

The Complete Phosphate Diester Hydrolytic Cleavage Mechanism Promoted by a Copper(II) Biomimetic Model of Catechol Oxidase

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Phosphate esters correspond to an ubiquitous group in biologic environments, and the study of its hydrolytic cleavage mechanism are subject of intense research¹. We present in this work a full theoretical analysis of the catalytic mechanism of a phosphate ester model (*bis*(2,4-dinitrophenyl)phosphate-**BDNPP**) by a dinuclear copper(II) complex originally designed to mimic the oxidase activity of catechol oxidase, revealing an interesting case of catalytic promiscuity in biomimetic systems. All the calculations (geometry optimizations, frequencies calculations and Intrinsic Reaction Coordinate-IRC) were performed at the B3LYP/6-31G(d)/LANL2DZ level in gas phase and single point corrections including the aqueous media contribution were done at B3LYP/6-31G(d)/LANL2DZ/PCM:UAHF level using the Gaussian09®. The theoretical investigation shows that the cleavage occurs via two preferential mechanisms, a *concerted* (the best agreement) and an *associative* one. The atomistic details of this hydrolytic cleavage following the *concerted mechanism* is presented on Figure 1(a) along with the first reaction intermediate structure on Figure 1(b). The *concerted mechanism* pass through a tight transition state, as revealed by the More O’Ferrall-Jencks diagram on Figure 1(c).

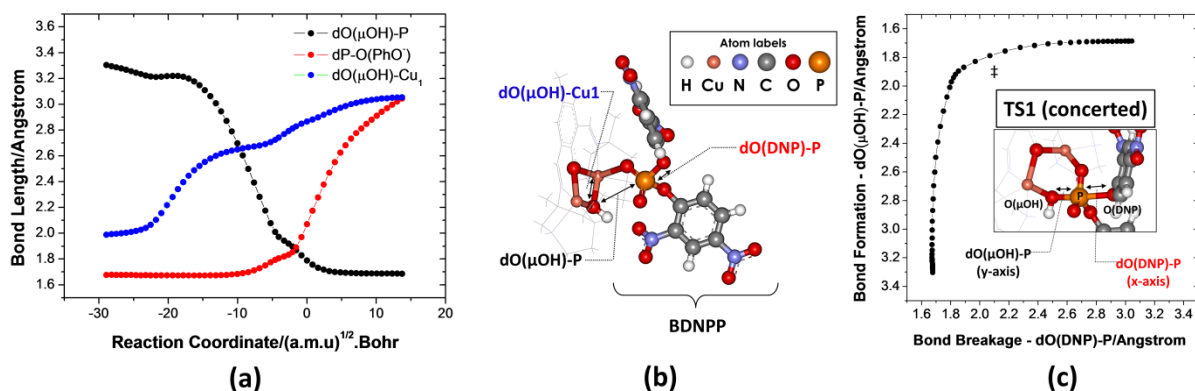


Figure 1. (a) Bond lengths (Angstrom) varying along the IRC coordinate. (b) Optimized structure for the first reaction intermediate following *concerted mechanism*. (c) More O’Ferrall-Jencks diagram showing the bond formation and bond breakage involving the oxygen atoms directly bonded to the phosphorus atom together with a close view of the first transition state (TS1).

Experimental results reveal a rate constant (k_{obs}) of $1.7 \times 10^{-5} \text{s}^{-1}$ and the free energy analysis for the *concerted mechanism*, using the Eyring equation, shows a rate constant of $2.6 \times 10^{-5} \text{s}^{-1}$. This work has been recently published by our research group and all the details regarding the other possible mechanism can be seen on reference 2.

- (1) Prasad, B. R.; Plotnikov, N. V.; Warshel, A. *J. Phys. Chem. B* **2013**, 117 (1), 153–163.
- (2) Esteves, L. F.; Rey, N. A.; Dos Santos, H. F.; Costa, L. A. S. *Inorg. Chem.* **2016**, 55 (6), 2806–2818.