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[Fe]-Hydrogenase and Models that Contain Iron–Acyl Ligation

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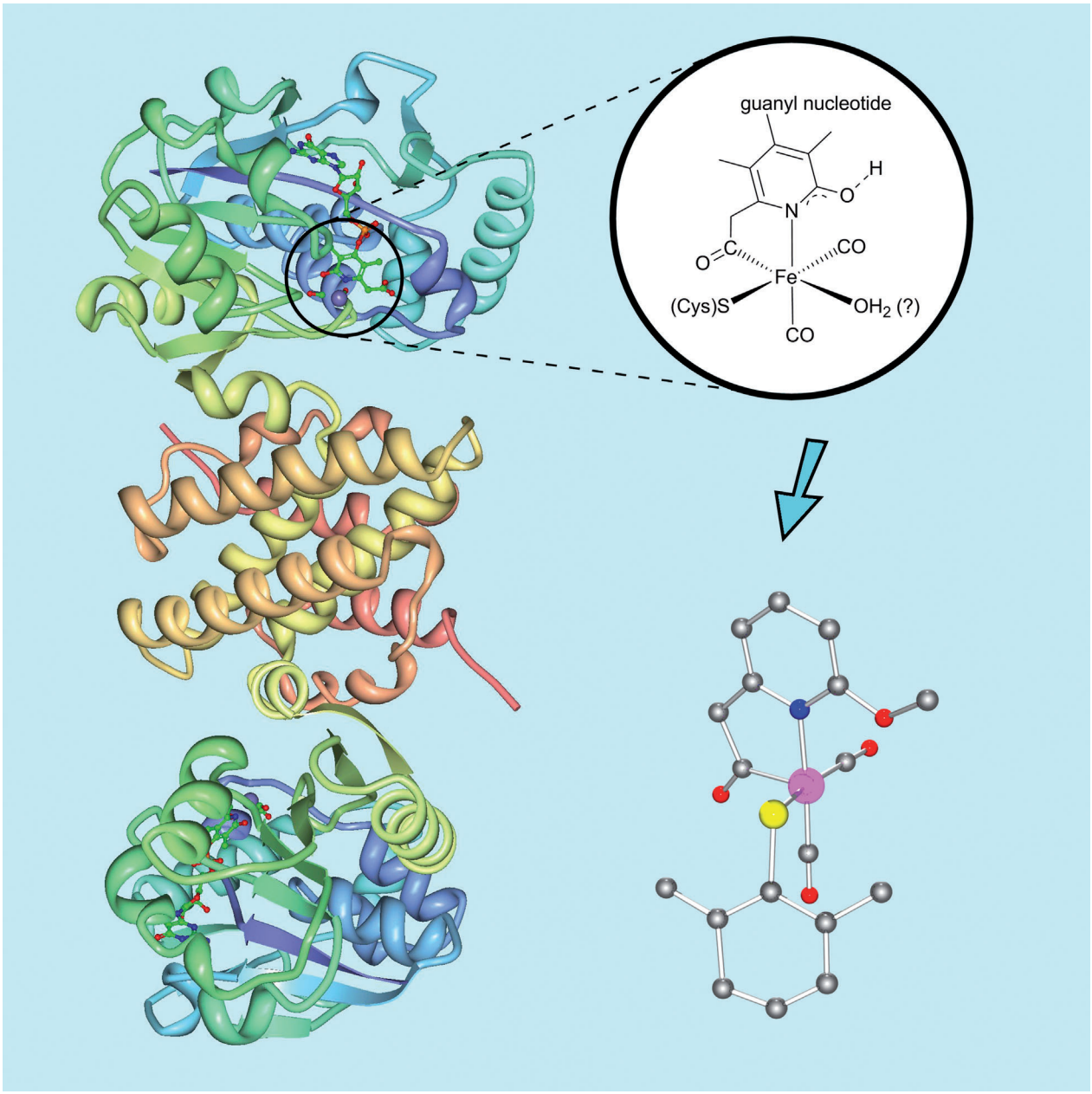
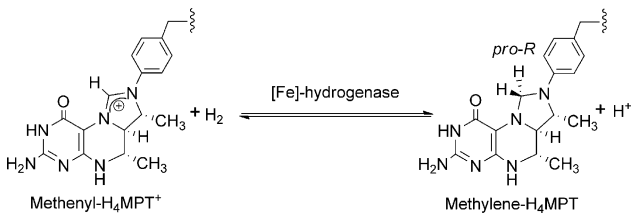


Abstract: [Fe]-hydrogenase is a newly characterized type of hydrogenase. This enzyme heterolytically splits hydrogen in the presence of a natural substrate. The active site of the enzyme contains a mono-iron complex with intriguing iron–acyl ligation. Several groups have recently developed iron–acyl complexes as synthetic models of [Fe]-hydrogenase. This Focus Review summarizes the studies of this enzyme and its model compounds, with an emphasis on our own research in this area.

Keywords: acyl ligands · carbonyl ligands · enzymes · hydrogenase · iron

Introduction

Hydrogenases are enzymes that catalyze the production and utilization of hydrogen. Three classes of phylogenetically unrelated hydrogenases, namely, [FeFe]-, [NiFe]-, and [Fe]-hydrogenases, are known.[1,2] [Fe]-hydrogenase, which is also termed H_2-forming methylene-tetrahydromethanopterin dehydrogenase (Hmd), catalyzes the reduction of methenyl-tetrahydromethanopterin (methenyl-H_4MPT^+) by H_2 into methylene-tetrahydromethanopterin (methylene-H_4MPT) and H^+ ions (Scheme 1), an intermediate step in the reduction of CO_2 into methane by methanogens, which are grown under nickel-limiting conditions.[3] Recent studies have revealed several unique features of this enzyme. Unlike [FeFe]- and [NiFe]-hydrogenases,[4] [Fe]-hydrogenase does not contain any Fe–S clusters and only requires one metal (Fe) for its function.[2] However, the Fe center in [Fe]-hydrogenase has a similar electronic structure (low-spin) and is ligated by similar ligands (sulfur and CO) to the distal Fe centers in [FeFe]- and [NiFe]-hydrogenases.[2]



Scheme 1. Hydride-transfer reaction catalyzed by [Fe]-hydrogenase.

The composition and structure of the Fe-containing active site in [Fe]-hydrogenase have been elucidated, albeit with some uncertainty, by using a wide range of spectroscopic and crystallographic methods, as discussed below. The currently accepted model suggests that the Fe ion is coordinated to two *cis*-CO ligands, one cysteine sulfur atom, one bidentate pyridone molecule, through its nitrogen and acyl-carbon atoms, and a possible sixth ligand, most likely a water molecule (Figure 1).[5]

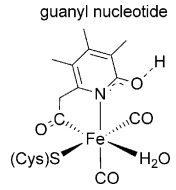


Figure 1. Proposed active site in the resting form of [Fe]-hydrogenase.

Although many synthetic models of [Fe]-hydrogenase have been reported in recent years, the scope of this Focus Review is limited to those models that contain acyl-ligand moieties because of their close structural similarity to the active site of the enzyme. Previous reviews have thoroughly covered more primitive models that do not contain an acyl ligand.[6,7] Special emphasis is given to our own contributions to this area. DFT calculations related to the reaction mechanism of the enzyme and small-molecule models will not be discussed herein.

[Fe]-Hydrogenase Enzyme

For many years, [Fe]-hydrogenase was regarded as a "metal-free" hydrogenase. In 2004, Lyon et al. showed that, when [Fe]-hydrogenase was inactivated by UV-A/blue light in the presence of ethylenediaminetetraacetic acid(EDTA), iron ions were released and the release increased linearly with a corresponding decrease in [Fe]-hydrogenase activity. After complete inactivation, the amount of released iron ions was almost identical to the initial content of the [Fe]-hydrogenase monomer, which indicated that there was one iron ion in each active site of [Fe]-hydrogenase.[8]

The decomposition of the iron-containing cofactor was further investigated and an organic product, which was assumed to coordinate to the Fe center, was identified (Figure 2).[9]

[Fe]-hydrogenase has also been studied by IR spectroscopy. Two strong bands at 2011 and 1944 cm^{-1} in water[10] (and at 1996 and 1928 cm^{-1} in the solid state)[5] with almost-equal intensities were attributed to two *cis*-CO ligands that were bound to the iron center. When changing the pH value from 9.5 to 5.5, additional peaks appeared at 2021 and 1952 cm^{-1} and, interestingly, the process was reversible. If the pH value was restored to 9.5, the two new bands completely dis-

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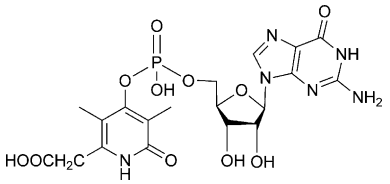

Figure 2. Structure of the organic decomposition product of the Fe-containing cofactor.

appeared. It was proposed that there was an acidic group proximal to the iron atom and that the change in protonation affected the electron density on the transition metal.[10] However, the possibility that the proximal group was an basic group (for example, a thiolate group) that reversibly accepted H^+ ions could not be excluded.

Exposure to CO reversibly changed the IR spectrum of [Fe]-hydrogenase and led to the appearance of three CO absorption bands at 2074, 2020, and 1981 cm^{-1}, thus indicating the presence of a tricarbonyl complex.[10] Interestingly, according to the absorptions of ^{13}CO-inhibited [Fe]-hydrogenase (at 2050, 1999, and 1980 cm^{-1}), only one ^{13}CO group existed. It was thought that the intrinsic CO ligands did not exchange with extrinsic CO groups. However, in 2012, when Schick et al. explored the biosynthetic pathway of [Fe]-hydrogenase, they found that, if an organism (*Methanobrevibacter smithii*) that contained [Fe]-hydrogenase was grown in the presence of ^{13}CO, not only the two terminal CO ligands, but also the acyl group, were labeled.[11] Thus, it is likely that complete CO exchange occurs in the enzyme, but that it is too slow to be detected on the monitored timescale.

Interestingly, the presence of H_2 did not influence the absorption of CO by [Fe]-hydrogenase, whereas that of methenyl-H_4MPT^+ alone showed small-but-noticeable changes. However, when H_2 and methenyl-H_4MPT^+ were mixed together, the band at 1944 cm^{-1} moved slightly to 1945 cm^{-1}, whereas the band at 2011 cm^{-1} shifted to 2015 cm^{-1}, which fit better as two Gaussian peaks at 2018 and 2011 cm^{-1} (in a 47:53 ratio). These results suggested that methenyl-H_4MPT^+ formed some interactions with the Fe center and that H_2 could only be activated by [Fe]-hydrogenase in the presence of this substrate.

Circular dichroism (CD) spectroscopy was also used to detect the interactions between [Fe]-hydrogenase and methenyl-H_4MPT^+.[12] The results showed that the presence of H_2 did not change the CD spectrum of [Fe]-hydrogenase. In the absence of H_2, the addition of methenyl-H_4MPT^+ resulted in about 10% of the [Fe]-hydrogenase containing bound methenyl-H_4MPT^+, thus giving rise to a slight change in the CD spectrum. However, in the presence of both H_2 and methenyl-H_4MPT^+, the CD spectrum changed substantially. These findings were consistent with the IR results, thus showing that methenyl-H_4MPT^+ is crucial for H_2 activation.

To investigate the electronic structure of iron in [Fe]-hydrogenase, Mössbauer spectra of the ^{57}Fe-labeled [Fe]-hydrogenase and its inhibited forms were recorded.[13] The zero-field Mössbauer spectrum of [Fe]-hydrogenase showed an isomeric shift of $\delta = +0.06\ mm\,s^{-1}$. Whereas the parameters were resistant to H_2, the binding of external CO or CN^- decreased the isomeric shift of the Fe ion ($\delta = -0.03\ mm\,s^{-1}$ for the CO-inhibited [Fe]-hydrogenase and $\delta = -0.01\ mm\,s^{-1}$ for the CN^--inhibited derivative). These small shifts indicated that the iron ions were all in a low oxidation state (0, +1, +2). In the presence of an external magnetic field, the Mössbauer spectra revealed the absence of an internal field, thus indicating that the iron ions were diamagnetic with spin $S = 0$, which excluded an oxidation state of Fe^I. Surprisingly, the addition of H_2 and/or methenyl-H_4MPT^+ did not show obvious changes in the Mössbauer parameters. This result led the authors to conclude that the two substrates did not interact with Fe as direct ligands.

Later, X-ray absorption spectroscopy (XAS) was used to reveal the composition of the Fe center in [Fe]-hydrogenase.[14] XAS analysis suggested there were two *cis*-CO ligands, one S ligand, and either one or two O/N ligands coor-

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Dafa Chen obtained his BS (2003) and PhD (2008) in Chemistry from Nankai University. He was a Postdoctoral Scholar in the group of Prof. Xile at the EPFL from 2008–2011, where he worked on the biomimetic chemistry of [Fe]-hydrogenase. Since 2011, he has been a Professor at the Harbin Institute of Technology, working in the field of bioinorganic chemistry.

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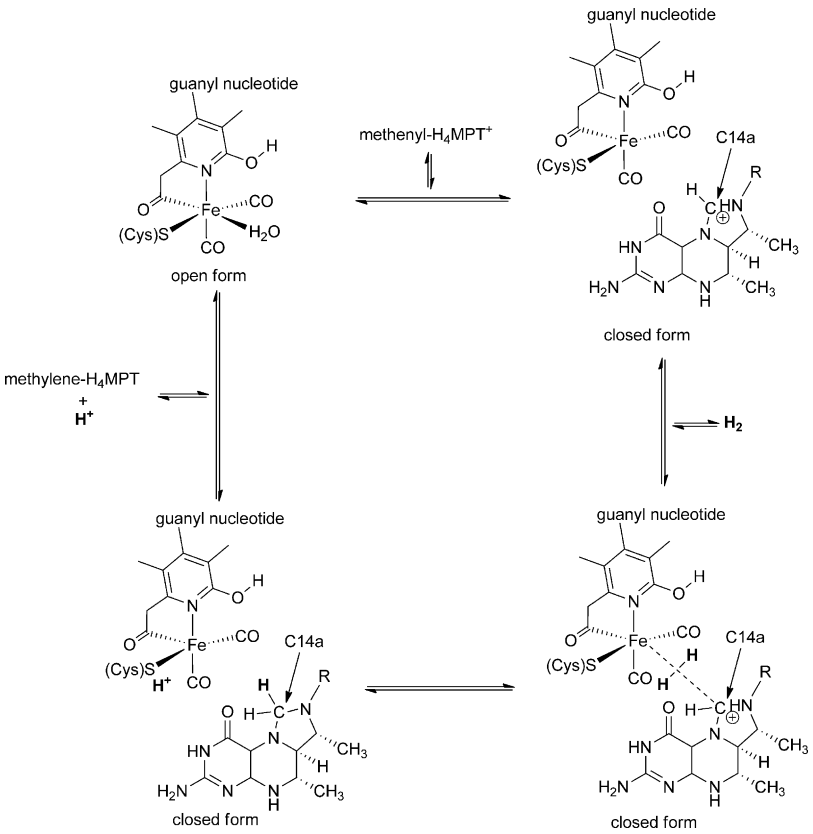
dinating to the Fe center. Cys176 was the mostly likely S ligand. The oxygen/nitrogen atom(s) might originate from the organic cofactor. In 2010, Salomone-Stagni et al. compared the XANES (X-ray absorption near-edge spectroscopy) spectra of several model complexes of [Fe]-hydrogenase. Together with Mössbauer spectroscopic analysis, the authors concluded that the oxidation state of the Fe center was +2.[15]

Although much progress had been made to that point, the nature of the active site in [Fe]-hydrogenase remained poorly understood. In 2008 and 2009, the main structure of the active site in [Fe]-hydrogenase was finally solved.[5,16] In 2008, Shima et al. reported a crystal structure of [Fe]-hydrogenase, which was revised in 2009. In this newly proposed structure, the Fe center is coordinated by two *cis*-CO ligands, a cysteine sulfur atom (Cys176), a bidentate pyridinol–acyl ligand, through its nitrogen and acyl donor atoms, and perhaps by a labile water molecule. The presence of this new acyl–iron bond was further supported by mass spectrometry and IR spectroscopy.[17]



Scheme 2. Proposed catalytic mechanism of hydrogen activation by [Fe]-hydrogenase.

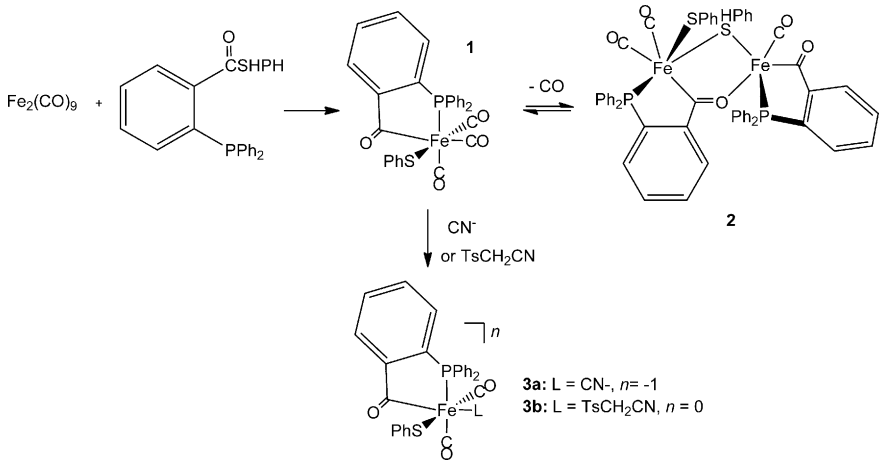
A crystal structure of the binary complex of [Fe]-hydrogenase with methylene-H_4MPT was also reported.[18] In its open form, the distance between the hydride-accepting atom (C14a) of methylene-H_4MPT and the iron center in the active site was 9.3 Å, which was too long for hydride transfer. However, in its closed form, the distance was only 3 Å, thus suggesting that H_2 was activated in this form. In addition, the C14a atom was next to the "solvent"-coordination site, thus indicating that this site was the H_2-binding site.

Based on these results, a catalytic mechanism was proposed (Scheme 2).[18] The cycle is initiated by the binding of methenyl-H_4MPT$^+$ to the open form of [Fe]-hydrogenase, thereby resulting in the formation of the closed form. Then, H_2 is captured at the "solvent"-coordination site of the Fe center and is heterolytically cleaved into a hydride and a proton. The hydride is accepted by the adjacent C14a carbocation of methenyl-H_4MPT$^+$, whilst the proton is accepted by [Fe]-hydrogenase. This proton is then delivered into the bulk solvent, thus completing the catalytic cycle. The proton-accepting group in [Fe]-hydrogenase might be the deprotonated form of the Cys176 thiol or the pyridinol hydroxy group.

Models that Contain Iron–Acyl Ligation

Several groups have accomplished the synthesis of Fe–acyl models of the [Fe]-hydrogenase active site in recent years. Rauchfuss and co-workers synthesized a phosphine-containing Fe–acyl complex (**1**) from the reaction of $Fe_2(CO)_9$ with a phosphine thioester (Scheme 3).[19] Complex **1** has labile CO ligands and decarbonylates to form a dimeric structure (**2**). Dimer **2** undergoes isomerization over time, which involves the reorientation of the bridging thiol ligands. Exposure of dimer **2** to CO at high pressures results in a mixture of compounds **1** and **2**. Complex **1** may be protonated by using $H(OEt_2)_2BArF_4$ (ArF = 3,5-$(CF_3)_2C_6H_3$) to produce a species in which either the thiol or acyl ligands is probably protonated. The reaction of this product with base regenerates complex **1**. The substitution of a CO ligand with CN or $TsCH_2CN$ groups produces complexes **3a** and **3b**, respectively. Anionic complex **3a** is quite stable, whereas neutral complex **3b** is only stable at low temperatures.[20]

Pickett and co-workers reported the synthesis and characterization of a series of phosphine-free carbamoyl-containing Fe complexes, starting from the reaction of $[Fe(CO)_4Br_2]$ with 2-aminopyridine.[21] The reaction between the amino group of the pyridine substrate and a metal-bound carbonyl ligand leads to the formation of complex **4**, which contains a pendant bound carbamoyl group (Scheme 4). The reaction of complex **4** with 2-mercaptoetha-

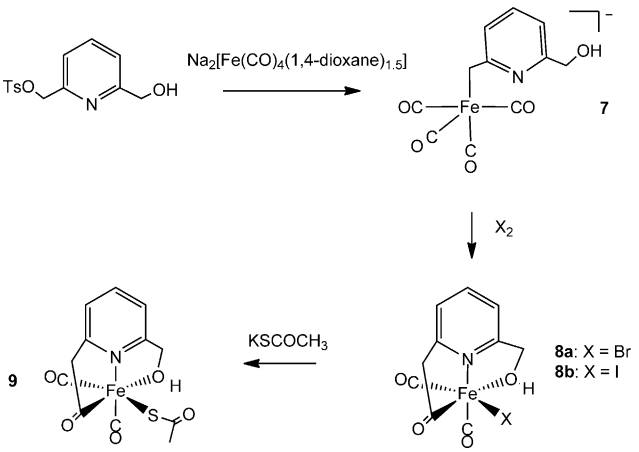


Scheme 3. Synthesis of iron–acyl–thiolato model complexes.

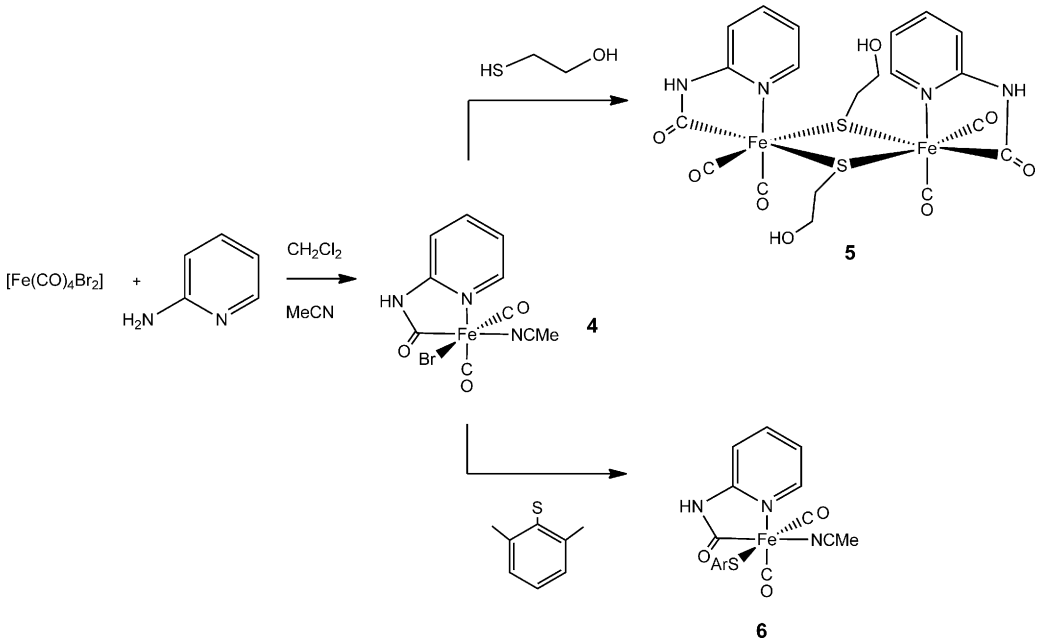
nol results in the formation of a dimeric complex with bridging thiol ligands (**5**) and the reaction of compound **4** with 2,6-dimethylbenzenethiol produces monomeric complex **6**. Both compounds **4** and **6** exhibit CO bands in their IR spectra that are similar to those in the spectrum of the wild-type enzyme.

A new type of [Fe]-hydrogenase model complex that contained a tridentate acylmethyl(hydroxymethyl)pyridine ligand was very recently reported by Song et al.[22] An initial reaction of the modified pyridine ligand with $Na_2[Fe(CO)_4(1,4\text{-dioxane})_{1.5}]$ in MeCN gave an unstable Fe^0 complex (**7**), in which the hydroxy group remained uncoordinated (Scheme 5). Following a migratory CO-insertion reaction and coordination of the hydroxy group, oxidation with a halogen atom afforded novel complexes **8a**,**b**. Substitution of the halide with a $^-SCOCH_3$ group yielded thiol complex **9**.

All of the aforementioned complexes structurally resemble the active site of the hydrogenase enzyme, although none of them have subsequently been reported to catalyze the hydrogenation reactions. Although these complexes are structurally diverse, they can be considered to be good spectroscopic models of the active site in [Fe]-hydrogenase, with re-



Scheme 5. Synthesis of model complexes that contain an acylmethyl(hydroxymethlyl)pyridine ligand.

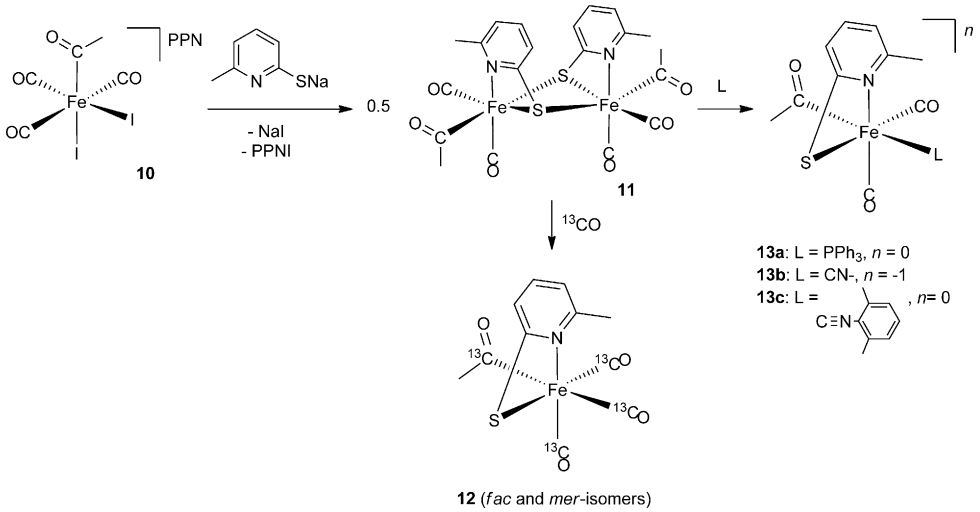


Scheme 4. Synthesis of carbamoyl-containing model complexes.

ported IR spectra and geometric parameters that match well with those of the enzyme.

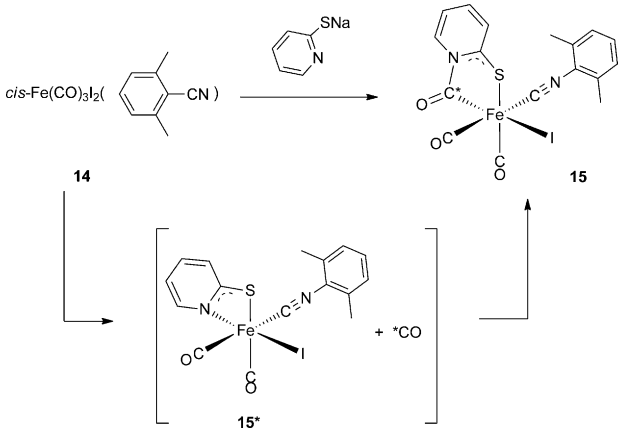
Iron–Acyl Model Complexes from Our Group

Initial work by our group on the development of models of the active site in [Fe]-hydrogenase focused on the use of pyridyl-2-tholate ligands to mimic the N and S ligands in the enzyme. Employing a strategy of an early installation of the acyl ligand, the reaction of complex **10** with sodium 6-methyl-2-mercaptopyridineate led to the synthesis of a di-iron dithiolate dimer (**11**, Scheme 6).[23] This complex was shown to reversibly bind CO through a series of isotopic labeling experiments, in which ^{13}CO was reacted with compound **11** to produce six-coordinate monomeric species that contained ^{13}C-labeled atoms on the carbonyl and acyl ligands. Based on NMR experiments, it is assumed that both the *fac* and *mer* isomers of compound **12** are formed. The reaction of complex **11** with cyano or phosphine ligands resulted in the formation of complexes **13a–13c**, which replicated the coordination environment of the Fe ion in the hydrogenase enzyme.



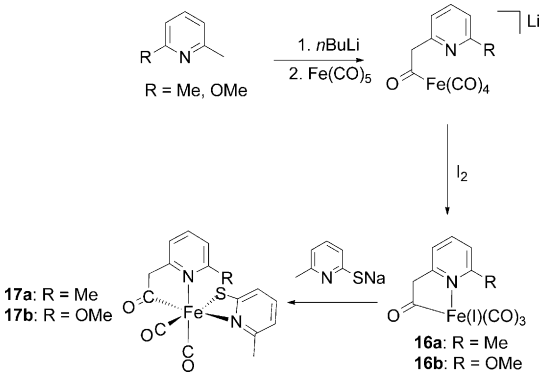
Scheme 6. Synthesis of compound **11** and its reactivity with CO and other ligands.

The use of isocyanide-substituted precursor $[Fe(CO)_3(2,6\text{-dimethyl-PhNC})I_2]$ resulted in different reactivity. The reaction of compound **14** with sodium pyridyl-2-thiolate gave complex **15**. The Fe ion contains an unexpected acyl–thiolate chelate (Scheme 7).[24] The formation of the acyl–thiolate ligand could be considered as the product of CO migration into the pyridyl-2-thiolate ligand; presumably, the reaction first yielded substitution product **15*** and one molecule of CO, which then inserted into the nucleophilic Fe–N bond to give compound **15**. Consistent with this hypothesis, the yield of compound **15** was higher when the reaction was carried out in the presence of CO.



Scheme 7. Formation of acyl–thiolate chelate **15**.

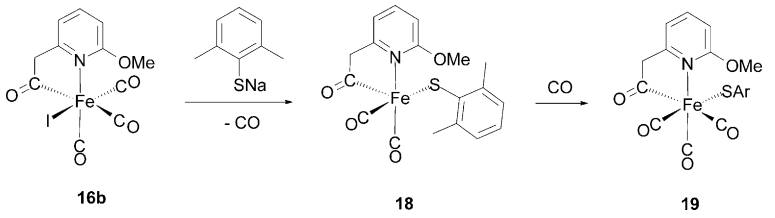
Subsequent work in this area focused on the use of an acylmethylpyridinyl ligand to more closely model the coordination sphere of the [Fe]-hydrogenase active site. A methylpyridinyl anion was generated in situ through the reaction of the pyridine starting material with *n*BuLi and was reacted with $Fe(CO)_5$. The subsequent addition of I_2 to the reaction solution led to the formation of $[(6\text{-R-PyCH}_2\text{CO})Fe(CO)_3I]$ (**16a,b**; Scheme 8).[25] The iodide ligand could be replaced with a sulfur moiety, through the reaction of complex **16** with sodium 6-methyl-2-mercaptopyridineate, thereby forming six-coordinate complexes **17a** and **17b**.



Scheme 8. Formation of acylmethylpyridinyl complexes **17a** and **17b**.

Similar to compound **11**, complexes **17a** and **17b** demonstrated CO exchange by performing labeling experiments, albeit more slowly. Photolysis experiments on compound **17b** resulted in an accelerated CO-exchange reaction, in which isomerization of the complex into a species with the acyl moiety *trans* to the sulfur ligand was observed.

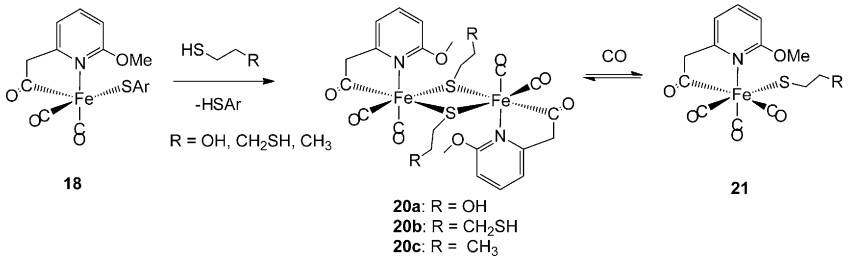
A five-coordinate Fe^{II} model complex was produced through the reaction of complex **16b** with sodium 2,6-dimethylbenzenethiolate (Scheme 9).[26] Complex **18** reacted with



Scheme 9. Formation of five-coordinate model complex **18**.

CO to give six-coordinate tricarbonyl complex **19**. Once again, the addition of ^{13}CO showed the incorporation of an isotopic label into all of the CO-ligand positions and the acyl group. The thiolate ligand in compound **18** was shown to be displaceable, as demonstrated by its reaction with 6-methyl-2-mercaptopyridine to generate complex **17b**. Complex **18** was unreactive in the presence of various ligands, such as water, MeCN, pyridine, and Et_3N.

The thiolate ligand in compound **18** could be displaced by other sulfur ligands. The reaction of compound **18** with $SHCH_2CH_2OH$ produced a dimeric complex (**20a**) with bridging thiolate ligands (Scheme 10).[27] Similar products



Scheme 10. Displacement of a thiol ligand in complex **18** to form a dimeric species.

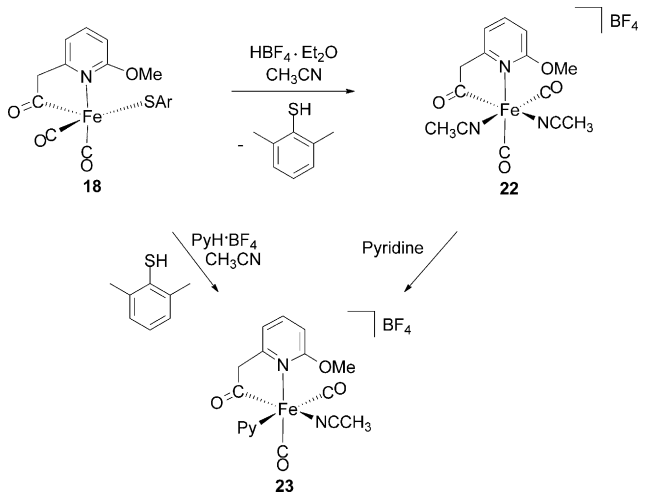
(**20b**, **20c**) were formed when the thiol was 1,3-propanedithiol or 1-propanethiol, respectively. Dimeric compound **20a** reversibly reacted with CO to give monomeric tricarbonyl product **21**.

Protonation reactions of complex **18** led to the formation of solvent-coordinated species, along with loss of the protonated thiol ligand. The reaction of complex **18** with $HBF_4{\cdot}Et_2O$ in MeCN produced the free thiol molecule and a yellow di-solvent-coordinated compound (**22**).[28] The addition of pyridine to a reaction solution that contained complex **22**, or the reaction of complex **18** with pyridinium tetrafluoroborate, produced pyridine-containing compound **23** (Scheme 11).

The protonation and coordination of the thiolate ligand in complex **18** are reversible. The treatment of compounds **22** and **23** with a mixture of NEt_3 and $HS(2,6\text{-}Me_2C_6H_3)$ in MeCN regenerated complex **18**. No reaction took place between NEt_3 and $HS(2,6\text{-}Me_2C_6H_3)$ alone in MeCN. Thus, $HS(2,6\text{-}Me_2C_6H_3)$ must first coordinate to the Fe ions in compounds **22** and **23** to form Fe–thiol species as intermediates. Upon the binding of sulfur to an Fe ion, the thiol proton became more acidic and could be deprotonated by Et_3N to give thiolate complex **18**.

Many of the model complexes that were developed in our group shared similar structures and reactivities to the various states of the [Fe]-hydrogenase enzyme. IR data of all of these compounds support the presence of *cis*-CO ligands with stretching frequencies within the range of the enzyme, with the exception of cationic compounds **22** and **23**, which are at slightly higher frequencies. Reversible CO-binding has been demonstrated for compounds **11** and **20a** and CO exchange can be seen in the reactions of compounds **17a**, **17b**, and **18** with ^{13}CO, thus forming tricarbonyl species that incorporate ^{13}C labels into both their acyl and carbonyl ligands. This reactivity is consistent with the ability of [Fe]-hydrogenase to bind extrinsic CO ligands and suggests that the lack of observed extrinsic/intrinsic-CO exchange in the enzyme is perhaps due to the observation times being much shorter than are needed for this potentially slow exchange reaction.

Complexes **11**, **13a**–**13c**, and **15** have been studied by using Mössbauer spectroscopy[24] and their isomeric shifts (δ) fall within a small range that is comparable to those found in [Fe]-hydrogenase and its CO/CN-inhibited forms, as well as those in other Fe^{II} models. These results indicate that the bis-carbonyl-coordination environment has a dominating influence on the electronic structure of these complexes and, thus, on the isomeric shifts. The field-dependent quadrupole splitting (ΔE_Q) parameter is much more sensitive to the ligand environment and these values were shown to vary



Scheme 11. Protonation of the thiol ligand in compound **18**.

significantly between models and between various enzyme states.

Attempts at H_2 activation under high pressures have been made for complexes **11**, **17a**,**b**, and **18**, with no observable success. Because the activation of H_2 by [Fe]-hydrogenase does not occur without the presence of the methenyl-H_4MPT^+ cofactor, we are currently exploring H_2-activation reactions with suitable substrate mimics.

Conclusions

A number of new model complexes of the active site of [Fe]-hydrogenase have been synthesized in recent years. The incorporation of the acyl-ligand moiety into these models more closely resembles the ligand environment in the enzyme. Spectroscopic characterization, including IR, Mössbauer, and CO-exchange experiments, confirms the similarity between the electronic environment of these models and the active site. The practical application of these models in H_2-activation and hydrogenation reactions has, until now, been impeded by the lack of suitable substrate/cofactor mimics, but the complexes have been shown to be good CO- and CN-reactivity models for the enzyme.

Acknowledgements

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[1] P. M. Vignais, B. Billoud, J. Meyer, *FEMS Microbiol. Rev.* **2001**, *25*, 455–501.
[2] S. Shima, R. K. Thauer, *Chem. Rec.* **2007**, *7*, 37–46.
[3] R. K. Thauer, A. R. Klein, G. C. Hartmann, *Chem. Rev.* **1996**, *96*, 3031–3042.
[4] a) A. Volbeda, M. H. Charon, C. Piras, E. C. Hatchikian, M. Frey, J. C. Fontecilla-Camps, *Nature* **1995**, *373*, 580–587; b) Y. Nicolet, C. Piras, P. Legrand, C. E. Hatchikian, J. C. Fontecilla-Camps, *Struct. Fold. Des.* **1999**, *7*, 13–23; c) J. W. Peters, W. N. Lanzilotta, B. J. Lemon, L. C. Seefeldt, *Science* **1998**, *282*, 1853–1858; d) F. A. Armstrong, *Curr. Opin. Chem. Biol.* **2004**, *8*, 133–140; e) K. A. Vincent, A. Parkin, F. A. Armstrong, *Chem. Rev.* **2007**, *107*, 4366–4413.
[5] T. Hiromoto, K. Ataka, O. Pilak, S. Vogt, M. S. Stagni, W. Meyer-Klaucke, E. Warkentin, R. K. Thauer, S. Shima, U. Ermler, *FEBS Lett.* **2009**, *583*, 585–590.
[6] For models without acyl ligands, see: a) X. F. Wang, Z. M. Li, X. R. Zeng, Q. Y. Luo, D. J. Evans, C. J. Pickett, X. M. Liu, *Chem. Commun.* **2008**, 3555–3557; b) B. V. Obrist, D. F. Chen, A. Ahrens, V. Schunemann, R. Scopelliti, X. L. Hu, *Inorg. Chem.* **2009**, *48*, 3514–3516; c) B. Li, T. Liu, C. V. Popescu, A. Bilko, M. Y. Darensbourg, *Inorg. Chem.* **2009**, *48*, 11283–11289; d) T. B. Liu, B. Li, C. V. Popescu, A. Bilko, L. M. Perez, M. B. Hall, M. Y. Darensbourg, *Chem. Eur. J.* **2010**, *16*, 3083–3089; e) S. Tanino, Y. Ohki, K. Tatsumi, *Chem. Asian J.* **2010**, *5*, 1962–1964.
[7] a) C. Tard, C. J. Pickett, *Chem. Rev.* **2009**, *109*, 2245–2274; b) J. A. Wright, P. J. Turrell, C. J. Pickett, *Organometallics* **2010**, *29*, 6146–6156; c) M. J. Corr, J. A. Murphy, *Chem. Soc. Rev.* **2011**, *40*, 2279–2292; d) S. Dey, P. K. Das, A. Dey, *Coord. Chem. Rev.* **2013**, *257*, 42–63.
[8] E. J. Lyon, S. Shima, G. Buurman, S. Chowdhuri, A. Batschauer, K. Steinbach, R. K. Thauer, *Eur. J. Biochem.* **2004**, *271*, 195–204.
[9] S. Shima, E. J. Lyon, M. L. Sordel-Klippert, M. Kauß, J. Kahnt, R. K. Thauer, K. Steinbach, X. Xie, L. Verdier, C. Griesinger, *Angew. Chem.* **2004**, *116*, 2601–2605; *Angew. Chem. Int. Ed.* **2004**, *43*, 2547–2551.
[10] E. J. Lyon, S. Shima, R. Boecher, R. K. Thauer, F. W. Grevels, E. Bill, W. Roseboom, S. P. J. Albracht, *J. Am. Chem. Soc.* **2004**, *126*, 14239–14248.
[11] M. Schick, X. Xie, K. Ataka, J. Kahnt, U. Linne, S. Shima, *J. Am. Chem. Soc.* **2012**, *134*, 3271–3280.
[12] S. Shima, S. Vogt, A. Göbels, E. Bill, *Angew. Chem.* **2010**, *122*, 10113–10117; *Angew. Chem. Int. Ed.* **2010**, *49*, 9917–9921.
[13] S. Shima, E. J. Lyon, R. K. Thauer, B. Mienert, E. Bill, *J. Am. Chem. Soc.* **2005**, *127*, 10430–10435.
[14] M. Korbas, S. Vogt, W. Meyer-Klaucke, E. Bill, E. J. Lyon, R. K. Thauer, S. Shima, *J. Biol. Chem.* **2006**, *281*, 30804–30813.
[15] M. Salomone-Stagni, F. Stellato, C. M. Whaley, S. Vogt, S. Morante, S. Shima, T. B. Rauchfuss, W. Meyer-Klaucke, *Dalton Trans.* **2010**, *39*, 3057–3064.
[16] S. Shima, O. Pilak, S. Vogt, M. Schick, M. S. Stagni, W. Meyer-Klaucke, E. Warkentin, R. K. Thauer, U. Ermler, *Science* **2008**, *321*, 572–575.
[17] S. Shima, M. Schick, J. Kahnt, K. Ataka, K. Steinbach, U. Linne, *Dalton Trans.* **2012**, *41*, 767–771.
[18] T. Hiromoto, E. Warkentin, J. Moll, U. Ermler, S. Shima, *Angew. Chem.* **2009**, *121*, 6579–6582; *Angew. Chem. Int. Ed.* **2009**, *48*, 6457–6460.
[19] A. M. Royer, T. B. Rauchfuss, D. L. Gray, *Organometallics* **2009**, *28*, 3618–3620.
[20] A. M. Royer, M. Salomone-Stagni, T. B. Rauchfuss, W. Meyer-Klaucke, *J. Am. Chem. Soc.* **2010**, *132*, 16997–17003.
[21] P. J. Turrell, J. A. Wright, J. N. T. Peck, V. S. Oganesyan, C. J. Pickett, *Angew. Chem.* **2010**, *122*, 7670–7673; *Angew. Chem. Int. Ed.* **2010**, *49*, 7508–7511.
[22] L.-C. Song, Z.-J. Xie, M.-M. Wang, G.-Y. Zhao, H.-B. Song, *Inorg. Chem.* **2012**, *51*, 7466–7468.
[23] D. Chen, R. Scopelliti, X. Hu, *J Am Chem. Soc* **2010**, *132*, 928–929.
[24] D. Chen, A. Ahrens-Botzong, V. Schunemann, R. Scopelliti, X. Hu, *Inorg. Chem.* **2011**, *50*, 5249–5257.
[25] D. Chen, R. Scopelliti, X. Hu, *Angew. Chem.* **2010**, *122*, 7674–7677; *Angew. Chem. Int. Ed.* **2010**, *49*, 7512–7515.
[26] D. Chen, R. Scopelliti, X. Hu, *Angew. Chem.* **2011**, *123*, 5789–5791; *Angew. Chem. Int. Ed.* **2011**, *50*, 5671–5673.
[27] B. Hu, D. Chen, X. Hu, *Chem. Eur. J.* **2012**, *18*, 11528–11530.
[28] D. Chen, R. Scopelliti, X. L. Hu, *Angew. Chem.* **2012**, *124*, 1955–1957; *Angew. Chem. Int. Ed.* **2012**, *51*, 1919–1921.

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