



Product Information

Z-Gly-Leu-Phe Chloromethyl Ketone

Product Number **C 9984**

Storage Temperature $-20\text{ }^{\circ}\text{C}$

Product Description

Molecular Formula: $\text{C}_{26}\text{H}_{32}\text{ClN}_3\text{O}_5$

Formula Weight: 502.0

Z-Gly-Leu-Phe Chloromethyl Ketone (Z-GLF-CMK, Z = benzyloxycarbonyl) is a cell permeable inhibitor of Granzyme B.¹

Granzyme B is a serine protease found in lytic granules of cytotoxic lymphocytes and plays a role in cell death or apoptosis.² Granzymes A and B are the most abundant granzymes and are expressed earlier than other granzymes. Granzyme B is an agent for rapid DNA fragmentation and can cleave several procaspases to activate the corresponding caspase. The Asp primary substrate specificity of granzyme B, also found in caspases, is unusual among proteases.³ Lamin B is another substrate for granzyme B.⁴

CMK is a trapping group responsible for irreversible inhibition and is also non-cytotoxic. Inhibition occurs when the CMK group covalently bonds to the $-\text{OH}$ of an serine adjacent residue, or the $-\text{SH}$ of an adjacent cysteine residue, on the target protein.

Z-Gly-Leu-Phe Chloromethyl Ketone is supplied as a white solid.

Preparation Instructions

Prepare 20 mM stock solutions in dry ($\geq 99.9\%$) DMSO to maintain product stability. Also soluble in DMF.

Storage/Stability

Store at $-20\text{ }^{\circ}\text{C}$. The product is reported to be stable at room temperature for one year in a desiccator. Allow container to warm to room temperature before opening to ensure stability.

Store stock solutions at $-20\text{ }^{\circ}\text{C}$ for 6-8 months.

References

1. Segal, D.M., et al., Substrate binding site in bovine chymotrypsin A-gamma. A crystallographic study using peptide chloromethyl ketones as site-specific inhibitors. *Biochemistry*, **10**, 3728-3737 (1971).
2. Pham, C. T., & Ley, T. J. The role of granzyme B cluster proteases in cell-mediated cytotoxicity. *Semin. Immunol.* **9**, 127-133 (1997).
3. Kam, C.-M., et al., Granzymes (lymphocyte serine proteases): characterization with natural and synthetic substrates and inhibitors. *Biochim. Biophys. Acta.* **1477**, 307-23 (2000).
4. Zhang, D., et al. Granzymes A and B directly cleave lamins and disrupt the nuclear lamina during granule-mediated cytolysis. *Proc. Natl. Acad. Sci. USA*, **9**, 5746-5751 (2001).

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