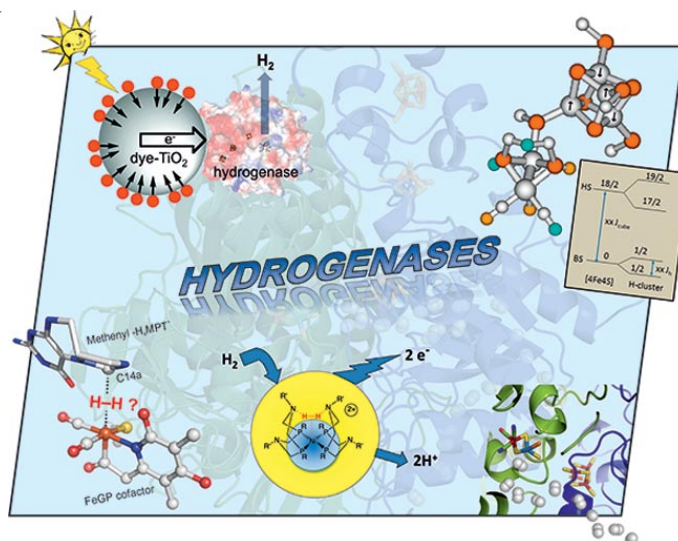


EurJIC is a journal of ChemPubSoc Europe, a union of 16 European chemical societies formed for the purpose of publishing high-quality science. All owners merged their national journals to form two leading chemistry journals, the *European Journal of Inorganic Chemistry* and the *European Journal of Organic 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 co-factor 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 H₂ production (top left-hand corner), as well as of cobalt and nickel functional models for H₂ 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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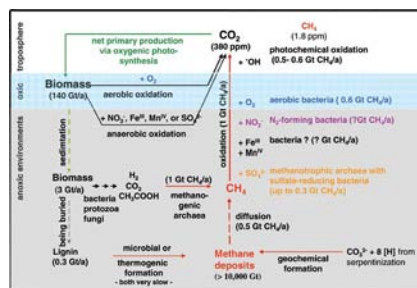
ESSAY

The Global Hydrogen Cycle

R. K. Thauer* 919–921

Hydrogenases and the Global H₂ Cycle

Keywords: Hydrogen / Nickel / Iron / Sulfur / Carbonyl ligands / Cyanide ligands



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.

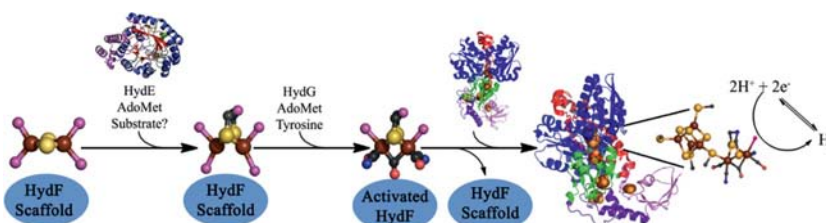
MICROREVIEWS

H-Cluster Biosynthesis

K. D. Swanson, B. R. Duffus,
T. E. Beard, J. W. Peters,*
J. B. Broderick* 935–947

Cyanide and Carbon Monoxide Ligand Formation in Hydrogenase Biosynthesis

Keywords: Enzymes / Cyanide / Carbon monoxide / Hydrogenase / H-cluster biosynthesis



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

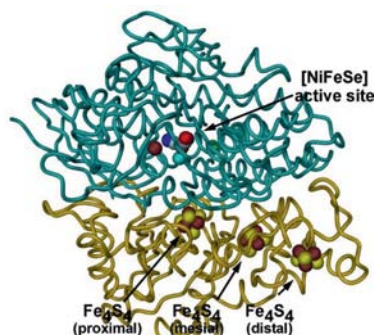
hydrogenase maturation systems, and it also describes cyanide and carbon monoxide biosynthetic systems. Particular focus is given to [FeFe]-hydrogenase H-cluster biosynthesis.

Biohydrogen Production

C. S. A. Baltazar, M. C. Marques,
C. M. Soares, A. M. DeLacey,
I. A. C. Pereira,*
P. M. Matias* 948–962

Nickel–Iron–Selenium Hydrogenases – An Overview

Keywords: Hydrogen / Structural Biology / Molecular modeling / Biological activity / Structure–activity relationships



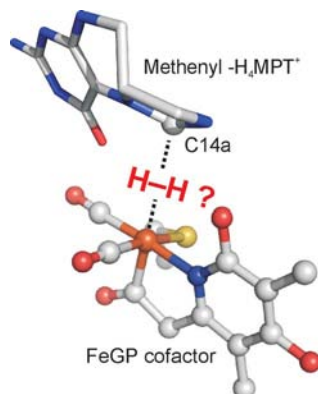
Herein we review the distribution, biochemical, catalytic, spectroscopic and structural properties of known [NiFeSe] hydrogenases of the Hys, Vhu and Fru classes and report on active-site models for the Vhu and Fru enzymes, for which there is no structural information. Hys hydrogenases are attractive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

Hydrogen Activation

S. Shima,* U. Ermler 963–972

Structure and Function of [Fe]-Hydrogenase and its Iron–Guanylylpyridinol (FeGP) Cofactor

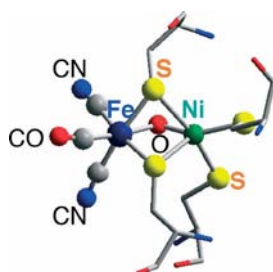
Keywords: Bioinorganic chemistry / Hydrogenases / Structure elucidation / Oxidoreductases / Structure–activity relationships



[Fe]-hydrogenase catalyzes the reversible reduction of methenyltetrahydromethanopterin with H₂. 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 H₂ 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.



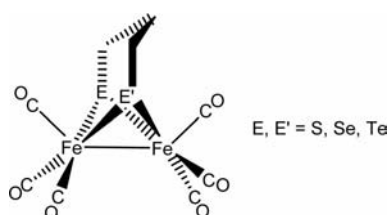
Y. Ohki, K. Tatsumi* 973–985

Thiolate-Bridged Iron–Nickel Models for 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 H₂ from weak acids.



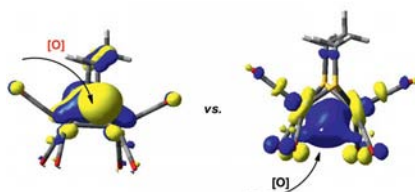
M. K. Harb, U.-P. Apfel,
T. Sakamoto,* M. El-khateeb,*
W. Weigand 986–993

Diiron Dichalcogenolato (Se and Te) Complexes: Models for the Active Site of [FeFe] Hydrogenase

Keywords: Iron / Selenium / Tellurium / Hydrogenases / Electrocatalysis

Sulfoxxygenation

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.

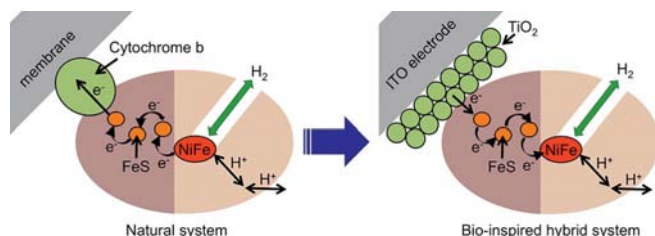


M. Y. Darensbourg,*
W. Weigand* 994–1004

Sulfoxxygenation of Active Site Models of [NiFe] and [FeFe] Hydrogenases – A Commentary on Possible Chemical Models of Hydrogenase Enzyme Oxygen Sensitivity

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

Hydrogen Production



Hydrogenases are enzymes that catalyze the reversible production of H₂ 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.

E. Reisner* 1005–1016

Solar Hydrogen Evolution with Hydrogenases: From Natural to Hybrid Systems

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

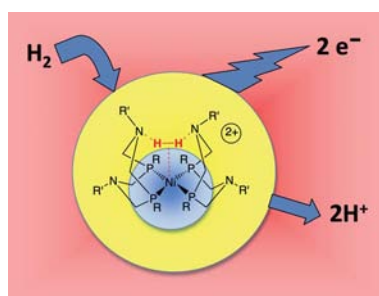
CONTENTS

Molecular Electrocatalysts

D. L. DuBois,
R. M. Bullock* 1017–1027

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 H₂, and a related series of Ni^{II} and Co^{II} complexes catalyze the production of H₂ by reduction of protons.

SHORT COMMUNICATIONS

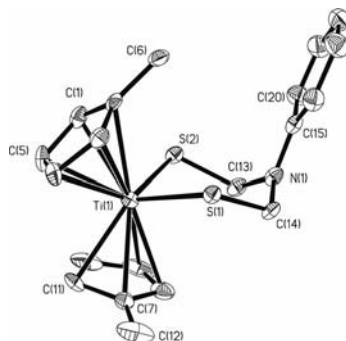
Azadithiolate Complexes

R. Angamuthu, M. E. Carroll, M. Ramesh,
T. B. Rauchfuss* 1029–1032



A New Route to Azadithiolato Complexes

Keywords: Iron / Titanium / Hydrogenases / Azadithiolates / Sulfur



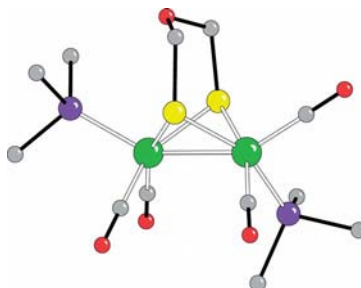
Azadithiolate ($\text{S}^- - \text{CH}_2 - \text{NH} - \text{CH}_2 - \text{S}^-$) is one of the unusual cofactors of the [FeFe]-hydrogenase enzyme. Reaction of $[(\text{MeC}_5\text{H}_4)_2\text{Ti}(\text{SH})_2]$ with cyclic imines with the formula $(\text{CH}_2\text{NR})_3$ gives 2-aza-1,3-dithiolato chelate complexes $[(\text{MeC}_5\text{H}_4)_2\text{Ti}\{(\text{SCH}_2)_2\text{NR}\}]$. These compounds demonstrate that azadithiolate ligands can exist on mononuclear metal centers.

Protonation Mechanisms

A. Jablonskytė, J. A. Wright,
C. J. Pickett* 1033–1037

[FeFe]-Hydrogenase Models: Unexpected Variation in Protonation Rate between Dithiolate Bridge Analogues

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 $\text{Fe}_2(\mu\text{-odt})(\text{CO})_4(\text{PMe}_3)_2$ (odt = 2-oxapropane-1,3-dithiolate) show that the identity of this atom has significant implications for the rate of protonation in model complexes.

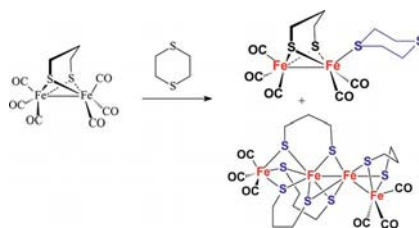
Bioinspired Organometallic Molecules

K. Charretier, J.-F. Capon, F. Gloaguen,*
F. Y. Pétillon, P. Schollhammer,*
J. Talarmin 1038–1042



Diiron Complexes with a [2Fe3S] Core Related to the Active Site of [FeFe]H₂ases

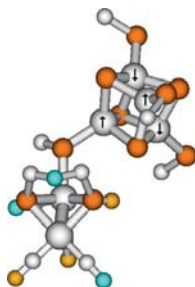
Keywords: Iron / Sulfur / Hydrogen / Electrochemistry / Hydrogenases / Bioinspired chemistry



Molecules in which a [2Fe3S] core is combined with six-membered heterocyclic sulfur ligands with well positioned heteroatoms, such as 1,4-dithiane ($\text{C}_4\text{H}_8\text{S}_2$) and 1,4-thioxane ($\text{C}_4\text{H}_8\text{OS}$) and an unexpected [4Fe8S] cluster have been elaborated.

FULL PAPERS

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.



Calculations on Hydrogenases

C. Greco,* A. Silakov,* M. Bruschi,
U. Ryde, L. De Gioia,
W. Lubitz 1043–1049

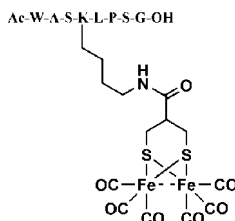
Magnetic Properties of [FeFe]-Hydrogenases: A Theoretical Investigation Based on Extended QM and QM/MM Models of the H-Cluster and Its Surroundings



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 metallocusters is presented. The dithiol side chain is then used to construct a peptide-ligated [FeFe]-hydrogenase model.



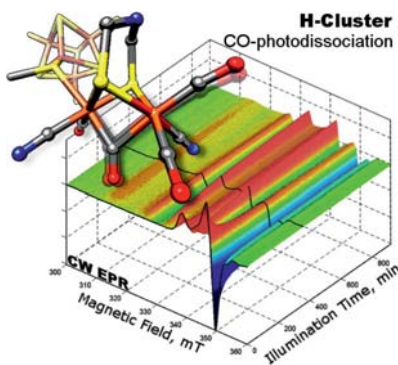
S. Roy, S. Shinde,
G. A. Hamilton, H. E. Hartnett,
A. K. Jones* 1050–1055

Artificial [FeFe]-Hydrogenase: On Resin Modification of an Amino Acid to Anchor a Hexacarbonyliron Cluster in a Peptide Framework



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

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.



Photodissociation in Fe Hydrogenases

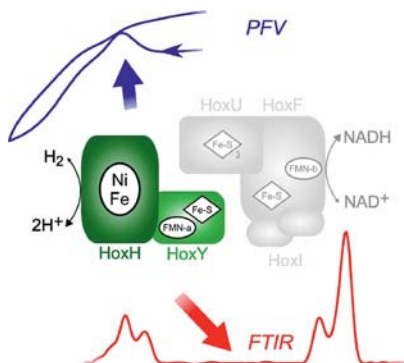
A. Silakov,* E. J. Reijerse,
W. Lubitz* 1056–1066

Unraveling the Electronic Properties of the Photoinduced States of the H-Cluster in the [FeFe] Hydrogenase from *D. desulfuricans*



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

The engineered subcomplex, HoxHY, of the NAD⁺-reducing soluble hydrogenase from *Ralstonia eutropha* is catalytically active for H⁺ reduction and H₂ 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.



[NiFe] Hydrogenase

L. Lauterbach, J. Liu, M. Horch,
P. Hummel, A. Schwarze, M. Haumann,
K. A. Vincent, O. Lenz,
I. Zebger* 1067–1079

The Hydrogenase Subcomplex of the NAD⁺-Reducing [NiFe] Hydrogenase from *Ralstonia eutropha* – Insights into Catalysis and Redox Interconversions



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

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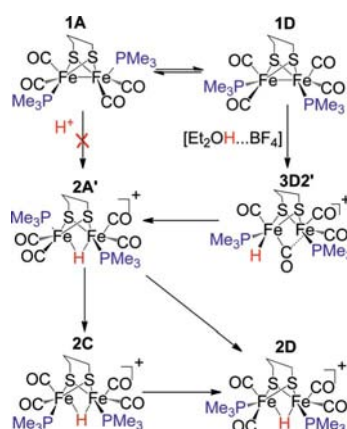
Protonation in Hydrogenase Model

C. Liu, J. N. T. Peck, J. A. Wright,
C. J. Pickett,* M. B. Hall* 1080–1093



Density Functional Calculations on Protonation of the [FeFe]-Hydrogenase Model Complex $\text{Fe}_2(\mu\text{-pdt})(\text{CO})_4(\text{PMe}_3)_2$ and Subsequent Isomerization Pathways

Keywords: [FeFe]-Hydrogenase / Protonation / Isomerization / Hydrides / Density functional calculations



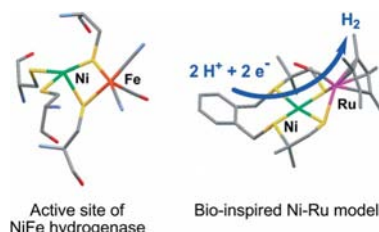
The initial protonation of a diiron model complex occurs terminally at one Fe on the basal/basal isomer **1D** rather than the apical/basal isomer **1A**. Then, rearrangement occurs to the bridging species **2A**, which then rearranges more slowly through two competing paths to the most stable isomer, **2D**.

Hydrogenase Models

S. Canaguier, M. Fontecave,
V. Artero* 1094–1099

Cp^{*-} -Ruthenium–Nickel-Based H_2 -Evolving Electrocatalysts as Bio-inspired Models of NiFe Hydrogenases

Keywords: Hydrogen / Biomimetic synthesis / Enzyme models / Metalloenzyme models / Electrocatalysis / Nickel / Ruthenium



The introduction of a pentamethylcyclopentadienyl (Cp^{*-}) ligand into the coordination sphere of Ru has led to the preparation of a new series of active and robust Ni–Ru catalysts for the evolution of H_2 as mimics of the active site of NiFe hydrogenases.

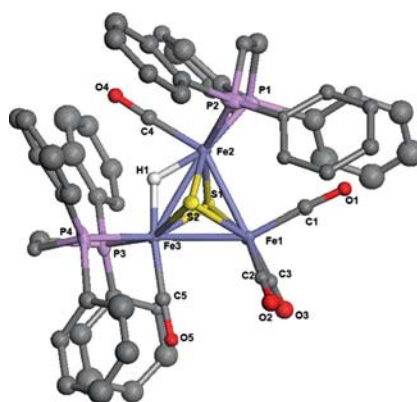
Synthesis of [3Fe2S] from [2Fe2S]

W. Gao,* J. Sun, M. Li,
T. Åkermar, K. Romare,
L. Sun, B. Åkermar* 1100–1105



Synthesis of a [3Fe2S] Cluster with Low Redox Potential from [2Fe2S] Hydrogenase Models: Electrochemical and Photochemical Generation of Hydrogen

Keywords: Enzyme models / Electrochemistry / Iron / Hydrogenases / Cluster compounds



An unexpected and efficient transformation of the [2Fe2S] complexes **1a** and **1b** into complex [3Fe2S(dppv)₂] (**2**) [dppv = bis(*cis*-Ph₂PCH=CHPh₂)] is described. Under acidic conditions, cyclic voltammetry experiments showed electrochemical activity for hydride **3**, formed by protonation of complex **2**, at -1 V vs. Fc/Fc^+ and catalysis of hydrogen evolution at -1.23 V vs. Fc/Fc^+ .

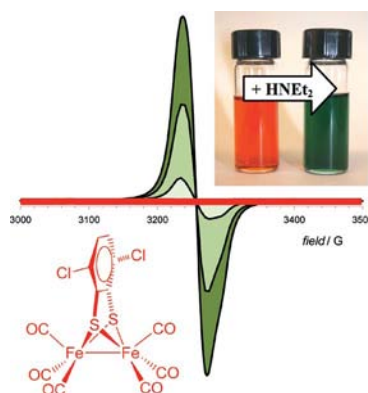
Bioinorganic Iron Carbonyls

D. Streich, M. Karnahl, Y. Astuti,
C. W. Cady, L. Hammarström,
R. Lomoth,* S. Ott* 1106–1111



Comparing the Reactivity of Benzenedithiolate- versus Alkyldithiolate-Bridged $\text{Fe}_2(\text{CO})_6$ Complexes with Competing Ligands

Keywords: Enzyme models / Hydrogenases / IR spectroscopy / S ligands / Carbonyl ligands



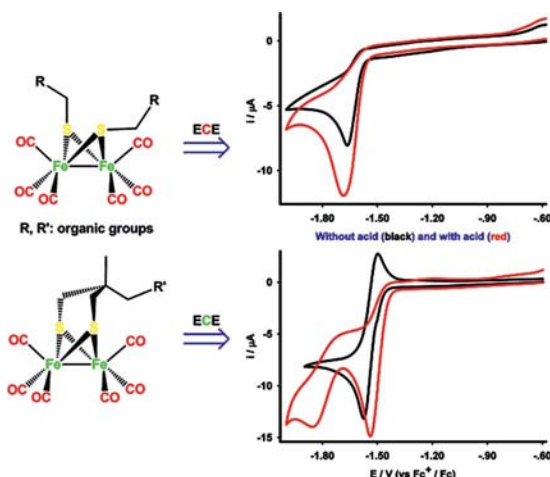
Exposure of $[(\mu\text{-bdt})\text{Fe}_2(\text{CO})_6]$, (**bdt**)**1**, to secondary amines or dmf results in major structural changes of the complex and formation of a magnetically uncoupled Fe^{I} species that carries the bdt and CO ligands. This reactivity contrasts that of $[(\mu\text{-edt})\text{Fe}_2(\text{CO})_6]$, (**edt**)**1**, and $[(\mu\text{-pdt})\text{Fe}_2(\text{CO})_6]$, (**pdt**)**1**, which are unreactive under identical conditions (bdt, edt, pdt = benzene-, ethyl-, propyldithiolate, respectively).

Mimics of [FeFe]-Hydrogenases

Y. Tang, Z. Wei, W. Zhong,
X. Liu* 1112–1120

Diiron Complexes with Pendant Phenol Group(s) as Mimics of the Diiron Subunit of [FeFe]-Hydrogenase: Synthesis, Characterisation, and Electrochemical Investigation

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



The bridging linkages of the diiron model complexes govern directly their electrochemistry and electrocatalytic reduction of

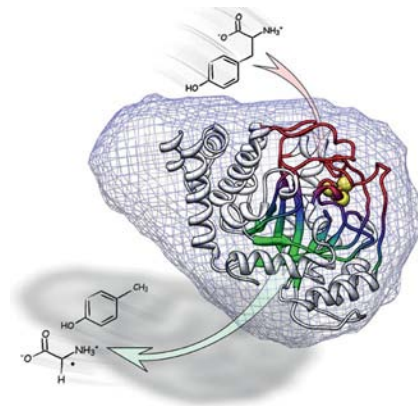
protons, as the linkages determine the nature of the coupled chemical reaction in the ECE processes.

[FeFe]-Hydrogenase

C. Tron, M. V. Cherrier, P. Amara,
L. Martin, F. Fauth, E. Fraga,
M. Correard, M. Fontecave, Y. Nicolet,
J. C. Fontecilla-Camps* 1121–1127

Further Characterization of the [FeFe]-Hydrogenase Maturase HydG

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



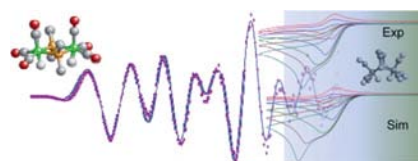
We have explored the CO/CN[−] synthesis catalyzed by [FeFe]-hydrogenase maturase HydG with site-directed mutants, and have performed functional studies, SAXS spectroscopy and homology modeling. We conclude that whereas CN[−] is made in the active site-containing TIM-barrel domain, the CO precursor follows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

Electrocatalytic Proton Reduction

M. H. Cheah, S. P. Best* 1128–1137

XAFS and DFT Characterisation of Protonated Reduced Fe Hydrogenase Analogues and Their Implications for Electrocatalytic Proton Reduction

Keywords: Hydrogenases / XAFS / Iron / Hydrides / Reduction



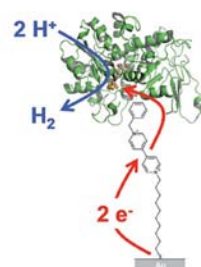
The two reaction paths for dihydrogen elimination from two-electron-reduced, protonated diiron compounds related to the hydrogenase H-cluster available from DFT calculations are considered in terms of a range of spectroscopic, electrochemical, DFT and XAFS studies of [FeH(CO)₃](μ-PPh₃)₂. Limitations are evident for the transition states associated with both of the calculated reaction paths.

Specific Immobilization of Proteins

H. Krassen, S. T. Stripp,* N. Böhm,
A. Berkessel, T. Happe, K. Ataka,
J. Heberle 1138–1146

Tailor-Made Modification of a Gold Surface for the Chemical Binding of a High-Activity [FeFe] Hydrogenase

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



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 H₂ at −450 mV vs. NHE, which was probed by electrochemistry and gas chromatography. Protein binding and electron transfer are discussed.

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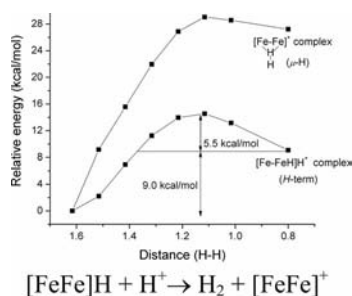
Protonation of Hydrogenases

M. G. I. Galinato, C. M. Whaley,
D. Roberts, P. Wang,
N. Lehnert* 1147–1154



Favorable Protonation of the $(\mu\text{-edt})[\text{Fe}_2(\text{PMe}_3)_4(\text{CO})_2(\text{H-terminal})]^+$ Hydrogenase Model Complex Over Its Bridging $\mu\text{-H}$ Counterpart: A Spectroscopic and DFT Study

Keywords: [FeFe] hydrogenases / Protonation / Enzyme models / Density functional calculations / Raman spectroscopy / IR spectroscopy / Potential energy surface / Electronic structure



A theoretical and spectroscopic study of the preferential protonation of the catalytically active terminal hydride (*H-term*) isomer of the hydrogenase model complex $(\mu\text{-edt})[\text{Fe}_2(\text{PMe}_3)_4(\text{CO})_2(\text{H})]^+$ is presented. Relative to the bridging hydride isomer, *H-term* has a lower activation energy barrier for protonation, due to a key MO that shows a relatively strong hydride (1s) contribution.

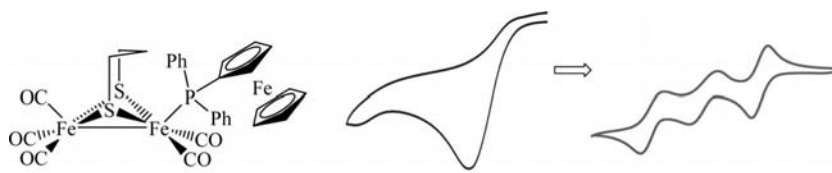
Redox Levels of [FeFe] Hydrogenases

Y.-C. Liu, C.-H. Lee, G.-H. Lee,
M.-H. Chiang* 1155–1162



Influence of a Redox-Active Phosphane Ligand on the Oxidations of a Diiron Core Related to the Active Site of Fe-Only Hydrogenase

Keywords: Fe-only hydrogenases / Metallo-enzymes / Electrochemistry / Iron / Phosphane ligands



Ligation of mppy to the $\{\text{Fe}_2\text{S}_2\}$ unit alters the oxidation levels of the Fe_2 core

and improves stability of the oxidized species.

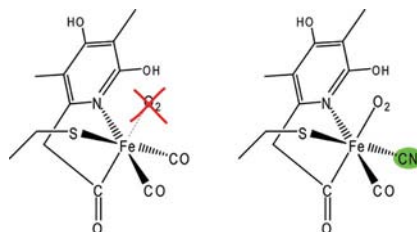
Oxygen-Sensitivity of Hydrogenases

M. T. Stiebritz, A. R. Finkelmann,
M. Reiher* 1163–1171



Oxygen Coordination to the Active Site of Hmd in Relation to [FeFe] Hydrogenase

Keywords: Hydrogenases / Oxygen / Iron / Density functional calculations / Thermodynamics



A DFT study of energy differences in oxygen coordination at the active sites of [FeFe] and monoiron (Hmd) hydrogenase reveals that first shell ligands determine O_2 coordination to the Hmd active site. Changing the first ligand shell but keeping the ligand sphere the same causes the oxygen coordination to become endo- or exothermic, which explains the difference in oxygen sensitivity of Hmd and [FeFe] hydrogenases.

* 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