A Survey of Nickel-Containing Metalloenzymes

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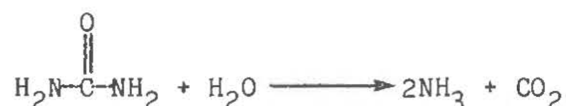
Only in recent years has there been evidence for a possible biological role for nickel. In contrast, almost every first row transition metal can be found in nature. Jack bean urease was the first nickel metalloenzyme to be recognized as such [1,2]. Nickel in jack bean urease is not redox active, but remains in the divalent state throughout its catalytic cycle. Ureases catalyze the hydrolysis of urea to ammonia and carbon dioxide.

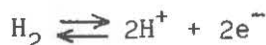


The ammonia produced is used by plants, rumen bacteria, and nitrogen-fixing bacteria as a source of nitrogen [3]. The exact geometry of the jack bean urease Ni(II) site is unknown, although electronic absorption spectroscopy combined with inhibition studies using β-mercaptoethanol suggest that the nickel atom is in a pseudo-octahedral environment with three nitrogens and three oxygens attached to the metal [4]. While the mechanism for urea hydrolysis has not been fully elucidated, substrate activation by coordination of the carbonyl oxygen is likely [5]. Since the enzyme has two nickel atoms per subunit, bimetallic mechanisms have also been proposed [3].

Carbon monoxide dehydrogenase (CODH) catalyzes the oxidation of CO to CO_2.

Nickel-containing CODH provides energy and a carbon source for acetogenic (acetate producing) and methanogenic (methane producing) bacteria [6]. Electron paramagnetic resonance (EPR) experiments with the enzyme from Clostridium thermoaceticum assign a rhombic signal to a Ni(III) species. Incubation of CODH with CO results in an axial signal and exchange of CO for $(^{13}C)CO$ and/or ^{61}Ni-enrichment (^{61}Ni, I = 3/2) confirms the existence of a Ni-C species [7]. Recently, CODH has been proven necessary for acetate metabolism. It appears that the enzyme catalyzes the conversion of coenzyme A to its acyl derivative [9].

Hydrogenase provides energy in the form of electrons for substrate reduction in sulfate-reducing and methanogenic bacteria.



Inactive hydrogenase from Desulfovibrio gigas exhibits a rhombic EPR signal assigned to Ni(III). X-ray absorption fine structure (EXAFS) and x-ray absorption near edge spectroscopy (XANES) conclude that a Ni(III) → Ni(II) reduction occurs upon incubation of the enzyme with hydrogen and that both Ni(III) and Ni(II) coordinate to approximately four sulfur atoms [9]. An intermediate in the hydrogen reduction of hydrogenase has been tentatively assigned to a nickel-hydride species. Two hypothetical redox schemes, one involving Ni(III) → Ni(II) and the other Ni(III) → Ni(0) are currently being investigated using EPR and electrochemical methods [10,11].

Methylreductase catalyzes the anaerobic reduction of C_1 compounds to methane [12]. Almost all methanogens can utilize CO_2 as their substrate.

$$4H_2 + CO_2 \longrightarrow CH_4 + 2H_2O$$

Methanogenesis is quite complex, although well characterized compared to the other systems mentioned so far. One mole of enzyme contains two mole of nickel in the form of two mole of F430, a nickel-containing tetrapyrrole so named because of its characteristic absorbance at 430 nm [12]. F430 from Methanobacterium thermoautotrophicum exists both in free form and protein bound. Freshly isolated protein-bound enzyme exhibits a short-lived EPR signal and the nickel atom appears to reside in a tetragonally-distorted octahedral environment with four equivalent nitrogen atoms in the equatorial plane [13]. Sodium dithionite reduces free F430 to give EPR signals matching those of the freshly isolated protein-bound form, suggesting a Ni(I) state. EXAFS experiments on protein-bound F430 provide evidence for octahedral coordination about nickel. Free F430 appears to consist of square planar Ni(II) [14]. In general, Ni(II) complexes with hydroporphinoid ligands exhibit a characteristic conformational ruffling of the ligand system due to the small size and electrophilicity of the nickel ion [15,16]. Axial ligation removes any remaining electrophilicity and thus flattens the tetrapyrrole ring [17].

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