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Influence of a Large σ-Donor Ligand on Structural and Catalytic Properties of Di-Iron Compounds Related to the Active Site of Fe-Hydrogenase – A DFT Investigation

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The complex $(S_2C_3H_6)[Fe_2(CO)_5P(NC_4H_8)_3]$ (**A**), a recently synthesized functional model of the active site of Fe-hydrogenases, is able to electrocatalyze proton reduction, leading to molecular hydrogen evolution. Experimental results suggested that the presence of the electron donor $P(NC_4H_8)_3$ ligand in **A** could favor the formation of a μ-CO species similar to that observed in the enzymatic cluster. However, insight into the structural features of key catalytic intermediates deriving from reduction and protonation of **A** was still lacking. Here we present results obtained using density functional theory to evaluate structures, relative stabilities, and spectroscopic properties of several species relevant for the electrocatalytic H_2 evolving process. The results enabled us to unravel the structure of the μ-CO complex experimentally detected after monoelectronic reduction of **A**. Moreover, we show that the introduction of the large electron-donor ligand $P(NC_4H_8)_3$ in the biomimetic complex does not favour the stabilization of terminal-hydrido adducts, which are expected to be very reactive in terms of H_2 production. The comparison of our findings with previous theoretical and experimental results obtained on similar model complexes suggests that the introduction of an electron donor ligand as good as $P(NC_4H_8)_3$, but less sterically demanding, could represent a better choice to facilitate the formation of μ-CO complexes more closely resembling the structure of the enzymatic cluster.

Introduction

The possibility of producing molecular hydrogen through eco-compatible, hydrocarbon-independent processes has been stimulating chemists towards the synthesis of inexpensive catalytic materials that could replace the currently used platinum-containing electrocatalysts.[1] The search for cheaper, but still efficient catalysts could take advantage from the study of hydrogenases,[2] which are metallo-enzymes that are able to catalyze the evolution of molecular hydrogen at high rates starting from protons and electrons.

Three classes of hydrogenases have been characterized so far: Ni–Fe hydrogenases, which include both iron and nickel atoms as metal centers of functional importance, and two classes of iron-dependent enzymes, i.e. the "iron-sulfur-cluster-free" hydrogenases,[3] and another group of proteins containing Fe_xS_x clusters, commonly referred to as "Iron-only" or Fe-hydrogenases. X-ray crystallographic studies on Fe-hydrogenases from *C. pasteurianum*[4] and *D. desulfuricans*[5] have shown that the active site of these enzymes includes an Fe_2S_2 sub-site bearing CO and CN^- ligands. The iron atoms of the sub-site are bridged by two sulfur atoms of a 1,3-propanedithiolato (pdt) or a related bis(thiomethyl)amino unit. One of the iron atoms shares a cysteinyl sulfur ligand with a classical Fe_4S_4 cluster; the resulting iron–sulfur complex is usually referred to as the H-cluster. Experimental results[6] indicate that the unprotonated, Fe^{I}-Fe^{II} form of the H-cluster di-iron subsite should correspond to a catalytically active state characterized by the presence of a carbonyl ligand bridging the two iron centers. As shown in Scheme 1, the coordination site *trans* to the bridging CO remains vacant, and this observation suggests that protons and dihydrogen could occupy such a position during the catalytic process. Upon monoelectronic reduction of the H-cluster, the bridging CO moves to a terminal position, but it still remains localized in the region of space between the iron ions (see Scheme 1).[6]

The above-mentioned studies have stimulated experimental chemists towards the synthesis of organometallic models that could reproduce the main structural and functional features of the H-cluster.[7] Unfortunately, the biomimetic clusters obtained so far fail to reproduce the precise orientation of ligands found in the H-cluster, a fact that is expected to be at the basis of the reduced catalytic efficiency of synthetic assemblies. For example, in the complex (μ-

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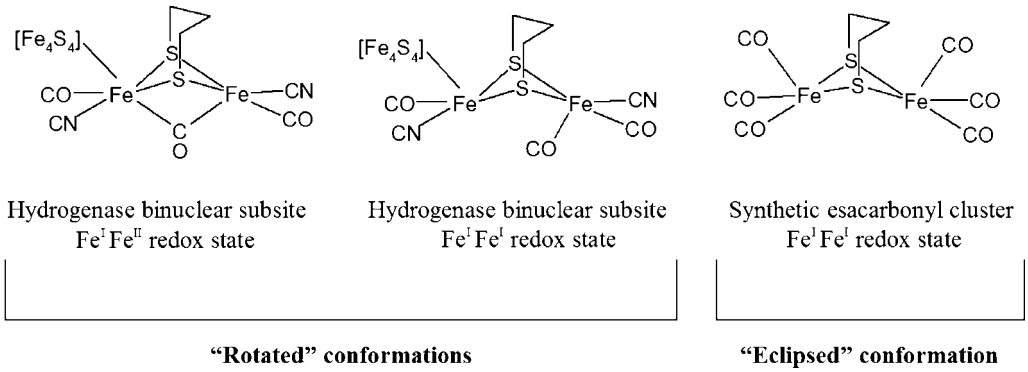


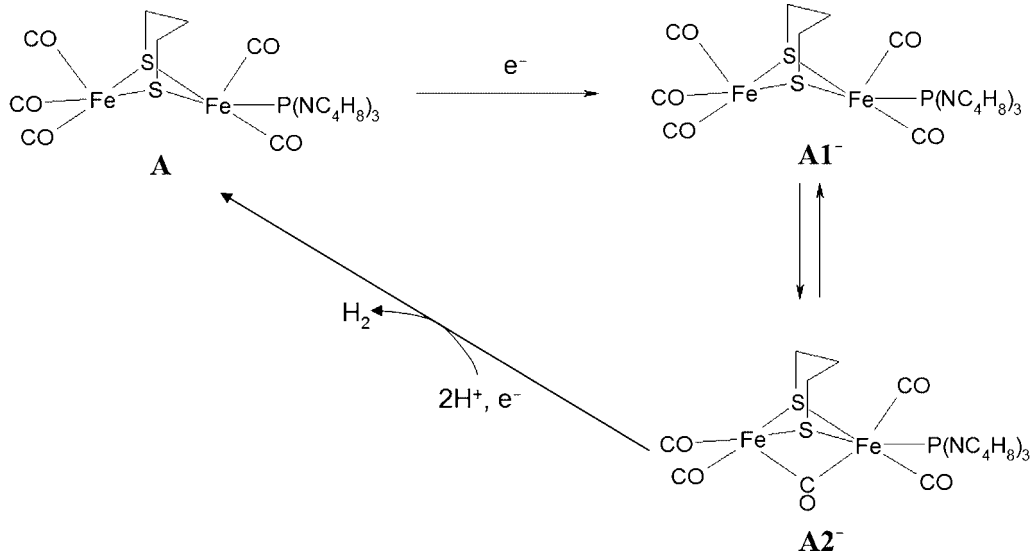
Scheme 1. Structures of the Fe-hydrogenase binuclear subsite in two different redox states, and geometry of the synthetic complex (μ-pdt)[Fe(CO)$_3$]$_2$.

pdt)[Fe(CO)$_3$]$_2$, the simplest functional model of the active site of Fe-hydrogenases, all the carbonyl groups are in the terminal position.[7h] Such an arrangement of ligands will be referred to as the "eclipsed conformation," as opposed to the "rotated conformation" that can be observed in Fe-hydrogenases (Scheme 1).

Theoretical studies have been carried out to understand the causes of the structural difference between synthetic models and the enzyme active site.[8,9] It turned out that the presence of good electron donor ligands bound to the metal centers can help in stabilizing the rotated conformation of di-iron clusters. Such observations have been recently taken into account by Hou and collaborators, who probed the effects of the introduction of tris(*N*-pyrrolidinyl)phosphane, a very good donor ligand, on the structural and functional properties of the synthetic species (μ-pdt)[Fe$_2$(CO)$_5$P(NC$_4$H$_8$)$_3$] (**A**).[10] It turned out that **A** (Scheme 2) is characterized by eclipsed conformation, while monoelectronic reduction leads to the formation of a μ-CO species that was tentatively assigned, on the basis of IR data, to a rotated conformer closely resembling the unprotonated form of the H-cluster (species **A2**$^-$, Scheme 2). Nothing is known about the regiochemistry of protonation of this synthetic cluster, an issue that is expected to be relevant to rationalize the electrocatalytic properties shown by (μ-pdt)[Fe$_2$(CO)$_5$P(NC$_4$H$_8$)$_3$] (for details on the mechanism proposed by Hou and collaborators for hydrogen evolution mediated by the di-iron assembly, see Scheme 2). In order to shed light on the structure-function relationships in **A**, we carried out a DFT investigation of structures, spectroscopic properties, and relative stabilities of several plausible isomers of this biomimetic compound, both in its protonated and unprotonated forms. Results allowed us to obtain a detailed structural characterization of key intermediate species, and a better understanding of the electrocatalytic cycle. DFT results are expected to be helpful also for the design of better bioinspired electrocatalytic compounds.

Methods

DFT calculations have been carried out using the pure functional BP86[11] in conjunction with a valence triple-ζ basis set with polarization on all atoms (TZVP).[12]



Scheme 2. The electrocatalytic mechanism of H_2 evolution mediated by (μ-pdt)[Fe$_2$(CO)$_5$P(NC$_4$H$_8$)$_3$], as proposed in ref.[10]

Calculations have been carried out with the TURBOMOLE 5.7 suite[13] applying the resolution-of-the-identity technique.[14]

Stationary points of the energy hypersurface have been located by means of energy gradient techniques and full vibrational analysis has been carried out to further characterize each stationary point. In order to characterize isomeric forms, DFT optimizations were repeated several times, starting from different initial geometries.

Free energy (G) values have been obtained from the electronic SCF energy considering three contributions to the total partition function (Q), namely $q_{translational}$, $q_{rotational}$, $q_{vibrational}$, under the assumption that Q may be written as the product of such terms.[15] In order to evaluate enthalpy and entropy contributions, the value for the temperature, pressure, and scaling factor for the SCF wavenumbers have been set to 298.15 K, 1 bar, and 0.9914, respectively. Rotations have been treated classically and vibrational modes described according to the harmonic approximation.

The optimized structures of the complexes reported in the present study always correspond to low spin states; high spin states are characterized by higher energies (not shown), as expected considering the characteristics of the ligands forming the coordination environment of the metal atoms.

The relative energies discussed in the present work are Gibbs free energies where the contributions described above are taken into account. The effect of the solvent (acetonitrile, ε = 36.64) has been evaluated according to the COSMO approach.[16]

Results and Discussion

For the sake of clarity, hereafter experimental complexes will be designated with capital bold letters, while computational models will be referred to using lower case bold letters. As for the nomenclature of the iron atoms, the metal center bound to the phosphane ligand will be referred to as the "proximal iron" (Fe_p), while the other iron ion will be named "distal" (Fe_d).

In order to validate the computational approach adopted in this paper (BP86/TZVP, see Methods), we initially opti-

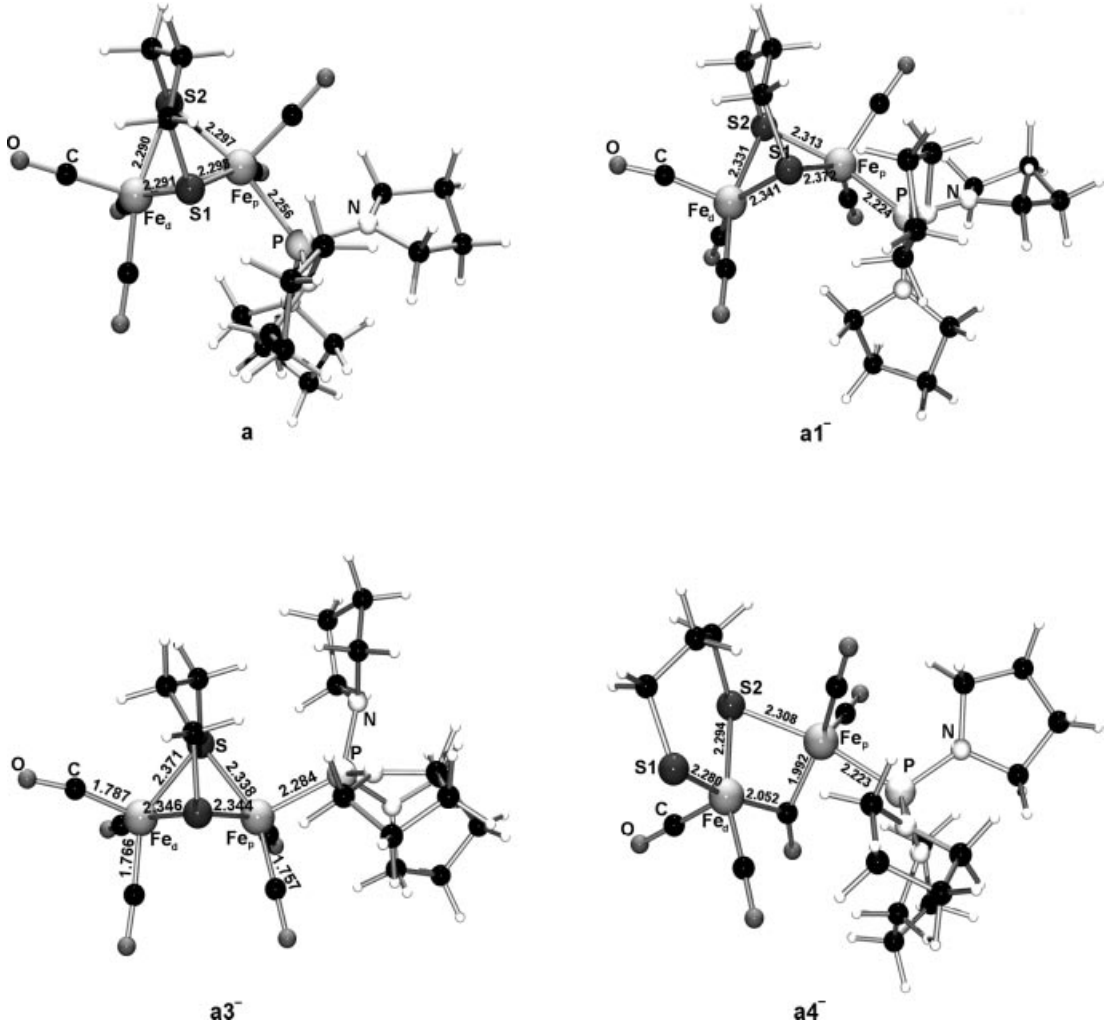


Figure 1. Optimized geometries of complexes **a**, **a1**$^-$, **a3**$^-$ and **a4**$^-$; S = 0 and 1/2 for neutral and monoanionic complexes, respectively. Selected distances are given in Å.

mized the geometry of complex **a**, and compared the resulting structure (see Figure 1) with its experimental counterpart. As shown in Table 1, the differences in bond lengths between **a** and **A** never exceed 0.059 Å. Similarly good results are obtained when bond angles are considered: in fact, the maximum difference between calculated and experimental values is very low (4.7 deg; for the Fe_p–Fe_d–C angle, the latter atom belonging to the carbonyl group *trans* to the S2 atom of pdt. See Figure 1).

Table 1. Comparison between experimental and computed bond lengths for complex **A**. Distances in Å.

Bond	Experimental bond lengths (**A**)	Calculated bond lengths (**a**)	Difference
Fe_d–Fe_p	2.5527	2.611	0.0583
Fe_p–S	2.2418; 2.2675	2.279; 2.300	0.0372; 0.0325
Fe_d–S	2.2542; 2.2615	2.286; 2.297	0.0318; 0.0355
Fe_p–P	2.2563	2.286	0.0297
P–N	1.662; 1.670; 1.682	1.711; 1.721; 1.731	0.049; 0.051; 0.049

An excellent correlation between computed and experimental CO stretching frequencies was also found, confirming that the BP86/TZVP level of theory is well suited to describe this class of compounds.[17] In fact, linear regression analysis gives rise to a R^2 value as large as 0.997 (Figure 2).

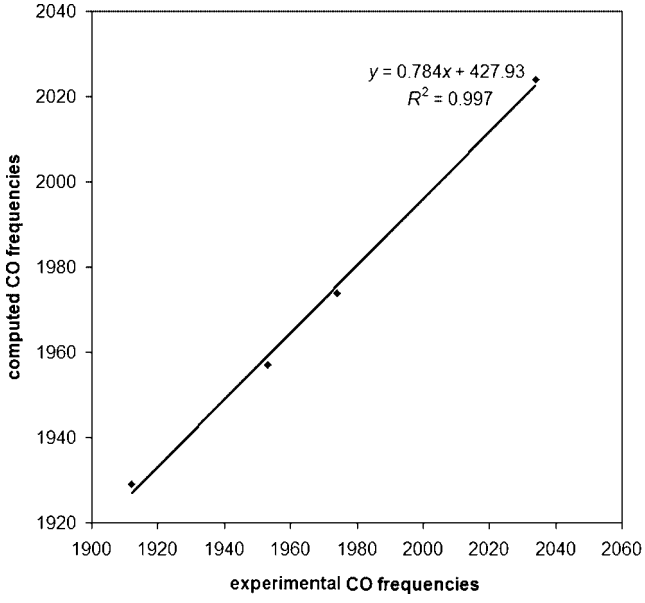


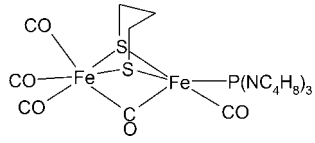
Figure 2. Linear fitting of calculated and experimental CO stretching frequencies for species **A**.

Structural Characterization of the Experimentally Observed Monoanionic Derivatives

The first optimized monoanionic isomer considered as a plausible product of the monoelectron reduction of **a** is **a1**$^-$, which shares a high degree of structural similarity with the parent complex **a**, the main differences being restricted to a limited decrease of the Fe_p–P bond length, while all the other bonds are slightly elongated in **a1**$^-$ (see Figure 1).

Hou et al.[10] proposed that **A1**$^-$ could undergo a conformational rearrangement leading to a μ-CO species structurally related to the enzymatic Fe_2S_2 subsite (complex **A2**$^-$, see Scheme 2). Prompted by these considerations, we carried out the geometry optimization of $(CO)_2Fe_d(\mu\text{-pdt})(\mu\text{-CO})Fe_p(CO)_2[P(NC_4H_8)_3]$ (**a2**$^-$), a species in which one of the terminal carbonyls bound to Fe_d in **a1**$^-$ has moved to a bridging position. However, it turned out that **a2**$^-$ (structure not shown) corresponds to a third-order saddle point on the potential energy surface (imaginary frequencies: 47.95i, 29.72i, 14.91i cm^{-1}). Moreover, **a2**$^-$ is 12.5 kcal mol^{-1} less stable than **a1**$^-$. DFT optimizations started from slightly different initial geometries converged on **a1**$^-$ or **a2**$^-$. Taken as a whole, these results indicate that **a2**$^-$ cannot correspond to the μ-CO species experimentally observed (**A2**$^-$).

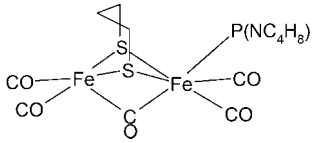
In principle, another isomer closely resembling the structure of the unprotonated enzymatic cofactor could be present in solution: in fact, a terminal CO bound to Fe_p could move to a bridging position, thus giving place to $(CO)_3Fe_d(\mu\text{-pdt})(\mu\text{-CO})Fe_p(CO)[P(NC_4H_8)_3]$, see Scheme 3. However, all the attempts to obtain such a geometry as a result of DFT optimization failed: several calculations were carried out starting from slightly different guess structures, but all of them fell back towards the **a1**$^-$ conformation. This indicates that a minimum corresponding to such a μ-CO geometry does not exist on the PES of $(\mu\text{-pdt})[Fe_2(CO)_5P(NC_4H_8)_3]$. The instability of this structure can be ascribed to the presence of a μ-CO group *trans* to another π-acid carbonyl ligand, and to a vacant coordination site.



Scheme 3. Schematic structure of a hypothetical adduct showing rotated conformation.

Previous computational studies[18,19] have shown that the stabilization of rotated conformations in di-iron biomimetic complexes can be achieved positioning a good σ-donating group *trans* to the incipient μ-CO. In view of this observation, we have evaluated (i) if the sterically impeded ligand $P(NC_4H_8)_3$ can move to assume an apical position on Fe_p in an eclipsed conformer, and (ii) if such a disposition of ligands on Fe_p can favor the rotation of ligands around Fe_d. In fact, an eclipsed geometry showing an apical $P(NC_4H_8)_3$ ligand corresponds to an energy minimum structure (adduct **a3**$^-$, Figure 1). **a3**$^-$ is 4.1 kcal mol^{-1} less stable than **a1**$^-$ due to the unfavorable interactions between the pyrrolidine rings of the phosphane ligand and the alkyl chain of pdt. These repulsive interactions played a relevant role in the optimization of the corresponding rotated species **a3-rotated**$^-$, see Scheme 4. In fact, the distortion of pdt geometry led one of its sulfur atoms to detach from the proximal

iron ion, a rearrangement accompanied by bridging-to-terminal movement of the μ-CO group, resulting in a four-coordinate Fe_p atom (structure not shown).



Scheme 4. Starting structure used for geometry optimization of **a3-rotated**$^-$.

The instability of μ-CO anionic complexes leaves unanswered the question of the nature of the spectroscopically characterized μ-CO species. Indeed, it was recently shown that hexacarbonyl di-iron complexes including a pdt ligand can assume a structure in which a sulfur atom of pdt has moved from a bridging to a terminal position;[20] such a rearrangement may allow one of the terminal CO ligands to become a μ-CO. Analysis of **a1**$^-$ suggests that this species might undergo a similar rearrangement: in fact, one of the Fe–S bonds (Fe_p–S1, 2.372 Å, see Figure 1) is significantly elongated with respect to the other three Fe–S bonds (2.313, 2.331, 2.341 Å). The weakening of the bonding interaction between Fe_p and S1 could favor isomerization, giving place to the DFT-optimized species **a4**$^-$ (see Figure 1). Notably, this isomer is only slightly less stable (2.9 and 5.0 kcal mol^{-1} when considering SCF energy differences and ΔG values, respectively) than **a1**$^-$; thus, these two adducts could be present simultaneously in solution, with **a1**$^-$ representing the main product of the monoelectronic reduction of **a**.

The co-existence of **a4**$^-$ and **a1**$^-$ is also supported by the comparison between the computed CO stretching frequencies of these two species and the experimental IR bands: in fact, the IR spectrum collected after electrochemical reduction of **a** is characterized by six distinct bands – five intense bands in the region between 1845 and 2015 cm^{-1}, and a weak absorption at lower wavenumbers (1778 cm^{-1}). In light of our computational results, we propose that the spectrum region above 1850 cm^{-1} is dominated by the stretching modes of the five terminal carbonyls included in the main reduction product **a1**$^-$; the less stable **a4**$^-$ species is detectable thanks to its bridging CO group, whose predicted IR stretching frequency (1742 cm^{-1}) is located largely below 1845 cm^{-1}. All the other computed CO peaks from **a4**$^-$ fall in a narrow region between 1872 and 1953 cm^{-1}, where the most populated **a1**$^-$ isomer gives place to intense absorption bands. As a further support to this hypothesis, a very good correlation between the selected six computed IR frequencies and the corresponding experimental bands could be evidenced after linear regression fitting analysis (R^2 = 0.990, see Figure 3).

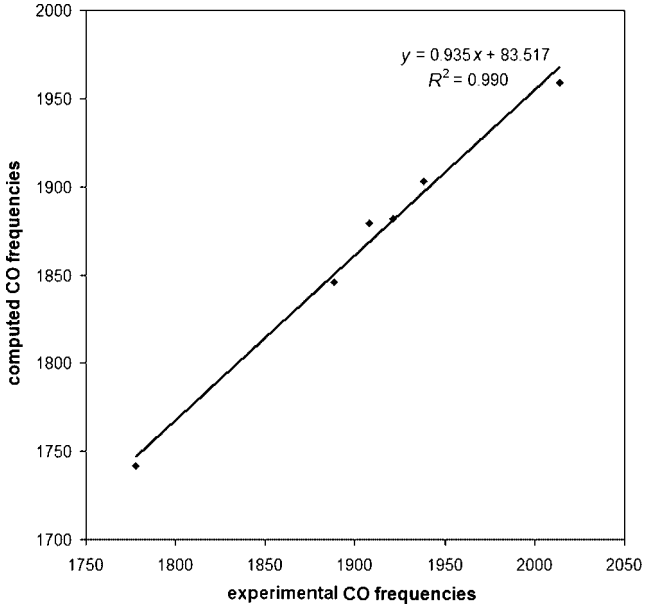
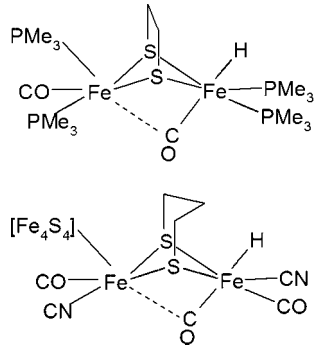


Figure 3. Linear fitting of the calculated and experimental CO frequencies for the anionic adducts coming from monoelectronic reduction of **A**.

Protonation of Monoanionic Derivatives

In the electrocatalytic cycle, monoelectronic reduction of **A** should be followed by protonation of the resulting monoanionic complex. The regiochemistry of protonation can influence the efficiency of hydrogen evolution, as shown recently for the biomimetic di-iron compound $[Fe_2(S_2C_2H_4)(\mu\text{-CO})(H)(CO)(PMe_3)_4]^+$, which revealed that a hydrido ligand terminally bound to one of the iron ions is much more reactive than a μ-H group.[21] This result supports the hypothesis that the formation of a terminal hydrido *trans* to a μ-CO or a semi-bridging carbonyl is crucial to explain the very high efficiency of Fe-hydrogenases (Scheme 5). However, in the case of simple Fe-hydrogenase functional models such as (μ-pdt)$[Fe(CO)_3]_2$, formation of μ-H derivatives (as opposed to terminal-hydrido adducts) is highly favored.[20a,22]



Scheme 5. Schematic structure of the synthetic complex obtained by Rauchfuss et al.,[21] and hypothetical structural features of the corresponding state of the active site of Fe-hydrogenase.

In view of these observations, we have studied the effects of the introduction of the donor ligand $P(NC_4H_8)_3$ on the relative stabilities of monoprotonated pentacarbonyl diiron complexes. To this end, we carried out geometry optimization of several different isomers, whose optimized structures are collected in Figure 4.

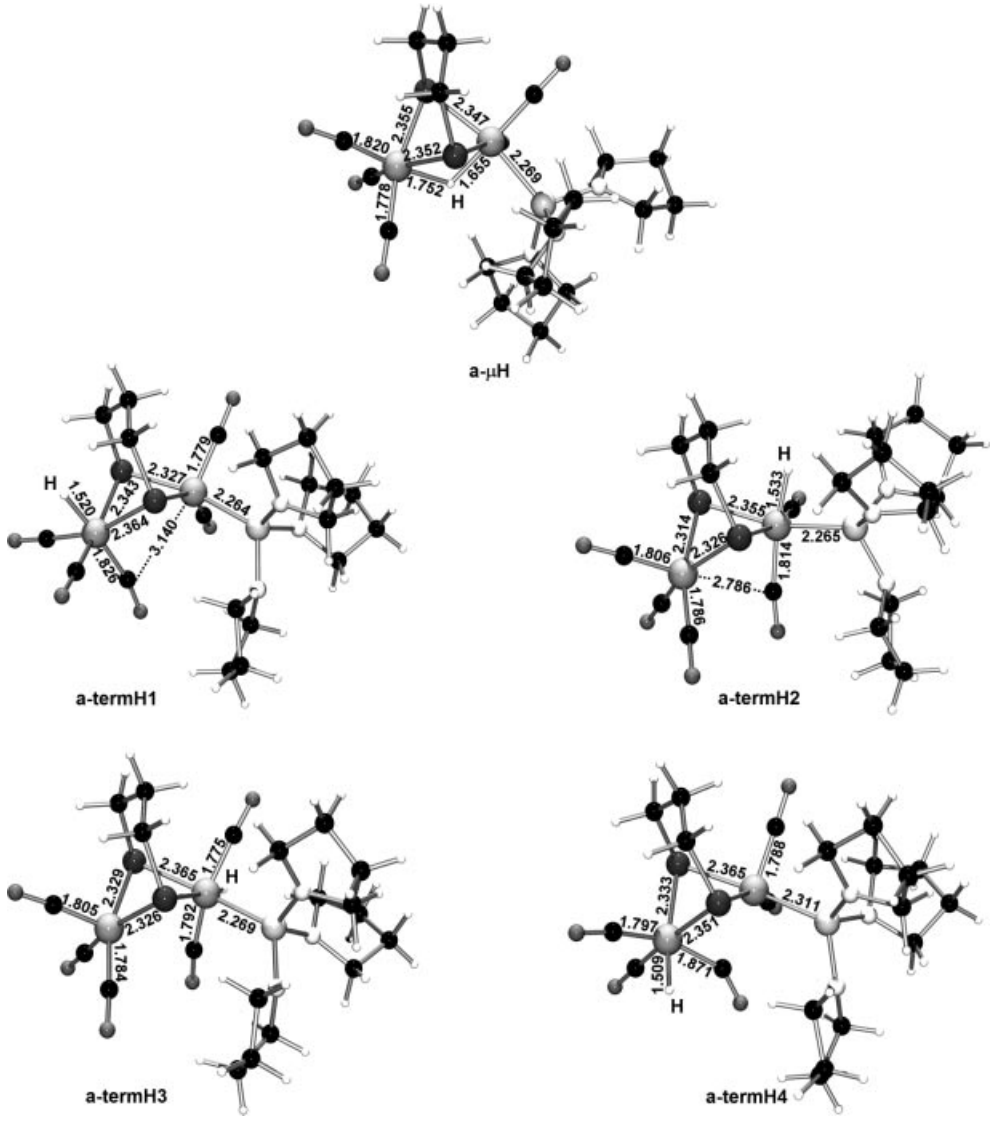


Figure 4. Optimized geometries of complexes **a-μH**, **a-termH1**, **a-termH2**, **a-termH3**, and **a-termH4**; for all these species $S = 1/2$. Selected distances are given in Å. The hydrido group has been labelled for the sake of clarity.

In line with previous observations regarding the protonated form of (μ-pdt)[Fe(CO)$_3$]$_2$,[20] the μ-H species **a-μH** is more stable than all the terminal-hydrido adducts considered in the present study (see Table 2 for a summary of the calculated ΔG values). Particularly relevant in the context of relative stabilities analysis are the cases of **a-termH1** and **a-termH2**: these complexes feature a terminal hydrido ligand *trans* to a carbonyl ligand, and can thus be considered the isomers with greater similarity to the most plausible protonated form of the enzymatic di-iron subsite (Figure 4). However, the free energy difference between **a-termH1** and **a-μH** is large ($\Delta G_{\mathbf{a\text{-}termH1-a\text{-}\mu H}}$ = 11.3 kcal mol^{-1}) and, more importantly, it is even larger than the energy difference between the corresponding monoprotonated hexacarbonyl complexes (**b-μH** and **b-termH**, see Figure 5; $\Delta G_{\mathbf{b\text{-}termH1-b\text{-}\mu H}}$ = 8.2 kcal mol^{-1}). The increase in the energy gap observed going from the hexacarbonyl to the pentacarbonyl species is due to steric repulsion between the carbonyl *trans* to the terminal hydrido in **a-termH1** and the phosphane ligand bound to Fe$_p$. In fact, this CO group can be considered a terminal carbonyl in the pentacarbonyl complex, since the Fe$_p$–C distance is as long as 3.140 Å, while the corresponding interatomic distance in (μ-pdt)[Fe(H)(CO)$_3$]$_2$ is significantly shorter (2.856 Å).

Table 2. Free energy difference between the μ-H adduct **a-μH** and the various terminal-hydrido isomers considered in this paper.

Adduct	Free energy difference relative to **a-μH** [kcal mol^{-1}]
a-termH1	11.3
a-termH2	10.3
a-termH3	11.2
a-termH4	18.0

When **a-termH2** is considered, a large energy difference relative to **a-μH** is also observed ($\Delta G_{\mathbf{a\text{-}termH1-a\text{-}\mu H}}$ = 10.3 kcal mol^{-1}). In this case, however, the CO *trans* to the

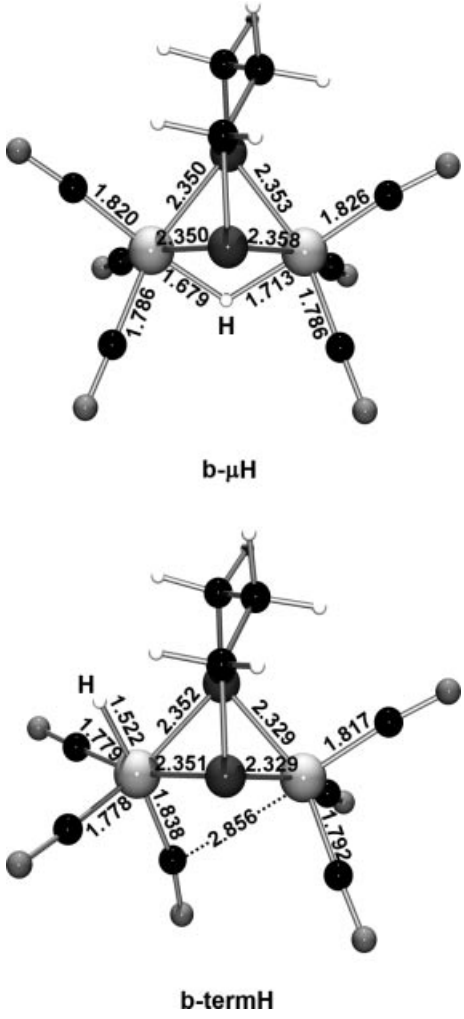


Figure 5. Optimized geometries of complexes **b-μH** and **b-termH**; for these two species $S = 1/2$. Selected distances are given in Å. The hydrido group has been labelled for the sake of clarity.

terminal hydrido on Fe_p remains closer to the second iron center (Fe_d–C bond length: 2.786 Å, see Figure 4), a behavior that is again correlated with the repulsive interactions between the carbonyl ligand and the pyrrolidine rings included in $P(NC_4H_8)_3$.

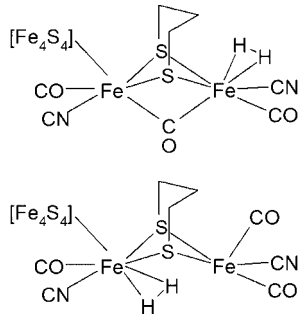
To complete the characterization of the monoprotonated species, we optimized also the structures of two adducts bearing a hydrido *trans* to the sulfur atoms of pdt (**a-termH3** and **a-termH4**, see Figure 4); both of them show free energy gaps larger than 11 kcal mol^{-1}, when compared to **a-μH**.

In summary, our computational results demonstrate that the formation of terminal-hydrido ligands should have small, if any, importance in the electrocatalytic cycle mediated by (μ-pdt)[$Fe_2(CO)_5P(NC_4H_8)_3$]. Moreover, the comparison between theoretical data obtained for (μ-pdt)[$Fe(CO)_3]_2$ and (μ-pdt)[$Fe_2(CO)_5P(NC_4H_8)_3$] indicates that the introduction of the electron donor ligand $P(NC_4H_8)_3$ does not lead to stabilization of terminal-hydrido complexes.

Diprotonated Neutral Complexes

Experimental data show that (μ-pdt)[$Fe_2(CO)_5P(NC_4H_8)_3$] undergoes two reduction and two protonation steps to allow H_2 evolution and closure of the catalytic cycle. Formation of diprotonated neutral species could thus have a role in electrocatalysis. In view of this, we studied neutral species derived from reduction and protonation of neutral, monoprotonated model complexes. In particular, we investigated the possible outcome of monoelectronic reduction and protonation of both a μ-H adduct (**a-μH**), and a terminal-hydrido compound (**a-termH1**).

It is important to note that the catalytic cycle of Fe-hydrogenases has been proposed to involve diprotonated intermediates in which a H_2 molecule is terminally bound to one of the iron centers in the binuclear subsite[23] (see Scheme 6). However, reduction and protonation of both **a-μH** and **a-termH1** does not lead to H_2-bound complexes: the addition of one electron and one proton to **a-μH** led to **a-H_2** (Figure 6), in which both hydrogen atoms, which are separated by 1.78 Å, occupy terminal positions on the two iron centers.



Scheme 6. The two possible versions of the H_2 bound H-cluster, as reported in ref.[23]

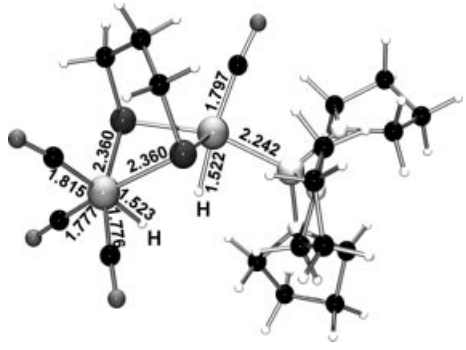


Figure 6. Optimized geometry of complex **a-H_2**, a diprotonated neutral complex in the singlet state ($S = 0$). Selected distances are given in Å. Labels are added only to metal-bound hydrogen atoms.

Interestingly, during the optimization of a species obtained by mono-electron reduction and protonation of **a-termH1**, the release of H_2 from the complex was observed. This result corroborates the hypothesis that the formation of **a-termH1** during electrocatalysis would give rise to a very efficient H_2 evolving route. Therefore, efforts aiming at the stabilization of pentacarbonyl diiron adducts bearing a ter-

minal hydrido ligand could assume great relevance for the development of better electrocatalytic materials.

Conclusions

In the first part of this work, we investigated the structural properties of several plausible isomers obtained by monoelectron reduction of the biomimetic complex (μ-pdt)[$Fe_2(CO)_5P(NC_4H_8)_3$]. Our computational study allowed us to show that complexes **a1**$^-$ and **a4**$^-$ should coexist in solution. The former adduct corresponds to a "classical" eclipsed conformation, while the second one is a μ-CO species structurally not related to the Fe-hydrogenases binuclear subsite. Therefore, the possibility that a rotated conformer closely resembling the H-cluster geometry can be formed during electrocatalysis is excluded. The ineffectiveness of $P(NC_4H_8)_3$ in stabilizing the rotated form of the synthetic assembly can be rationalized in light of recent theoretical results regarding monosubstituted derivatives of (μ-pdt)[$Fe(CO)_3$]$_2$ (i.e., adducts in which only one carbonyl has been replaced by a good σ-donor).[18,19] In fact, it has been shown that a good electron-donating ligand (L) is able to stabilize the rotated conformation of (μ-pdt)[$Fe(CO)_3$-$Fe(CO)_2(L)$]$^-$ complexes, when L is *trans* to the incipient bridging CO group.[18,19] Nevertheless, if L corresponds to $P(NC_4H_8)_3$, it is not possible to place the σ-donor *trans* to the incipient μ-CO, since in such a configuration the alkyl chain of pdt would cause steric clashes with the pyrrolidine rings included in $P(NC_4H_8)_3$. These observations suggest that the introduction of an electron donor ligand as good as $P(NC_4H_8)_3$, but less sterically demanding, could represent a better choice to facilitate the formation of more stable rotated adducts.

In the second part of the study, we have shown that the most stable protonated, uncharged form of (μ-pdt)-[$Fe_2(CO)_5P(NC_4H_8)_3$] corresponds to a μ-H adduct (**a-μH**), and that terminal-hydrido complexes – which turned out to be highly reactive according to DFT results – are not involved in the electrocatalytic cycle. In fact, all the terminal-hydrido species here investigated are less stable than the hydrido-bridged isomer **a-μH** by at least 10 kcal mol^{-1}. The steric repulsion between the $P(NC_4H_8)_3$ ligand and the carbonyl ligands plays a relevant role in determining such large energy gaps.

In conclusion, DFT results allowed us to rationalize why the synthetic complex (μ-pdt)[$Fe_2(CO)_5P(NC_4H_8)_3$] is significantly less efficient then the enzyme in H_2 production,[10,24] and might contribute to the design and synthesis of novel functional models of the active site of Fe-hydrogenase.

[1] M. Y. Darensboug, *Nature* **2005**, *433*, 589.

[2] S. P. Albracht, *Biochim. Biophys. Acta* **1994**, *167*, 1188; E. G. Graf, R. K. Thauer, *FEBS Lett.* **1981**, *136*, 165; M. W. W. Adams, *Biochim. Biophys. Acta* **1990**, *115*, 1020; R. Cammack, *Nature* **1999**, *397*, 214; Y. Nicolet, B. J. Lemon, J. C. Fontecilla-Camps, J. W. Peters, *Trends Biochem. Sci.* **2000**, *25*, 138; J. W. Peters, *Curr. Opin. Struct. Biol.* **1999**, *9*, 670; D. S. Horner, B. Heil, T. Happe, T. M. Embley, *Trends Biochem. Sci.* **2002**, *27*, 148; Y. Nicolet, C. Cavazza, J. C. Fontecilla-Camps, *Inorg. Biochem.* **2002**, *91*, 1; R. Cammack, M. Frey, R. Robson, *Hydrogen as Fuel – Learning from Nature*, Taylor and Francis, London, **2001**; F. A. Armstrong, *Curr. Opin. Chem. Biol.* **2004**, *8*, 133.

[3] E. J. Lyon, S. Shima, G. Buurman, S. Chowdhuri, A. Batschauer, K. Steinbach, R. K. Thauer, *Eur. J. Biochem.* **2004**, *271*, 195; O. Pilak, B. Mamat, S. Vogt, C. H. Hagemeier, R. K. Thauer, S. Shima, C. Vonrhein, E. Warkentin, U. Ermler, *J. Mol. Biol.* **2006**, *358*, 798.

[4] J. W. Peters, W. N. Lanzilotta, B. J. Lemon, L. C. Seefeldt, *Science* **1998**, *282*, 1853.

[5] Y. Nicolet, C. Piras, P. Legrand, C. E. Hatchikian, J. C. Fontecilla-Camps, *Structure* **1999**, *7*, 13.

[6] Y. Nicolet, A. L. de Lacey, X. Vernede, V. M. Fernandez, E. C. Hatchikian, J. C. Fontecilla-Camps, *J. Am. Chem. Soc.* **2001**, *123*, 1596.

[7] a) W. Gao, J. Liu, C. Ma, L. Weng, K. Jin, C. Chen, B. Akermark, L. Sun, *Inorg. Chim. Acta* **2006**, *359*, 1071; b) L.-C. Song, C. Jea, J. Yan, H.-T. Wang, X.-F. Liu, X. Q.-M. Hu, *Organometallics* **2006**, *25*, 1544; c) S. Jiang, J. Liu, L. Sun, *Inorg. Chem. Commun.* **2006**, *9*, 290; d) J.-F. Capon, F. Gloaguen, P. Schollhammer, J. Talarmin, *Coord. Chem. Rev.* **2005**, *249*, 1664; e) C. Tard, X. Liu, S. K. Ibrahim, M. Bruschi, L. De Gioia, S. C. Daview, X. Yang, L.-S. Wang, G. Sawers, C. J. Pickett, *Nature* **2005**, *433*, 610; f) L.-C. Song, Z.-Y. Yang, H.-Z. Bian, Y. Liu, H.-T. Wang, X.-F. Liu, Q.-M. Hu, *Organometallics* **2005**, *24*, 6126; g) J. W. Tye, J. Lee, H.-W. Wang, R. Mejia-Rodriguez, J. H. Reibenspies, M. B. Hall, M. Y. Darensbourg, *Inorg. Chem.* **2005**, *44*, 5550; h) S. J. Borg, T. Behrsing, S. P. Best, M. Razavet, X. Liu, C. J. Pickett, *J. Am. Chem. Soc.* **2004**, *126*, 16988; i) S. Ott, M. Kritikos, B. Akermark, L. Sun, R. Lomoth, *Angew. Chem. Int. Ed.* **2004**, *43*, 1006; j) T. Liu, M. Wang, Z. Shi, H. Cui, W. Dong, J. Chen, B. Akermark, L. Sun, *Chem. Eur. J.* **2004**, *10*, 4474; k) R. Mejia-Rodriguez, D. Chong, J. H. Reibenspies, M. P. Soriaga, M. Y. Darensborg, *J. Am. Chem. Soc.* **2004**, *126*, 12004; l) J.-F. Capon, F. Gloaguen, P. Schollhammer, J. Talarmin, *J. Electroanal. Chem.* **2003**, *566*, 241; m) D. Chong, I. P. Georgakaki, R. Mejia-Rodriguez, J. Sanabria-Chinchilla, M. P. Soriaga, M. Y. Darensbourg, *Dalton Trans.* **2003**, 4158; n) F. Gloaguen, J. D. Lawrence, T. B. Rauchfuss, M. Bénard, M.-M. Rohmer, *Inorg. Chem.* **2002**, *41*, 6573; o) F. Gloaguen, J. D. Lawrence, T. B. Rauchfuss, *J. Am. Chem. Soc.* **2001**, *123*, 9476.

[8] M. Bruschi, P. Fantucci, L. De Gioia, *Inorg. Chem.* **2004**, *43*, 3733.

[9] J. W. Tye, M. Y. Darensbourg, M. B. Hall, *Inorg. Chem.* **2006**, *45*, 1552.

[10] J. Hou, X. Peng, Z. Zhou, S. Sun, X. Zhao, S. Gao, *J. Org. Chem.* **2006**, *71*, *691*, 4633.

[11] A. D. Becke, *Phys. Rev. A* **1988**, *38*, 3098; J. P. Perdew, *Phys. Rev. B* **1986**, *33*, 8822.

[12] A. Schafer, C. Huber, R. Ahlrichs, *J. Chem. Phys.* **1994**, *100*, 5829.

[13] R. Ahlrichs, M. Bar, M. Haser, H. Horn, C. Kolmel, *Chem. Phys. Lett.* **1989**, *162*, 165.

[14] K. Eichkorn, F. Weigend, O. Treutler, R. Ahlrichs, *Theor. Chem. Acc.* **1997**, *97*, 119.

[15] F. Jensen, *Introduction to Computational Chemistry*, John Wiley & Sons, Chichester, England.

[16] A. Klamt, *J. Phys. Chem.* **1995**, *99*, 2224; A. Klamt, *J. Phys. Chem.* **1996**, *100*, 3349.

[17] G. Zampella, M. Bruschi, P. Fantucci, M. Razavet, C. J. Pickett, L. De Gioia, *Chemistry* **2005**, *11*, 509.

[18] M. Y. Darensbourg, E. J. Lyon, X. Zhao, I. P. Georgakaki, *Proc. Natl. Acad. Sci. USA* **2003**, *100*, 3683; I. P. Georgakaki, L. M. Thomson, E. J. Lyon, M. B. Hall, M. Y. Darensbourg, *Coord. Chem. Rev.* **2003**, *238–239*, 255.

[19] It is interesting to note that a similar stabilizing effect exerted by the ligand *trans* to the μ-CO could be operative also in the enzyme active site. In fact, the Fe_4S_4 subcluster included in the H-cluster proved to be a good electron-donating group (see ref.[7e]) and it has been demonstrated that good donors localized at the position occupied by the Fe–S cubane can favor the rotation of ligands bound to the distal iron center (see ref.[8]).
[20] S. J. Borg, J. W. Tye, M. B. Hall, S. P. Best, *Inorg. Chem.* **2007**, *46*, 384; C. Greco, G. Zampella, L. Bertini, M. Bruschi, P. Fantucci, L. De Gioia, *Inorg. Chem.* **2007**, *46*, 108.
[21] J. I. van der Vlugt, T. B. Rauchfuss, C. M. Whaley, S. R. Wilson, *J. Am. Chem. Soc.* **2005**, *127*, 16012.
[22] T. Zhou, Y. Mo, A. Liu, Z. Zhou, K. R. Tsai, *Inorg. Chem.* **2004**, *43*, 923.
[23] M. Bruschi, G. Zampella, P. Fantucci, L. De Gioia, *Coord. Chem. Rev.* **2005**, *249*, 1620.
[24] J. N. Butt, M. Filipiak, W. R. Hagen, *Eur. J. Biochem.* **1997**, *245*, 116.

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