Biomimetic models of [NiFe] hydrogenase for electrocatalytic hydrogen evolution

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Chapter 1

Introduction

Hydrogenases are enzymes which can catalyze the reversible oxidation of dihydrogen. Since H_2 gas might be used as a sustainable energy source, the structure and mechanism of hydrogenases have received the attention of many chemists. In this introductory chapter an overview is given of the different types of hydrogenases and their catalytic activities. Furthermore, structural and functional models of the active sites of the hydrogenases are described. The aim of the research described in this thesis concerns the synthesis and characterization of new complexes as mimics of [NiFe] hydrogenases. At the end of this chapter a short overview is given of the contents of thesis.

1.1 The Energy Challenge

The global daily energy consumption is increasing with the growing population, and providing an abundant, environmentally friendly and renewable energy source is one of the major challenges of contemporary research.[1,2] Molecular hydrogen (H_2) is a perfect candidate energy carrier as an alternative to fossil fuels. The "Hydrogen Economy" has been proposed to be the ultimate solution for future energy demands as dihydrogen is a 'clean' fuel producing only water upon combustion, and because it is chemically simple to store energy in the dihydrogen molecule.[3] Although platinum can be used as a very efficient and robust catalyst for dihydrogen production, it is an expensive metal and not a sustainable material due to its limited reserves on Earth.[4] In order to obtain cheap and efficient catalysts for dihydrogen production, earth abundant metals should be used. For the activation and production of dihydrogen gas, nature uses hydrogenase enzymes containing nickel and/or iron ions in their active sites; these enzymes regulate the electron and proton concentrations of the cell by dihydrogen uptake or evolution. In the past few decades, chemists have been trying to mimic the active sites of the hydrogenase enzymes in order to develop cheap and efficient electrocatalysts for dihydrogen evolution.[5]

1.2 Hydrogenases

1.2.1 General

Hydrogenases enzymes play an important role in the metabolism of bacteria, catalyzing the reversible oxidation of dihydrogen according to the reaction shown in eq. 1.[6]

$$2H^+ + 2e^- \rightleftarrows H_2 \qquad \text{Eq [1]}$$

Understanding of the hydrogenase enzymes is relevant for future energy applications since dihydrogen is a clean source of energy. In order to produce dihydrogen gas for the application in fuel cells, new catalysts may be developed by using biomimetic, functional models of hydrogenases.[7] Three types of hydrogenases are known, which are classified based on the metal center in the active site which are [FeFe], [Fe] and [NiFe] hydrogenases, as described in the following sections.

1.2.2 [FeFe] Hydrogenase

From the three classes of hydrogenases the [FeFe] hydrogenase and their model complexes have been studied most intensively.[3] These enzymes play a central role in microbial energy metabolism catalyzing the hydrogen evolution reaction (HER). The [FeFe] hydrogenase show the highest catalytic activity for proton reduction, but are also extremely sensitive to irreversible inactivation by dioxygen. The active site of the [FeFe] hydrogenase is buried deeply within the protein. The active site of [FeFe] hydrogenase contains a dinuclear iron center comprising the unusual CO, CN^- and an azadithiolate ligand, and is linked via a cysteine thiolate to an Fe_4S_4 cluster (Figure 1.1). Dihydrogen can enter and leave the active site through hydrophobic channels.[8,9] The active site of the [FeFe] hydrogenase contains a bridging azadithiolate ligand between the two iron centers. The central secondary amine group in this dithiolate ligand is believed to play a crucial role as a proton relay and might be part of the explanation of the extremely high activity of this hydrogenase enzyme.[3]

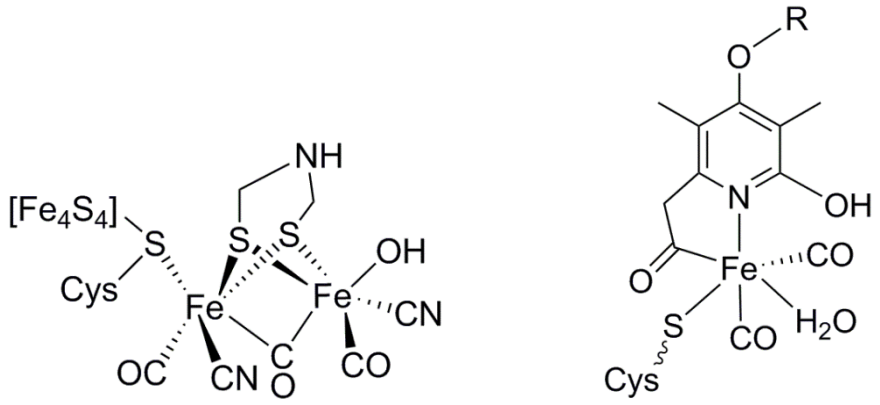


Figure 1.1: Schematic drawing of the active sites in [FeFe] hydrogenase (left) and [Fe] hydrogenase (right).

1.2.3 [Fe] Hydrogenase

Some methanogenic archaea bacteria contain a hydrogenase enzyme that does not contain a nickel center nor iron-sulfur clusters. These [Fe] hydrogenase contains a mononuclear iron catalytic center (Figure 1.1) and catalyzes the transfer of hydride groups. The absence of a nickel center in this hydrogenase is induced by the nickel-deficient environment in which the single-celled microorganisms grow.[8,9] In the hydrogenases containing a bimetallic active site iron-sulfur clusters function as channels to shuttle electrons from the active site to the electron accept or/donor protein partner. The [Fe] hydrogenase does not release electrons but rather

uses the coenzyme tetrahydromethanopterin as a hydride acceptor.[3,8] In contrast to the [FeFe] and [NiFe] hydrogenases the [Fe] hydrogenase does not catalyze the oxidation of H_2 to protons.[8]

1.2.4 [NiFe] Hydrogenase

The third class of hydrogenases comprises the [NiFe] hydrogenase containing a heterodimetallic Ni-Fe active site. Although this enzyme is mostly involved in the uptake of H_2, it is also able to catalyze the production of H_2.[9] The active site of [NiFe] hydrogenase contains a nickel center with four bonds to cysteine thiolates which is connected via two cysteine thiolate bridges to an iron center with CO and CN^- ligands (Figure 1.2).[10] The [NiFe] hydrogenases generally show lower activities in proton reduction than the [FeFe] hydrogenases, but they are much less sensitive for inactivation by dioxygen. Furthermore, generally they are able to recover from oxidative inactivation.[8]

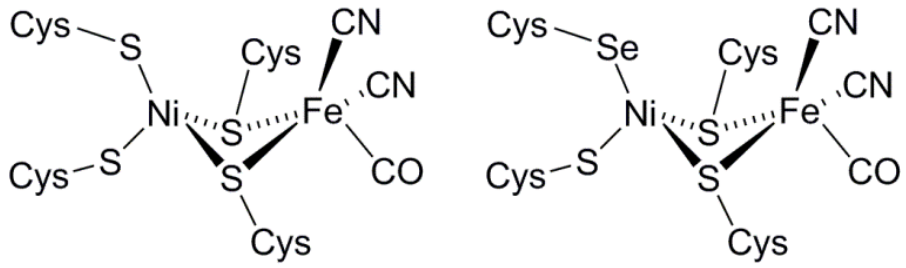


Figure 1.2: Schematic drawing of the active sites of [NiFe] hydrogenase (left) and [NiFeSe] hydrogenase (right).

The [NiFe] hydrogenase is built up from two subunits; a large subunit of 62.5 kDa containing the dinuclear active site and a small subunit of 28.8 kDa containing three iron-sulfur clusters distributed from the active site to the surface of the protein. These iron-sulfur clusters function as the electron shuttle pathway from the active site to a redox protein.[8] No consensus is apparent in literature concerning the exact catalytic mechanism of the [NiFe] hydrogenase.[3] One of the proposed mechanisms for the HER catalyzed by [NiFe] hydrogenase is depicted in Figure 1.3. The catalytic cycle starts from an initial epr-silent state called the Ni-SI state. Binding of a proton to the metal centers with a concurrent uptake of an electron results in a bridging hydride ligand between the iron and the nickel center. This Ni-C state then accepts an electron to reduce the Ni(III) center to Ni(II). A second proton can be brought in close

proximity to the bridging hydride via a cysteine ligand acting as a so-called proton relay. The proton and the hydride combine to evolve dihydrogen, with the regeneration of the Ni-SI state.[3,8]

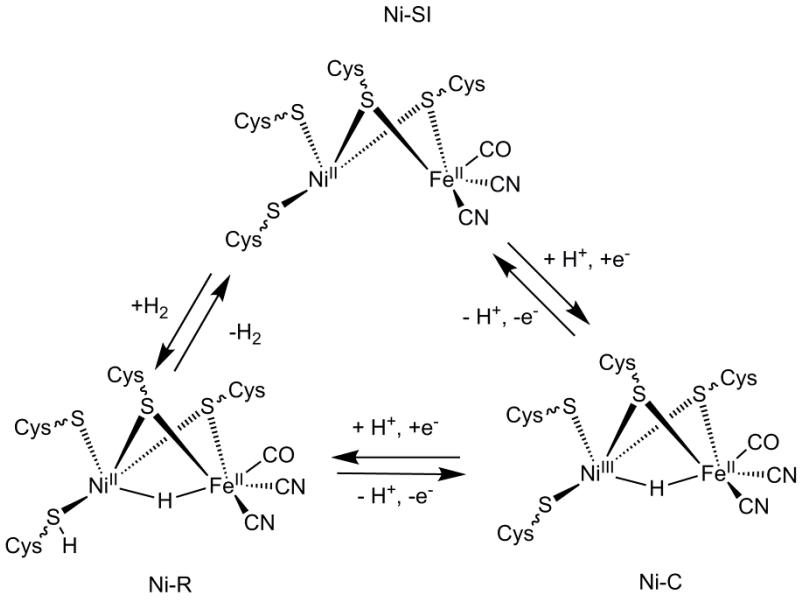


Figure 1.3: Postulated catalytic mechanism of the reversible HER catalysis by [NiFe] hydrogenases.[8]

1.2.5 [NiFeSe] Hydrogenase

The [NiFeSe] hydrogenase forms a subclass of the [NiFe] hydrogenase, in which one of the cysteines (Cys) in the active site of the enzyme is replaced by selenocysteine (Sec).[11] Selenocysteine is found in all three domains of life, however not many organisms use this aminoacid.[12] Generally, the Sec-containing redox proteins show higher catalytic activities than their Cys-containing homologues. The relevant properties of selenium that could explain this difference in activity are the higher nucleophilicity of selenium, the lower redox potentials of the Sec-homologues and the higher acidity of Sec; the pKa of Sec is 5.3 whereas that of Cys is 8.3. The increased acidity of Sec allows selenol groups to be active at lower pH ranges. Selenium is also a softer donor atom than sulfur, the polarizable volume of selenium is 3.8 $Å^3$ vs 2.9 $Å^3$ of sulfur.[13] Thus, due to the different electronic properties of selenium it is possible that the Sec ligand makes a better proton relay, and hence increases the activity of the enzyme as a whole.[3] A schematic representation of the active site of [NiFeSe] hydrogenase in the Ni-C state of the enzyme is shown in Figure 1.2.

1.3 Synthetic Models of the Active Site in [NiFe] Hydrogenase

1.3.1 Structural Models of [NiFe] Hydrogenase

After the determination of the first crystal structure of a hydrogenase enzyme, chemists used the insight gained from the active site as inspirations for the design of new molecular catalyst for proton reduction. By using either the biomimetic approach or the bio-inspired approach, several organometallic complexes have been designed and synthesized.[5] Whereas many structural and functional models for the active site in [FeFe] hydrogenase have been reported, synthetic models of the active site of the [NiFe] hydrogenase are less prevalent.[15]

The first structural model for the heterodinuclear active site in [NiFe] hydrogenase was reported by Darensbourg and coworkers,[16] and comprised a Ni(II) complex of a tetradentate N_2S_2 ligand, of which one of the thiolate sulfurs formed a bridge to an $Fe(CO)_4$ group. In this compound the Ni-Fe distance is 3.76 Å, which is significantly longer than that found in the biological system (2.6-2.9 Å).[16] Pohl and coworkers reported the first example of an Ni-Fe complex with two thiolate bridges between the metal centers, resulting in an Ni-Fe distance of 2.8 Å, which is in the range found in the biological system (Figure 1.4).[17]

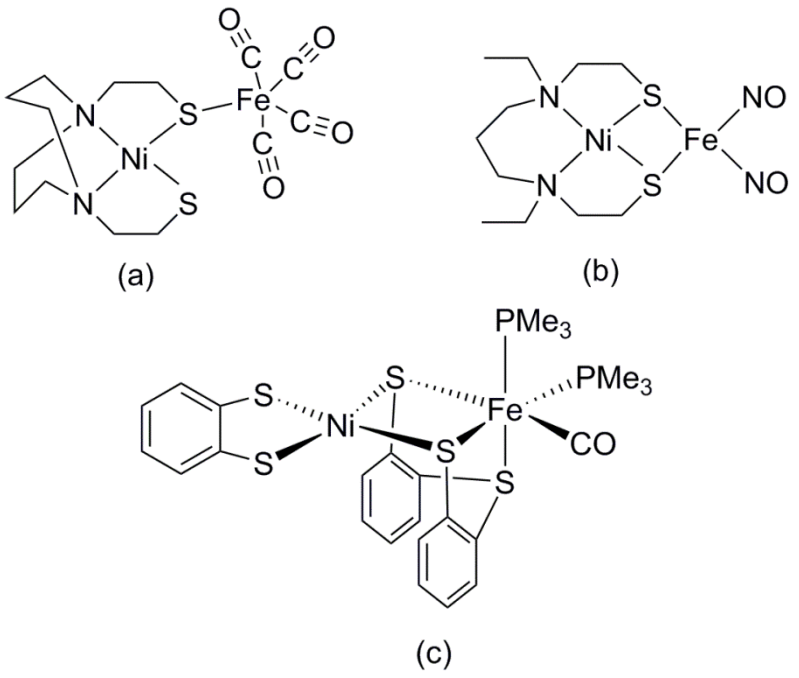


Figure 1.4: Structural models for the active site in [NiFe] hydrogenase reported by Darensbourg et al. (a),[16] Pohl et al. (b),[17] and Sellmann et al (c).[18]

In 2002 Sellmann and coworkers reported the first structural mimic comprising an NiS_4 coordination sphere with a low-spin Ni(II) center bridged by two thiolate donor atoms of a tridentate ligand to a low-spin Fe(II)-carbonyl moiety (Figure 1.4c).[18]

Although several structural models were reported with different ligand environments, none of them have been reported as catalysts either for H_2 oxidation or for proton reduction to H_2 until 2006.[10,19-21]

1.3.2 Functional Models of [NiFe] Hydrogenase

In 2004 Sellmann and coworkers reported a trinuclear Ni_2Fe complex as the first functional model of [NiFe] hydrogenase, although the catalytic activity is not clearly described (Figure 1.5).[22] The activity of this compound for proton reduction was observed using a solution of HBF_4 in dichloromethane, which resulted in oxidation of the complex with the formation of H_2 as identified by ^1H NMR.[22] The group of Schröder reported a functional model of [NiFe] hydrogenase in 2006. The trinuclear complex contained one nickel ion in a tetradentate ligand bridging to two iron centers that are each additionally bound to three carbonyl ligands in a six-coordinate, distorted octahedral geometry (Fig.1.5).[23] This compound was reported to catalyze the reduction of protons from a solution of trifluoroacetic acid (Htfa) in dichloromethane to form H_2 with an activity of 6 turnovers per hour at a potential of −1.64 V *vs* $Fc^{+/0}$. However, the compound appeared to be stable only for 1 h.[23]

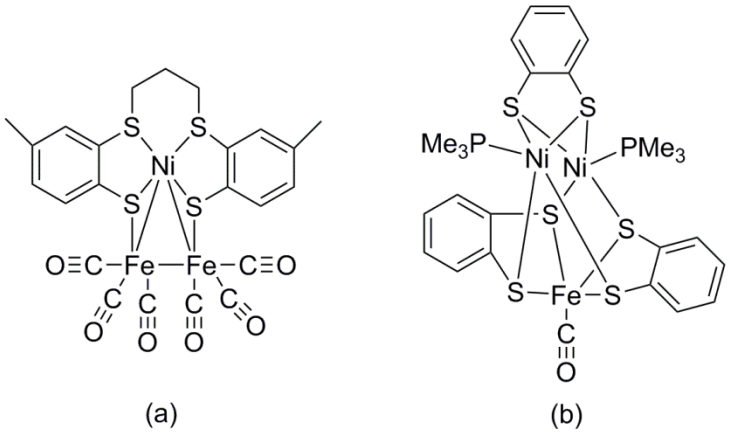


Figure 1.5: First functional models for [NiFe] hydrogenases reported by the group of Schröder (a)[23] and Sellmann et al. (b).[22]

In 2009 the group of Rauchfuss reported the compound [(dppe)Ni(μ-H)(μ-pdt)$Fe(CO)_3$] (dppe = 1,2-bis(diphenylphosphanyl)ethane; pdt = 1,3-propanedithiolate) and derivatives of this

complex by substituting CO ligands for phosphorous-based ligands (Fig. 1.6a).[24] This compound was found to be an active catalyst for proton reduction upon addition of Htfa to a dichloromethane solution as indicated by electrochemical measurements, but no quantitative results were reported.[24] In 2010 Artero and Fontecave reported the use of the compound [Ni(xbSmS)], described by the group of Bouwman in 2002, to create a NiFe species in which the iron center is substituted with a Cp^- ligand and a carbonyl group. This complex was reported to catalyze the HER in a solution of Htfa in DMF: in a 4 h experiment 20 turnovers were achieved (Fig. 1.6b).[25]

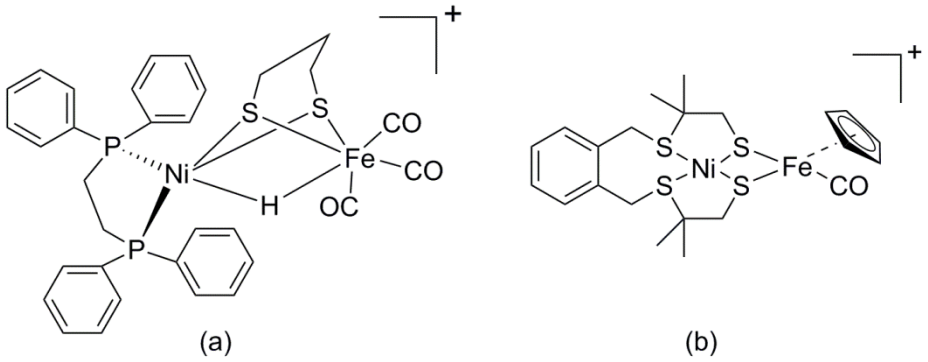


Figure 1.6: Examples of reported complexes as functional mimics of the [NiFe] hydrogenase active site.[24,25]

After these early examples of functional models, many new investigations have been reported that were aimed at understanding of the catalytic mechanism [NiFe] hydrogenase and the development cheap, high efficient catalysts.[26,27] Although a variety of model compounds have been reported until now, only few of them efficiently catalyze the hydrogen evolution reaction as functional mimics of hydrogenases.[28-33] All complexes have structural similarities with [NiFe] hydrogenase comprising either an NiS_4 or an NiS_2N_2 environment further bound to various iron centers. Two of these complexes are shown in Figure 1.7, being NiFe complexes with different nickel environments (NiS_4 and NiS_2N_2) bound to the $FeCp^*CO$ moiety (HCp^* = pentamethylcyclopentadiene). The complex comprising an NiS_4 environment appeared to have better catalytic activity in proton reduction than the complex with an NiS_2N_2 environment in the presence of HBF_4 in acetonitrile solution according to the results of electrochemical studies.[33] These differences in catalytic activity of highly similar compounds show the importance of further studies to model systems with different ligand environments. Until now the geometry of the metal centers, ligand flexibility and environment have been found to play an important role in the efficiency of electrocatalytic proton reduction.

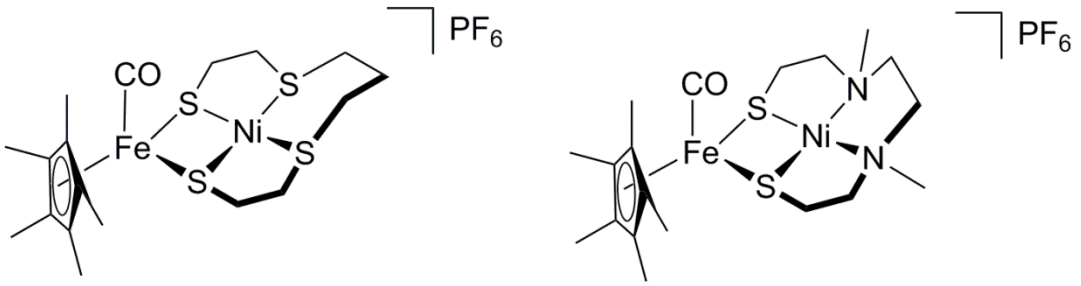
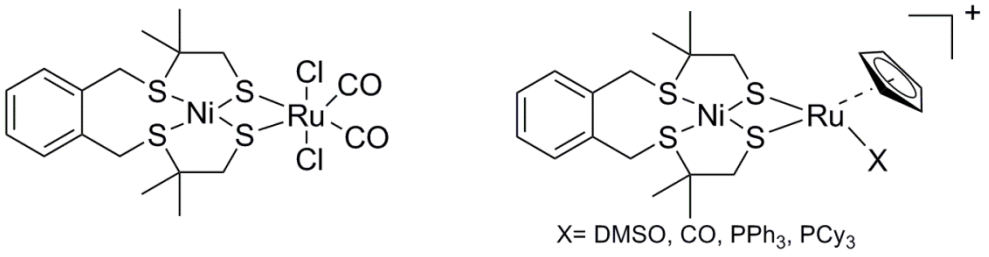


Figure 1.7: Two models of [NiFe] hydrogenases with NiS_4 and NiS_2N_2 environment.[33]

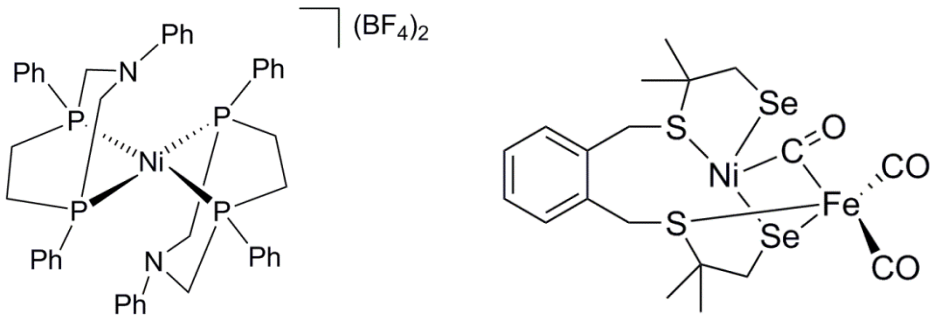
The structural and functional models for [NiFe] hydrogenase are not limited to [NiFe] species. In the further development of structural and functional mimics for the active site in [NiFe] hydrogenase, dinuclear [NiRu] compounds were also prepared.[8,34-37] The choice of replacing iron by ruthenium in mimicking the active site of the [NiFe] hydrogenase is based on the fact that many ruthenium complexes are active (homogeneous) catalysts in hydrogenation and hydrogen transfer reactions. Most significant is the fact that Ru(II) ions are able to accept both hard and soft ligands such as hydride and dihydrogen, which makes its suitable for replicating the function of the iron center in the active site of the [NiFe] hydrogenase.[8] In 2006 the group of Fontecave reported a bioinspired [NiFe] hydrogenase mimic that was prepared by combining the nickel complex [Ni(xbSmS)] with a $[Ru(CO)_2(Cl)_2]$ moiety to obtain the dinuclear NiRu complex shown in Figure 1.8a.[38,39] Following this approach another [NiRu] compound was reported comprising a ruthenium center with a Cp^- ligand (HCp = cyclopentadiene) and a variety of monodentate ligands (Figure 1.8b).[35] By using the compound $[Ni(xbSmS)RuCp(dmso)]PF_6$ as an electrocatalyst for the hydrogen evolution reaction in DMF, the overpotential of the reaction was reduced by180 mV (which is 660 mV) vs Ag/AgCl electrode compared to previously reported complexes with different ligands on ruthenium center ($[Ni(xbSmS)Ru(CO)_2Cl_2]$ and $[Ni(xbSmS)Ru(p\text{-}cymene)Cl]^+$).[35]



(a) (b)

Figure 1.8: Examples of [NiRu] complexes as bio-inspired models for the active site in [NiFe] hydrogenase.[35,38]

In 2011, DuBois and coworkers reported a highly efficient electrocatalyst for proton reduction based on a mononuclear nickel compound comprising the ligand 1,3,6-triphenyl-1-aza-3,6-diphosphacycloheptane (Figure 1.9a). This electrocatalyst catalyzes the production of dihydrogen with a turnover frequency of 33,000 s^{-1} in acetonitrile in the presence of protonated dimethylformamide and even 106,000 s^{-1} in the presence of 1.2 M water in acetonitrile.[40] The mechanistic investigations revealed that the pendant amines situated above and below the plane of coordination play a crucial role as protons relays.[40]



(a) (b)

Figure 1.9: The mononuclear nickel electrocatalyst for proton reduction reported by the group of DuBois (a)[40] and first structural model of [NiFeSe] hydrogenase reported by the group of Reisner (b).[11]

While many synthetic models were developed for the active site in [NiFe] hydrogenase, the group of Reisner focused their attention on mimics for the [NiFeSe] hydrogenase. The first approach in mimicking the [NiFeSe] hydrogenase active site was reported in 2014.[41] A mononuclear nickel compound containing a tetradentate dithioether-diselenolate ligand was reported as a mimic of the nickel part of the active site. Later the same group described a structural mimic of the [NiFeSe] hydrogenase active site containing both nickel and an iron center (Figure 1.9b).[11] The nickel part of this compound is based on the [Ni(xbSmS)] complex in which the terminal sulfurs of the S_4-ligand were replaced by selenium to obtain [Ni(xbSmSe)]. The iron part constitutes an iron(II) center with three CO ligands, of which one is bridging between the nickel and iron center. This model is the first structural model for the active site in [NiFeSe] hydrogenase.[11]

1.4 Aim and Outline of This Thesis

The aim of the research described in this thesis concerns the synthesis and characterization of new Ni, NiFe and NiRu complexes as structural and functional mimics of the active site in [NiFe] hydrogenase for electrocatalytic proton reduction.

In Chapter 2 the synthesis and characterization are described of new nickel complexes of two tetradentate S_2Se_2 ligands and the corresponding NiFe complexes obtained after reaction with $[FeCp(CO)_2]I$ as mimics of the active site in [NiFeSe] hydrogenase. The electrochemical and electrocatalytic properties towards proton reduction have been investigated and are also reported.

In Chapter 3 two NiRu complexes are reported as mimics of [NiFe] and [NiFeSe] hydrogenases. The NiRu complexes described in this chapter were obtained by the reaction of the nickel complexes [Ni(xbSmS)] and [Ni(xbSmSe)] with $[RuCp(PPh_3)_2Cl]$. The ligands only differ in the presence of either two thiolates or two selenolate groups in an attempt to get insight in the role of the selenolate group in the activation of protons by the isostructural [NiRu] compounds. The electrochemical properties of the complexes and their activities as electrocatalyst in the hydrogen evolution reaction are compared.

In Chapter 4 the synthesis and characterization is reported of a number of new nickel dithiolate/diselenolate complexes. These compounds appeared to be unstable in light. The light-induced C-S / C-Se bond cleavage that occurs in these compounds is described. This reactivity is relevant for the understanding of the the mechanism of methyl-coenzyme M reductase (MCR).

In Chapter 5 the reaction of [Ni(xbSmS)] and [Ni(xbSmSe)] with the compound cis-$[Ru(phen)_2(Cl)_2]$ is described. The electrochemical properties of the resulting trinuclear [NiRu] complexes are described, and their activity as electrocatalysts for proton reduction is compared.

Finally, in Chapter 6 a summary is presented of the findings described in this thesis, followed by general conclusions and an outlook for further research.

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