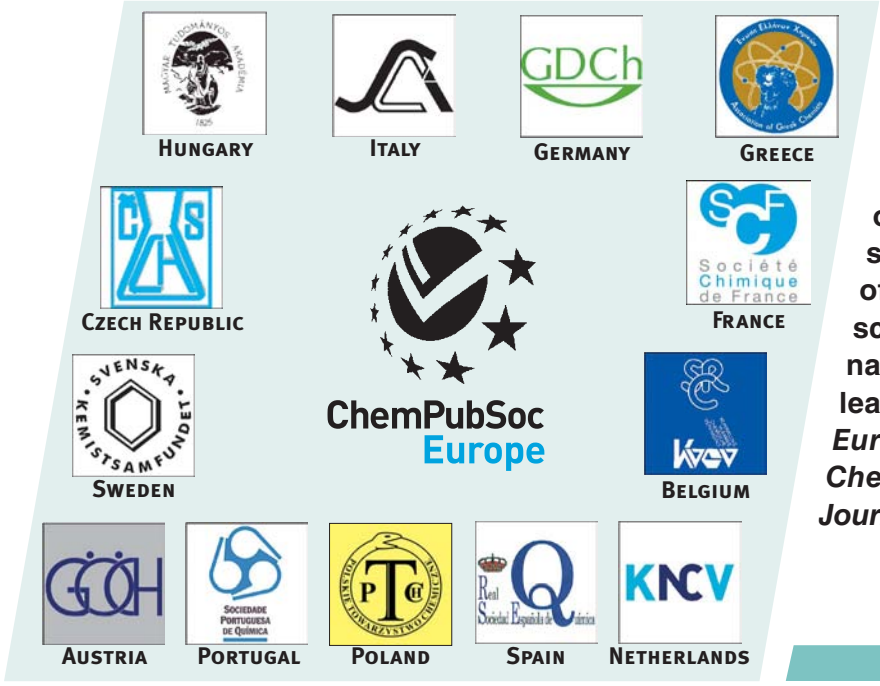
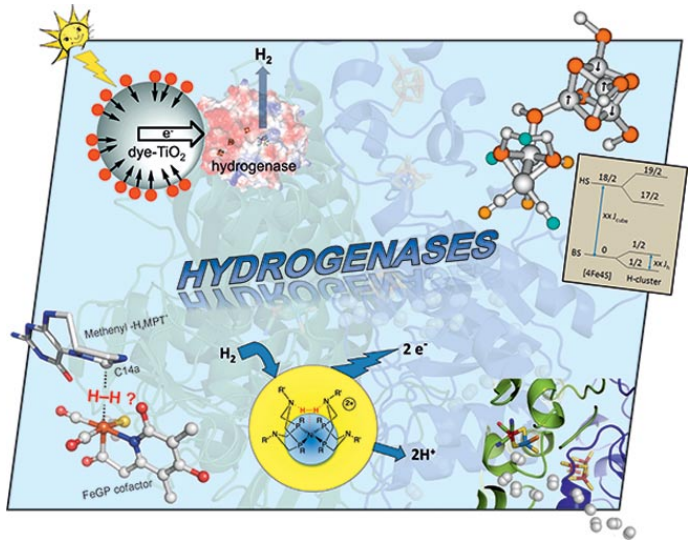


EurJIC is a journal of ChemPubSoc Europe, a union of 16 European chemical societies formed for the purpose of publishing high- quality science. All owners merged their national journals to form two leading chemistry journals, the *European Journal of Inorganic Chemistry* and the *European Journal of Organic Chemistry*.

Other ChemPubSoc Europe journals are *Chemistry – A European Journal*, *ChemBioChem*, *ChemPhysChem*, *ChemMedChem*, *ChemSusChem* and *ChemCatChem.*

COVER PICTURE

The background of the cover picture shows a schematic representation of a hydrogenase, the topic of this cluster issue, as a watermark. Superimposed are illustrations that highlight the scope of the articles: [NiFeSe] hydrogenases (bottom right-hand corner and background) are the focus of the Microreview by Inês Pereira and Pedro Matias et al. (p. 948ff). Seigo Shima et al. (p. 963ff) examine the iron guanylylpyridinol cofactor of [Fe] hydrogenase (bottom left-hand corner). From a theoretical point of view, Claudio Greco and Alexey Silakov et al. (p. 1043ff) probe the magnetic properties of [FeFe]-hydrogenases (top right-hand corner). The use of hydrogenases in vivo and as hybrids for H_2 production (top left-hand corner), as well as of cobalt and nickel functional models for H_2 oxidation and production (bottom middle), are covered in the Microreviews by Erwin Reisner (p. 1005ff) and Morris Bullock et al. (p. 1017ff), respectively. Many thanks to the authors for their creative designs.



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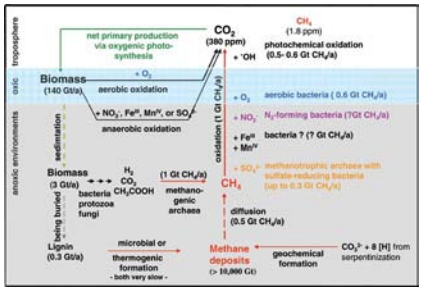
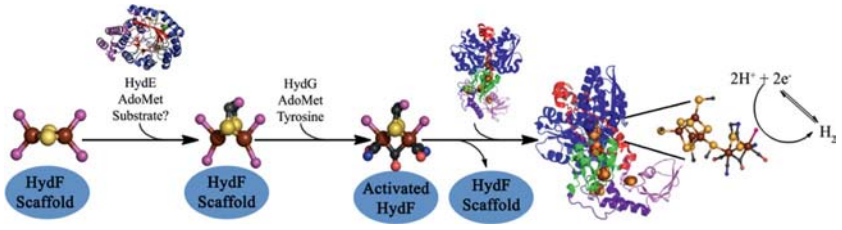
ESSAY

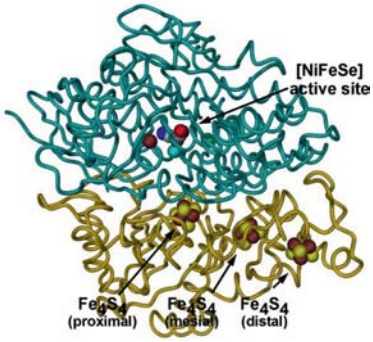


The collection of contributions in this cluster issue on hydrogenases deals with the mechanism, biosynthesis, evolution, and application of hydrogenases. This essay introduces the reader to the global hydrogen cycle and the types of hydrogenases that are used for proton reduction and dihydrogen oxidation.

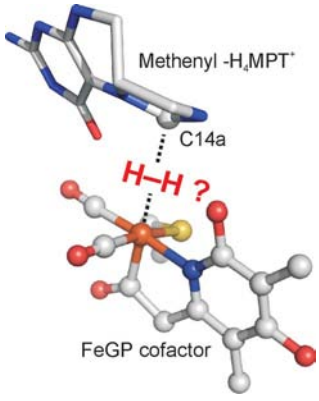
MICROREVIEWS



Hydrogenase active site (H-cluster) ligands are synthesized by maturation enzymes to generate an active enzyme capable of catalyzing the formation or oxidation of hydrogen. This review discusses the different hydrogenase maturation systems, and it also describes cyanide and carbon monoxide biosynthetic systems. Particular focus is given to [FeFe]-hydrogenase H-cluster biosynthesis.



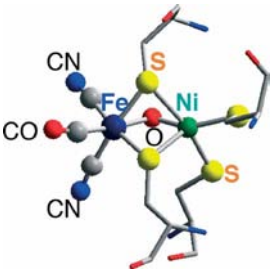
Herein we review the distribution, biochemical, catalytic, spectroscopic and structural properties of known [NiFeSe] hydrogenases of the Hys, Vhu and Fru classes and report on active-site models for the Vhu and Fru enzymes, for which there is no structural information. Hys hydrogenases are attractive catalysts for technological applications such as biohydrogen production.



[Fe]-hydrogenase catalyzes the reversible reduction of methenyltetrahydromethanopterin with H_2. This third type of hydrogenase contains a unique iron–guanylylpyridinol (FeGP) cofactor. In the closed model of the enzyme, the iron ligation site *trans* to the acyl carbon atom is next to the C14a carbon atom and is therefore considered to be the H_2 binding site.

Models for the [NiFe] Hydrogenase

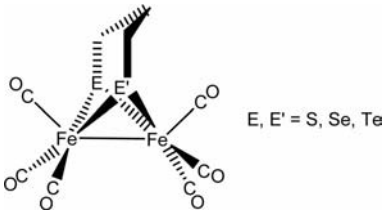
[NiFe] hydrogenase is the most common type among the currently known hydrogenases, and its active site consists of an "organometallic" Fe−Ni complex supported by cysteinyl thiolate ligands. This review presents an overview of the synthesis, properties, and reactions of thiolate-bridged iron−nickel complexes that model the active site of [NiFe] hydrogenase.



Keywords: Hydrogenases / Iron / Nickel / Thiolates / Enzyme models

[FeFe] Hydrogenases

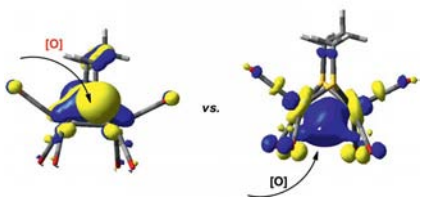
[FeFe] hydrogenase models containing different chalcogens such as S, Se, or Te are reviewed and compared with diiron dithiolato compound analogues for their ability to catalyze the formation of H_2 from weak acids.



Keywords: Iron / Selenium / Tellurium / Hydrogenases / Electrocatalysis

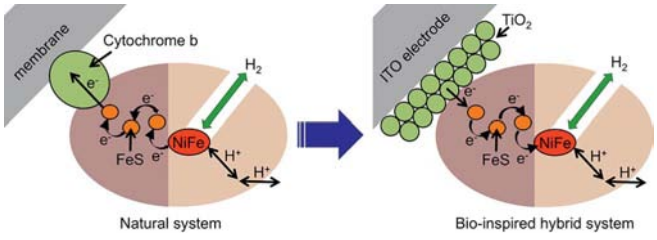
Sulfoxygenation

An overview of the oxygen sensitivity of [NiFe] and [FeFe] hydrogenase and studies of oxygen reactivity with synthetic analogues of the enzyme active site are presented. Discrete S-oxygenate complexes that maintain the Ni-S or Fe-S connectivity could signify reversible oxygen damage, and a protective, "antioxidant" role of the sulfur atoms in the active sites.



Keywords: Hydrogenases / Biomimetics / Iron / Nickel / Oxygen / Sulfur

Hydrogen Production



Hydrogenases are enzymes that catalyze the reversible production of H_2 from aqueous protons at an iron or nickel/iron active site. The utilization of these enzymes in vivo and by man-made hybrid systems for photochemical hydrogen production is reviewed.

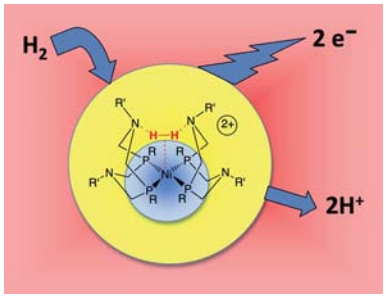
Keywords: Hydrogen / Hydrogenases / Artificial photosynthesis / Electrochemistry / Photochemistry

CONTENTS

Molecular Electrocatalysts

Molecular Electrocatalysts for the Oxidation of Hydrogen and the Production of Hydrogen – The Role of Pendant Amines as Proton Relays

Keywords: Hydrogen / Electrochemistry / Hydrides / Homogeneous catalysis / Proton transport

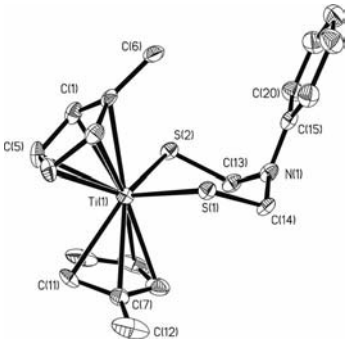


Pendant amines function as proton relays in molecular electrocatalysts, facilitating transfer of protons to and from the metal. A series of Ni^{II} complexes with diphosphanes bearing pendant amines are catalysts for oxidation of H_2, and a related series of Ni^{II} and Co^{II} complexes catalyze the production of H_2 by reduction of protons.

SHORT COMMUNICATIONS

Azadithiolate Complexes

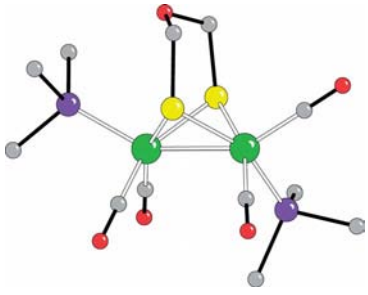
Keywords: Iron / Titanium / Hydrogenases / Azadithiolates / Sulfur



Azadithiolate ($S^- – CH_2 – NH – CH_2 – S^-$) is one of the unusual cofactors of the [FeFe]-hydrogenase enzyme. Reaction of $[(MeC_5H_4)_2Ti(SH)_2]$ with cyclic imines with the formula $(CH_2NR)_3$ gives 2-aza-1,3-dithiolato chelate complexes $[(MeC_5H_4)_2Ti\{(SCH_2)_2NR\}]$. These compounds demonstrate that azadithiolate ligands can exist on mononuclear metal centers.

Protonation Mechanisms

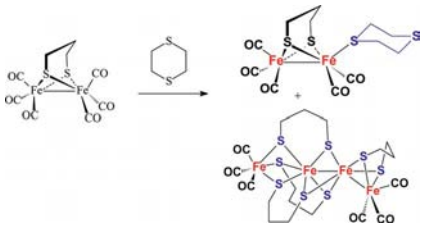
Keywords: [FeFe]-Hydrogenase / Metalloenzymes / Protonation / Kinetics / Reaction mechanisms



The identity of the central atom in the dithiolate bridge of the [FeFe]-hydrogenase {2Fe2S} subsite is a key question in the activity of the enzyme. Protonation kinetics studies on the simple model $Fe_2(\mu\text{-odt})(CO)_4(PMe_3)_2$ (odt = 2-oxapropane-1,3-dithiolate) show that the identiy of this atom has significant implications for the rate of protonation in model complexes.

Bioinspired Organometallic Molecules

Keywords: Iron / Sulfur / Hydrogen / Electrochemistry / Hydrogenases / Bioinspired chemistry

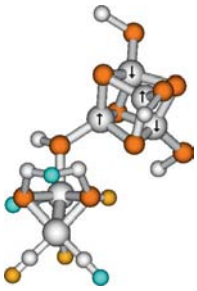


Molecules in which a [2Fe3S] core is combined with six-membered heterocyclic sulfur ligands with well positioned heteroatoms, such as 1,4-dithiane ($C_4H_8S_2$) and 1,4-thioxane (C_4H_8OS) and an unexpected [4Fe8S] cluster have been elaborated.

FULL PAPERS

Calculations on Hydrogenases

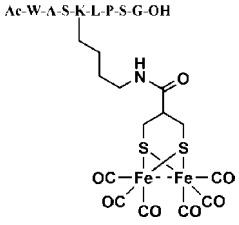
Magnetic properties of [FeFe]-hydrogenases are computed, based on purely QM and on QM/MM enzyme models. Calculated *g* values are highly dependent on the broken-symmetry coupling scheme and on the level of theory used; theoretical hyperfine couplings are more stable, and indicate the presence of an exogenous ligand like a water molecule in the partially oxidized active site.



Keywords: Computer chemistry / Density functional calculations / Magnetic properties / EPR parameters calculation / Quantum mechanics / Enzymes / Hydrogenases / Hydrogen

Enzyme Models

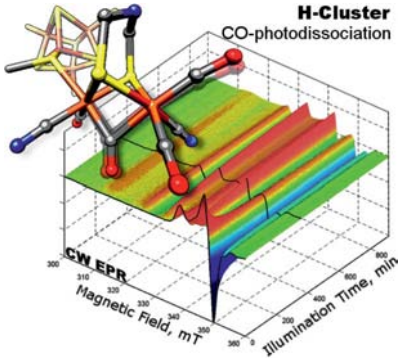
A general method for modification of a primary amine in peptides to create a dithiol anchor for metalloclusters is presented. The dithiol side chain is then used to construct a peptide-ligated [FeFe]-hydrogenase model.



Keywords: Bioinorganic chemistry / Bioorganometallic chemistry / Enzyme models / Hydrogenase / Peptidomimetics / Designed peptide

Photodissociation in Fe Hydrogenases

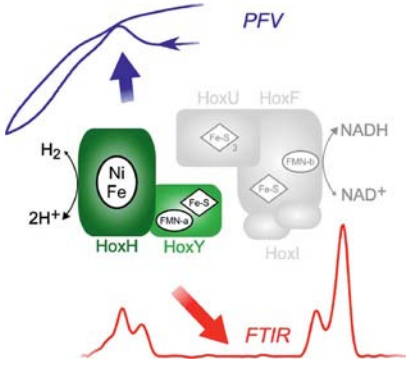
Photodissociation of the CO ligands of the active site of the [FeFe] hydrogenase from *D. desulfuricans* was studied by advanced pulse EPR methods. Two light-induced states were found. One of them is characterized by removal of the external CO ligands, while another by removal of the bridging CO ligand. The electronic structure of the latter was found to be different from the other EPR active states.



Keywords: [FeFe] hydrogenases / EPR spectroscopy / Photodissociation / Electronic structure / Structure elucidation

[NiFe] Hydrogenase

The engineered subcomplex, HoxHY, of the NAD^+-reducing soluble hydrogenase from *Ralstonia eutropha* is catalytically active for H^+ reduction and H_2 oxidation. Spectroscopic analyses revealed one FeS cluster, a [NiFe] active site with standard ligation, and substoichiometric amounts of FMN. Redox dependent transitions between active and inactive states were examined by IR and electrochemistry.



Keywords: Hydrogen / Enzyme catalysis / [NiFe] hydrogenase / IR spectroscopy / Redox chemistry / Electrochemistry / Metabolism

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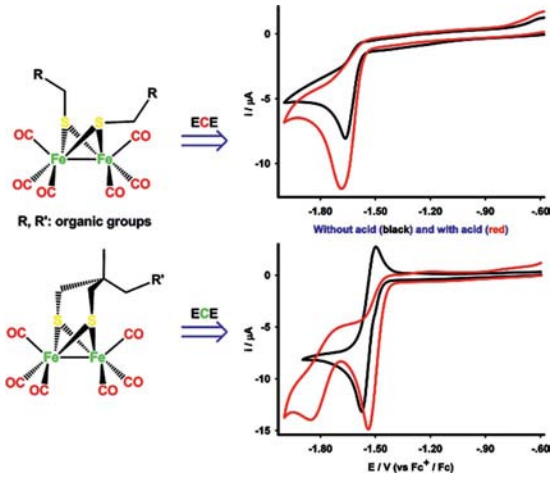
Mimics of [FeFe]-Hydrogenases

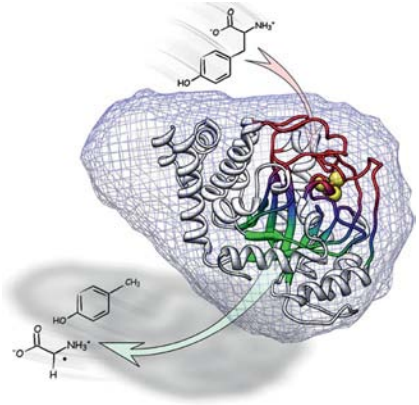


The bridging linkages of the diiron model complexes govern directly their electrochemistry and electrocatalytic reduction of protons, as the linkages determine the nature of the coupled chemical reaction in the ECE processes.

Keywords: [FeFe]-hydrogenases / Enzyme models / Iron / Bridging ligands / Electrochemistry / Reduction

[FeFe]-Hydrogenase

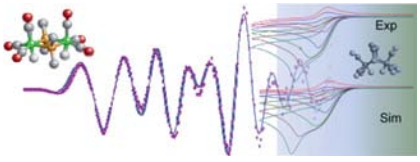
We have explored the CO/CN^- synthesis catalyzed by [FeFe]-hydrogenase maturase HydG with site-directed mutants, and have performed functional studies, SAXS spectroscopy and homology modeling. We conclude that whereas CN^- is made in the active site-containing TIM-barrel domain, the CO precursor follows an internal path from this site to a catalytic [4Fe-4S] cluster in the tightly bound C-terminal domain.



Keywords: Enzymes / [FeFe]-Hydrogenase / Carbon monoxide / Cyanide / Active site maturation

Electrocatalytic Proton Reduction

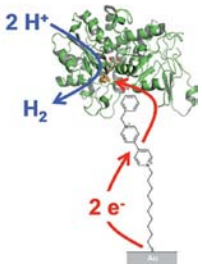
The two reaction paths for dihydrogen elimination from two-electron-reduced, protonated diiron compounds related to the hydrogenase H-cluster available from DFT calculations are considered in terms of a range of spectroscopic, electrochemical, DFT and XAFS studies of $[FeH(CO)_3](\mu\text{-}PPh_3)_2$. Limitations are evident for the transition states associated with both of the calculated reaction paths.



Keywords: Hydrogenases / XAFS / Iron / Hydrides / Reduction

Specific Immobilization of Proteins

We demonstrated the specific binding of a [FeFe] hydrogenase to a modified gold surface by IR spectroscopy. A novel linker thiol, 1-(10-mercaptodecyl)-1′-benzyl-4,4′-bipyridinium dibromide (MBBP), was synthesized and characterized. The hydrogenase layer releases H_2 at −450 mV vs. NHE, which was probed by electrochemistry and gas chromatography. Protein binding and electron transfer are discussed.



Keywords: Hydrogen / Metalloenzymes / Immobilization / Electrochemistry / IR spectroscopy

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* Author to whom correspondence should be addressed.

Supporting information on the WWW (see article for access details).

If not otherwise indicated in the article, papers in issue 6 were published online on February 14, 2011

