>Formula</strong></td>
<td>C28H50N4O7</td>
</tr>
<tr>
<td><strong>Synonyms</strong></td>
<td>Epoxomicin, BU4061T, BU-4061 T</td>
</tr>
<tr>
<td><strong>Chemical Name</strong></td>
<td>(2S,3S)-2-[[2(S,3S)-2-[acetyl(methyl)amino]-3-methylpentanoyl]amino]-N-[(2S,3R)-3-hydroxy-1-[(2S)-4-methyl-1-[(2R)-2-methyloxiran-2-yl]-1-oxopentan-2-yl]amino]-1-oxobutan-2-yl]-3-methylpentanamide</td>
</tr>
<tr>
<td><strong>Canonical SMILES</strong></td>
<td>CCC(C(C(=O)NC(C(O)C(=O)NC(CC(C)C(=O)C1(CO1)C)NC(=O)C(C(CCC)N(C)(=O)C)</td>
</tr>
<tr>
<td><strong>Solubility</strong></td>
<td>&gt;27.7mg/mL in DMSO</td>
</tr>
<tr>
<td><strong>Storage</strong></td>
<td>Store at -20°C</td>
</tr>
<tr>
<td><strong>General tips</strong></td>
<td>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.</td>
</tr>
<tr>
<td><strong>Shopping Condition</strong></td>
<td>Evaluation sample solution: ship with blue ice</td>
</tr>
<tr>
<td></td>
<td>All other available size: ship with RT, or blue ice upon request</td>
</tr>
</tbody>
</table>

### Biological Activity

**Targets:** Proteasome

**Pathways:** Ubiquitination/Proteasome >> Proteasome

**Description:**

Epoxomicin was originally isolated from the culture medium of an Actinomycetes strain based on its in vivo antitumor activity against murine B16 melanoma. Epoxomicin is a naturally occurring selective proteasome inhibitor with anti-inflammatory activity. [1] Epoxomicin primarily inhibits the activity of CTRL (chymotrypsin-like proteasome).
The novel α-epoxy ketone moiety of Epoxomicin forms covalent bonds with residues in particular catalytic subunits of the enzyme, disabling activity. The trypsin-like and peptidyl-glutamyl peptide hydrolyzing behaviors of the proteasome were both inhibited by Epoxomicin as well (at 100 and 1,000-fold slower rates, respectively). The ubiquitin-proteasome pathway heavily regulates bone formation, and Epoxomicin was shown to increase both bone volume and bone formation rates in rodents.

Another study demonstrates that exposure to Epoxomicin and other proteasome inhibitors leads to dopaminergic cell death, producing a model of Parkinson's disease in vivo. Epoxomicin is an inhibitor of 20S Proteasome. [2]

Reference:
2. Epoxomicin, Santa Cruz Biotechnology.

Protocol

Cell experiment:

Cell lines
HEK293T cells

Preparation method
The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reacting conditions
Incubated at 0.2 μM or 2 μM epoxomicin for 1 hour

Applications
Peptides were degraded by proteasome from cytosolic, mitochondrial, and nuclear proteins. Epoxomicin is a proteasome inhibitor. It decreased the levels of the majority of intracellular peptides, companying with inhibition of the proteasome beta-2 and beta-5 subunits in HEK293T cells.

Animal experiment [3]:

Animal models
C57BL6

Dosage form
Epoxomicin (0.58 mg/kg) solubilized in 10% DMSO/PBS were injected i.p. daily for 6 days

Applications
Epoxomicin reduced inflammation in response to picrylchloride. Epoxomicin potently inhibited the irritant-associated inflammatory response by 95% when ear edema measurements were made 24 hr postchallenge.
Other notes

Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

Reference:

Product Citations


Product Validation
HeLa cells were untreated (-) or treated with 10 μm Epoxomicin (+) as indicated, 4 h later the cells were harvested and the lysates were subjected to immunoblot analysis with anti-ubiquitin or anti-p53 antibodies.

Analysis of proteasome activity and proteasome complex formation in response to treatment of phLF with 20 μM epoxomicin for 4.5 h. Dose dependent inhibition of the CT-L catalytic site, resulted in enhanced recruitment of PA28γ and PA200 to 20S and 26S proteasomes. Interference with total proteasome activity by treatment with proteasome inhibitor epoxomicin resulted in an even more pronounced formation of alternative proteasome complexes.
