A dinuclear zinc(II) complex of a new unsymmetric ligand with an N_5O_2 donor set; a structural and functional model for the active site of zinc phosphoesterases.

Autorzy

Biswanath Das

Henrik Daver

Monika Pyrkosz-Bulska

Elke Persch

Suman K. Barman

Rabindranath Mukherjee

Elżbieta Gumienna-Kontecka

Martin Jarenmark

Fahmi Himo

Ebbe Nordlander

Rok wydania

2014

Czasopismo

Journal of Inorganic Biochemistry

Numer woluminu

132

Strony

6-17

DOI

10.1016/j.jinorgbio.2013.08.001

Kolekcja

Naukowa

Streszczenie

The dinuclear complex [Zn2(DPCPMP)(pivalate)](ClO4), where DPCPMP is the new unsymmetrical ligand [2-(N-(3-((bis((pyridin-2-yl)methyl)amino)methyl)-2-hydroxy-5-methylbenzyl)-N-((pyridin-2-yl)methyl)amino)acetic acid], has been synthesized and characterized. The complex is a functional model for zinc phosphoesterases with dinuclear active sites. The hydrolytic efficacy of the complex has been investigated using bis-(2,4-dinitrophenyl)phosphate (BDNPP), a DNA analog, as substrate. Speciation studies using potentiometric titrations have been performed for both the ligand and the corresponding dizinc complex to elucidate the formation of the active hydrolysis catalyst; it reveals that the dinuclear zinc(II) complexes, [Zn2(DPCPMP)](2+) and [Zn2(DPCPMP)(OH)](+) predominate the solution above pH4. The relatively high pKa of 8.38 for water deprotonation suggests that a terminal hydroxide complex is formed. Kinetic investigations of BDNPP hydrolysis over the pH range 5.5-11.0 and with varying metal to ligand ratio (metal salt:ligand=0.5:1 to 3:1) have been performed. Variable temperature studies gave the activation parameters ΔH(‡)=95.59kJmol(-1), ΔS(‡)=-44.82Jmol(-1)K(-1), and ΔG(‡)=108.00kJmol(-1). The cumulative results indicate the hydroxido-bridged dinuclear Zn(II) complex [Zn2(DPCPMP)(μ-OH)](+) as the effective catalyst. The mechanism of hydrolysis has been probed by computational modeling using density functional theory (DFT). Calculations show that the reaction goes through one concerted step (SN2 type) in which the bridging hydroxide in the transition state becomes terminal and performs a nucleophilic attack on the BDNPP phosphorus; leaving group dissociates simultaneously in an overall inner sphere type activation. Calculated free energy barrier is in good agreement with the experimentally determined activation parameters.

Język

Angielski

Typ publikacji

Artykuł

Słowa kluczowe

zinc phosphoesterases, dinuclear active sities, DNA analog, transition state

Adres publiczny

http://dx.doi.org/10.1016/j.jinorgbio.2013.08.001

Strona internetowa wydawcy

http://www.elsevier.com