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CARBON DIOXIDE HIDRATION: MECHANISTIC LESSONS FROM ENZYMATIC SYSTEMS

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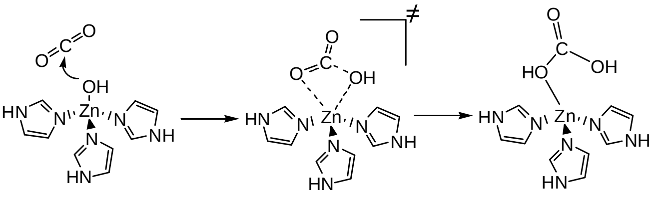
ABSTRACT. Carbon dioxide is arguably one of the most significant challenges for bioremediation, given its involvement in global warming. One reaction that would remove CO_2 from the atmosphere is hydration to bicarbonate. Living organisms have found a way to efficiently catalyze this reaction, employing the enzyme carbonic anhydrase, which employs a tetrahedral zinc active site. Here, we employ density functional (DFT) calculations in order to understand why nature has chosen this particular metal and this particular coordination geometry for CO_2 hydration. We ask the question whether other metals, such as iron or cooper, would be able to catalyze the same reaction in coordination environments such as seen in other metalloproteins. We find that the key of the carbonic anhydrase reaction lies not so much in the choice of metal, as in geometrical elements which allow the metal-bound carbonate to become a proper product.

Keywords: *carbon dioxide, carbonic anhydrase, density functional, hydration*

INTRODUCTION

Hydration of CO_2, a major metabolite in vivo as well as a major pollutant from an environmental point of view, is catalyzed in vivo by carbonic anhydrases (CANH) to produce bicarbonate, employing a tetrahedral zinc active site whose ligands are three endogenous histidine ligands and a hydroxide/aqua ligand. The active form of this site is the hydroxo one, and the metal-bound OH group is responsible for a nucleophylic attack on the CO_2 in the key step of the catalytic mechanism, wherein the nascent bicarbonate ligand becomes bidentate to the zinc (cf. scheme 1) [1, 2].



Scheme 1

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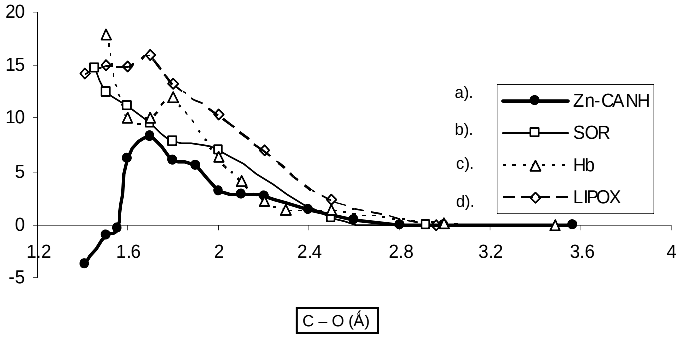
The choice of a tetrahedral zinc site for the CANH reaction is typically discussed in the general terms of the choice of zinc for non-redox, hydration/hydrolysis reaction. Here, we employ density functional theory (DFT) methods to explore the advantages of employing a tetrahedral zinc active site for the hydration of carbon dioxide. We find that zinc appears to be preferred by living organisms for the CANH active site due to its preference for tetrahedral coordination geometry (as opposed to the more sterically-demanding octahedral geometry preferred with other metals such as Fe). Other factors favoring zinc (such as redox activity of some metals, or intrinsic nucleophilicity of the metal-bound OH group) may also be at play but are seen to be mere side-benefits compared to the sterical argument.

RESULTS AND DISCUSSION

Scheme 2 shows the calculated potential energy surface for CO_2 hydration by the carbonic anhydrase active (CANH) site. The very low activation barrier is in good agreement with experiment and with previous computational results [2]. There is a rearrangement of the OH ligand throughout the reaction (with the transition state featuring the nascent bicarbonate ligand as bidentate): it is ligated to zinc in the reactants but is no longer a zinc ligand in the product (it is substituted by an oxygen atom originating from CO_2). Also shown are similar reaction curves for three other metalloprotein active sites which, like CANH, feature a metal bound-hydroxide at least under some conditions: lipoxygenase (LIPOX) [3], hemoglobin (Hb) [4] and superoxide reductase (SOR) [5]. With all three models the attack of the iron-bound hydroxide onto the carbon atom in carbon dioxide is extremely facile, implying that Zn-CANH is not unique in its ability to catalyze CO_2 hydration. However, the iron systems (Hb, SOR, LIPOX) do not feature a product stable enough to make the reaction feasible. This latter shortcoming is NOT due to the metal: it is rather due to the octahedral environment around the iron, which is more sterically demanding than the tetrahedral environment around the Zn in CANH, and therefore does not allow facile reorientation of the OH group away from the metal, as required by the mechanism presented schematically in scheme 1. Consistent with this, we also find (results not shown) that (1) water or ammonia instead of imidazole as ligands to the zinc model do not raise the reaction barrier to any significant extent, and (2) placing Co, Fe or Cu instead of Zn in the carbonic anhydrase model does not lower the reaction barrier to any significant extent.



Scheme 2

CONCLUSIONS

The key of the carbonic anhydrase reaction is not so much the choice of metal or ligand, as in geometrical elements which allow the metal-bound carbonate to become a proper product.

EXPERIMENTAL SECTION

The BP86 functional, which uses the gradient-corrected exchange functional proposed by Becke [6], the correlation functional by Perdew [7], 6-31G** were used as implemented in Spartan [8].

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REFERENCES

1. S. Schenk, J. Notni, U. Kohn, K. Wermann, E. Anders, *Dalton Trans.*, **2006**, 4191.
2. G. Parkin, *Chem. Rev.*, **2004**, *104*, 699.
3. N. Lehnert, E. I. Solomon, *J. Biol. Inorg. Chem.*, **2003**, *8*, 294.
4. J. Dunne, D. A. Svistunenko, A. I. Alayash, M. T. Wilson, C. E. Cooper, *Adv. Exp. Med .Biol.*, **1999**, *471*, 9.
5. R. Silaghi-Dumitrescu, I. Silaghi-Dumitrescu, E. D. Coulter, D. M. Kurtz, Jr., *Inorg. Chem.*, **2003**, *42*, 446.
6. A. D. Becke, *Phys. Rev.*, **1988**, 3098.

7. J. P. Perdew, *Phys. Rev.*, **1986**, *B33*, 8822.
8. SPARTAN '04 for Windows, Wavefunction Inc., 18401 Von Karman Avenue, Suite 370 Irvine, CA 92612.