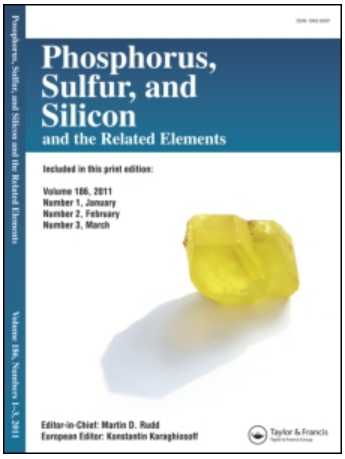

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Calixarene Methylenebisphosphonic Acids: Alkaline Phosphatase Inhibition and Docking Studies

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Calixarene Methylenebisphosphonic Acids: Alkaline Phosphatase Inhibition and Docking Studies

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The inhibition of alkaline phosphatase from bovine intestine mucosa and bovine kidney by calix[4]arenes functionalized at the marcocyclic upper rim by one or two methylene bisphosphonic acid fragments have been investigated. The mechanisms of enzyme inhibition have been discussed using a molecular docking approach by computational modeling of inhibitors into active centers of E. coli *alkaline phosphatase.*

Keywords Calixarene; methylenebisphosphonic acid; alkaline phosphatase; inhibition; docking

Calix[4]arenes bearing one or two methylenebisphosphonic acid fragments were characterized as efficient calf intestine alkaline phosphatase inhibitors.[1] In this article, kinetics of interaction of these compounds with alkaline phosphatase isoenzymes are analyzed.

Calix[4]arene bis-methylenebisphosphonic acid **1** displayed stronger inhibition of alkaline phosphatase from bovine intestine mucosa than calix[4]arene methylenebisphosphonic acid **2**. At the same time these macrocyclic compounds showed almost identical affinities to bovine kidney isoenzyme. For elucidation of the molecular mechanism of inhibition the tested compounds **1** and **2,** as well as methylenebisphosphonate and 4-hydroxyphenyl methylenebisphosphonate were docked computationally to the active site of *E. Coli* alkaline phosphatase. On the basis of experimental and theoretical results obtained, the possible role of functionally important amino acid residues in formation of enzyme-inhibitor complex at the active centre of alkaline phosphatase is discussed.

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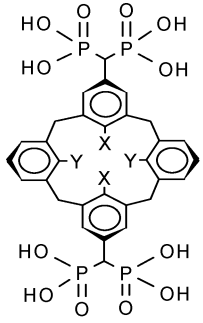
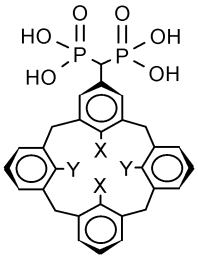


1



2

X=OH,

Y=OPr

REFERENCE

[1] A. I. Vovk, V. I. Kalchenko, S. A. Cherenok, V. P. Kukhar, O. V. Muzychka, and M. O. Lozynsky, *Org. Biomol. Chem.*, **2,** 3162 (2004).