TimTec Diversity Library of 10,000 compounds was screened in research collaboration between Department of Veterinary Molecular Biology at Montana State UniVersity, Bozeman, Montana, and Department of Chemistry at Altai State Technical UniVersity, Barnaul, Russia.

Published screening results identified 18 hit compounds, most potent inhibitors of Anthrax Lethal Factor.

Schepetkin, I., et al., Novel Small-molecule Inhibitors of Anthrax Lethal Factor Identified by High-throughput Screening. J. Med. Chem. 49: 5232-5244 (2006)

Abstract

Anthrax lethal factor (LF) is a key virulence factor of anthrax lethal toxin. We screened a chemolibrary of 10 000 drug-like molecules for their ability to inhibit LF and identified 18 novel small molecules with potent LF inhibitory activity. Three additional LF inhibitors were identified through further structureactivity
relationship (SAR) analysis. All 21 compounds inhibited LF with an IC50 range of 0.8 to 11 Ã*ƒ*Â-M, utilizing mixed-mode competitive inhibition. An evaluation of inhibitory activity against a range of unrelated proteases showed relatively high specificity for LF. Furthermore, pharmacophore modeling of these
compounds showed a high degree of similarity to the model published by Panchal et al. (Nat. Struct. Mol. Biol. 2004, 11, 67-72), indicating that the conformational features of these inhibitors are structurally compatible with the steric constraints of the substrate-binding pocket. These novel LF inhibitors and the structural scaffolds identified as important for inhibitory activity represent promising leads to pursue for further LF inhibitor development.

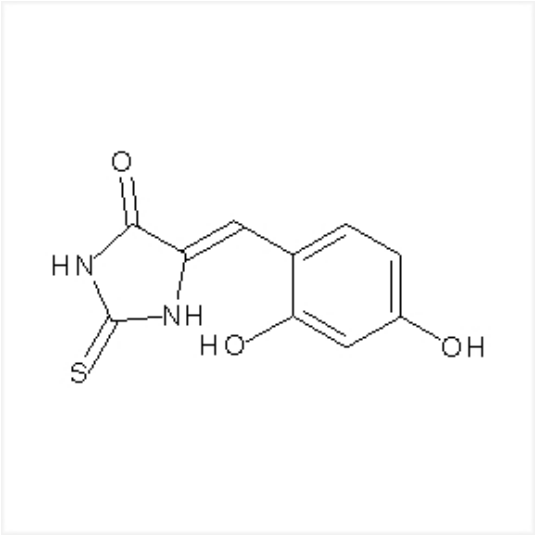
Activators of Neutrophils analogs

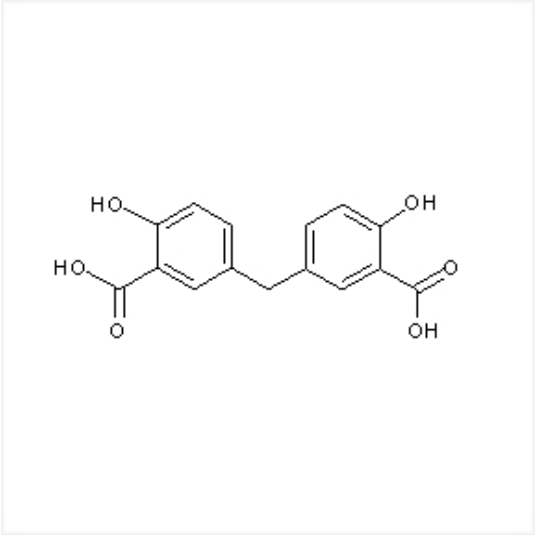
Inhibitors of Anthrax Lethal Factor

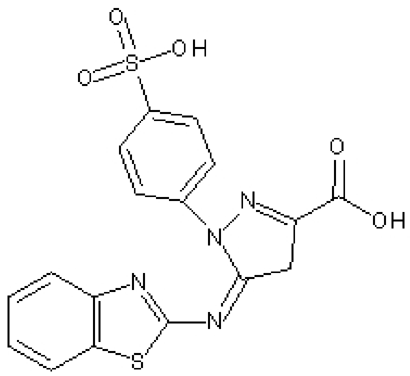
ST003272
C10H8N2O3S
236.25

ST018515
C15H12O6
288.26

ST019413
C17H12N4O5S2
416.44



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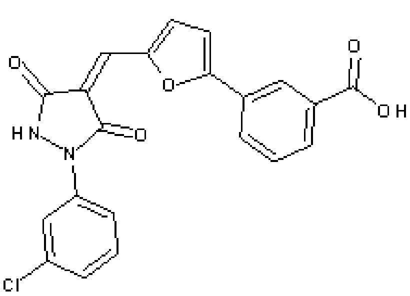
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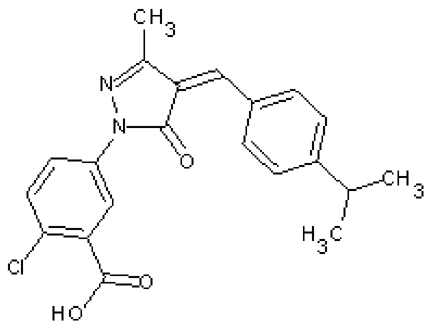
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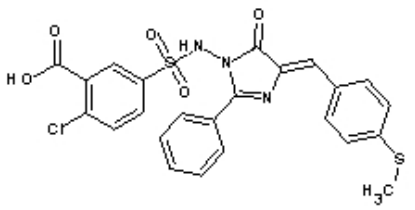

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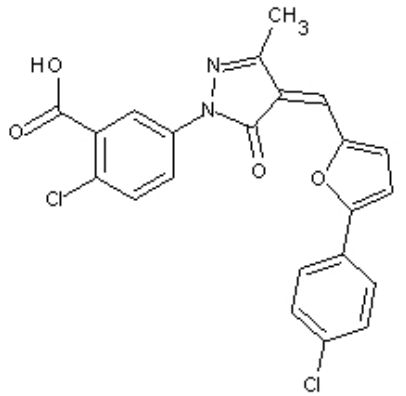

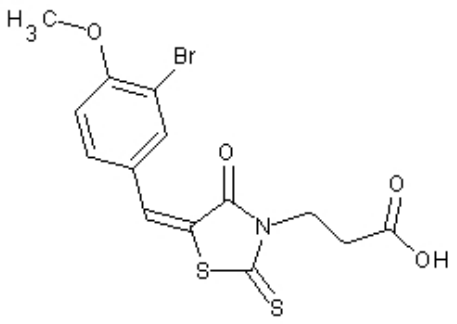

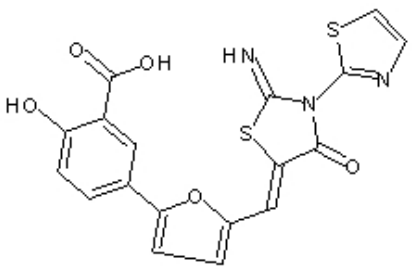

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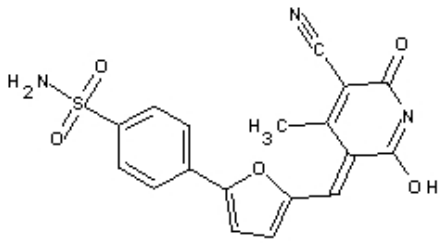

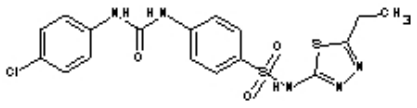

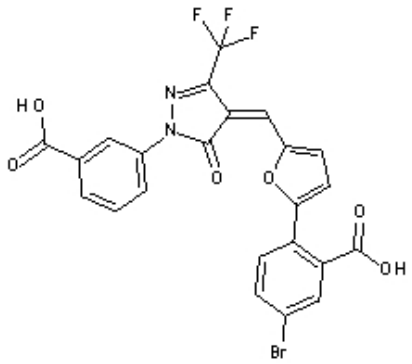

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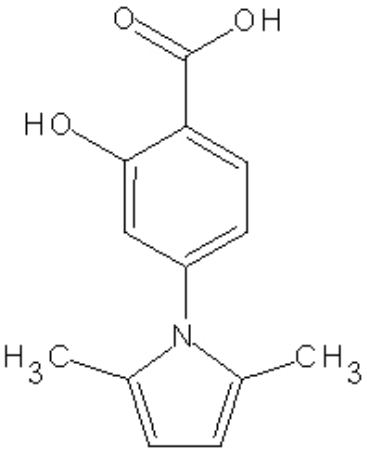

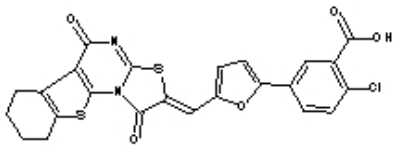

[Activators of Neutrophils analogs]