A New Mechanism for the Function of Heme Oxygenase

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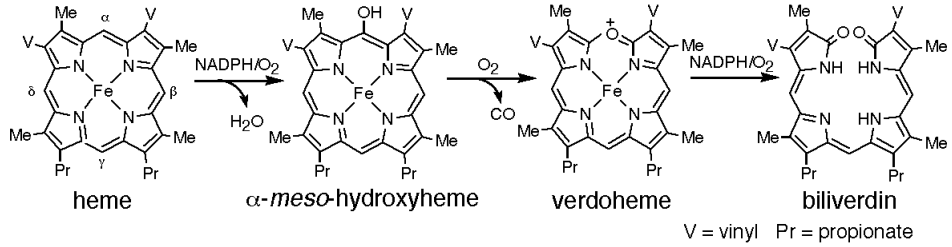
Heme oxygenase (HO) is distributed in a wide variety of organisms such as bacteria, plants, and mammal. A major function of this enzyme is iron homeostasis, freeing iron from heme for reuse. A porphyrin ring is regioselectively oxidized at the α-position to produce biliverdin, carbon monoxide, and free iron using dioxygen and NADH in these reactions. The hydroxylation at the α-carbon atom mediated by the iron-hydroperoxo and iron-oxo species are discussed on the basis of quantum mechanical calculations.[1] The initial reaction by the iron-hydroperoxo species is the direct attack of the distal OH group to the α-carbon. The O-O bond cleavage requires an activation energy of more than 40 kcal/mol at the B3LYP level of density functional theory, due to the low reactivity of the iron-hydroperoxo species.[2] On the other hand, the reaction by the iron-oxo species is initiated by a distortion of the porphyrin ring to allow the direct attack of the oxo group to the α–carbon. The activation energy for this reaction is also about 40 kacal/mol. Although the reactivity of the iron-oxo species is sufficient for the abstraction of an H atom from alkanes, this reaction is unlikely to occur because of the highly bent structure of the porphyrin ring in the transition state. A new mechanism for the function of this enzyme is proposed using quantum mechanics/molecular mechanics (QM/MM) calculations.



(1) T. Kamachi, A. F. Shestakov, and K. Yoshizawa, *J. Am. Chem. Soc.*, **126**, 3672 (2004).
(2) T. Kamachi, Y. Shiota, T. Ohta, and K. Yoshizawa, *Bull. Chem. Soc. Jpn.*, **76**, 721 (2003).