INVESTIGATION OF THE BIOLOGICAL ROLE OF SELENIUM: INSIGHT FROM DFT STUDIES ON MODEL CHALCOGENIDES

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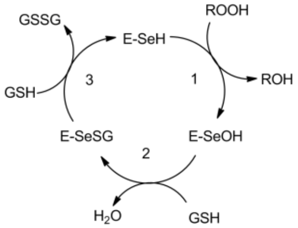
Selenocysteine (Sec), a modified amino acid containing selenium, is found in 25 proteins in the human body. The real reason for the presence of this unusual residue is still not clear, considered that its insertion mechanism is much more complicated than those of the more common amino acids. [1] What is clear, though, is that in glutathione peroxidases (GPx), an important class of proteins, a considerable loss of activity is found if Sec is substituted with Cys. The role of GPx enzymes is to catalyze the reduction of organic hydroperoxides via a three-step mechanism (Scheme 1). [2] The importance of this task in the prevention of many degenerative diseases has led scientists to try to emulate the efficiency of these enzymes through novel, chalcogen based molecules. [3] The main goal is to discover the relevant features of the enzymatic active site and to transfer them to small molecules for an efficient drug design. To achieve this, we are studying the elementary enzymatic reactions in model organic chalcogenides, in cysteine, selenocysteine and tellurocysteine and also in small cluster modelled on the GPx active site with current DFT techniques and activation strain analyses. Focus was centered on Step 3, a nucleophilic attack of a chalcogenolate to a dichalcogenide, which is considered to be rate determining and results on mechanism and energetics of these reactions are presented [4] together with novel findings from the investigation of the oxidation of chalcogenides with H_2O_2 (Step 1).



Scheme 1. Catalytic mechanism of GPx enzyme (E).

References

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