# Carbon dioxide Reduction: A Bioinspired Catalysis Approach

Yun Li, Maria Gomez-Mingot, Thibault Fogeron, Marc Fontecave

# Carbon dioxide Reduction: A Bioinspired Catalysis Approach

**Yun Li[a], Maria Gomez-Mingot[a], Thibault Fogeron[a,b] and Marc Fontecave[a,*]**

[a]Laboratoire de Chimie des Processus Biologiques, UMR 8229 CNRS, Collège de France, Université Paris 6, 11 Place Marcelin Berthelot, 75231 Paris Cedex 05, France.

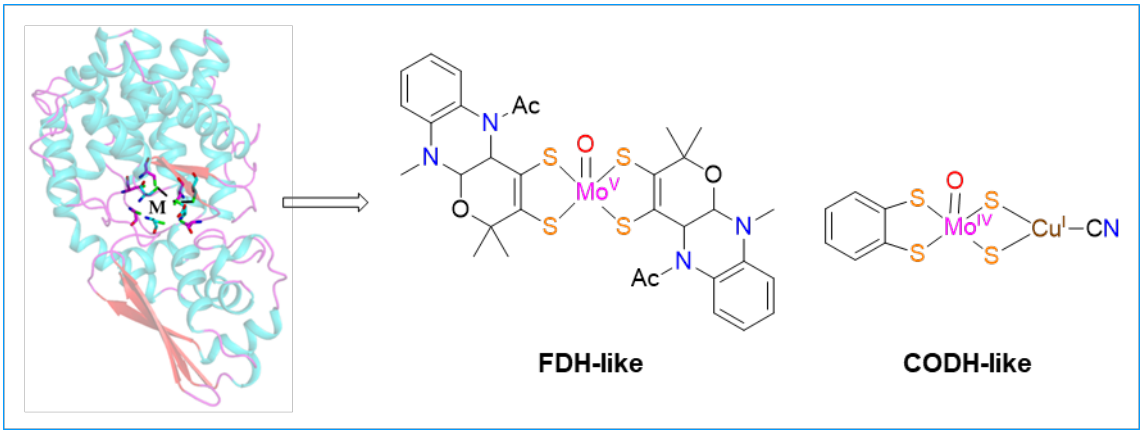
[b]Current address: Laboratoire de Chimie, Ecole Normale Supérieure de Lyon, Université de Lyon, CNRS UMR 5182, 46 allée d'Italie, 69364 Lyon, France

Corresponding author's email address: marc.fontecave@college-de-france.fr

**CONSPECTUS:** While developed in a number of directions, bioinspired catalysis has been explored only very recently for $CO_2$ reduction, a challenging reaction, of prime importance in the context of the energetic transition to be built up. This approach is particularly relevant as Nature teaches us that $CO_2$ reduction is possible, with low overpotentials, high rates and large selectivity, and gives us unique clues to design and discover new interesting molecular catalysts. Indeed, based on our relatively advanced understanding of the structures and mechanisms of the active sites of fascinating metalloenzymes such as formate dehydrogenases (FDHs) and CO dehydrogenases (CODHs), it is possible to design original, active, selective and stable, molecular catalysts using the bioinspired approach. These metalloenzymes use fascinating metal centers: in FDHs, a Mo(W) mononuclear ion is coordinated by four sulfur atoms provided by a specific organic ligand, molybdopterin (MPT), containing a pyranopterin heterocycle (composed of a pyran ring fused with a pterin unit) and two sulfhydyl groups for metal chelation; in CODHs, catalytic activity depends on either a unique nickel-iron-sulfur cluster or a dinuclear Mo-Cu complex, in which the Mo ion is chelated by a MPT ligand. As a consequence, the novel class of catalysts, designed by bioinspiration, consists of mononuclear Mo, W and Ni and as well as dinuclear Mo-Cu and Ni-Fe complexes, in which the metal ions are coordinated by sulfur ligands, more specifically dithiolene chelates mimicking the natural MPT cofactor. In general, their activity is evaluated in electrochemical systems (cyclic voltammetry and bulk electrolysis) or in photochemical systems (in the presence of a photosensitizer and a sacrificial electron donor) in solution. This research is multidisciplinary as it implies detailed biochemical, functional and structural characterization of the inspiring enzymes together with synthetic organic and organometallic chemistry and molecular catalysis studies. The most important achievements in this direction, starting from the first report of a catalytically active biomimetic bis-dithiolene-Mo complex in 2015, are discussed in this Account, highlighting the challenging issues associated with synthesis of such sophisticated ligands and molecular catalysts, as well as the complexity of reaction mechanisms. While the very first active biomimetic catalysts require further improvement, in terms

of performances, they set a stage in which molecular chemistry and enzymology can synergistically cooperate for better understanding why nature has selected these sites and for developing highly active catalysts.

## CONSPECTUS GRAPHIC




## KEY REFERENCES:


- Porcher, J.-P.; Fogeron, T.; Gomez-Mingot, M.; Derat, E.; Chamoreau, L.-M.; Li, Y.; Fontecave, M. A Bioinspired Molybdenum Complex as a Catalyst for the Photo- and Electroreduction of Protons. *Angew. Chem. Int. Ed.* **2015**, 54, 14090–14093[1]. This paper reports the first catalytically active bis-ditholene Mo-based complex mimicking the active site of formate dehydrogenase.
- Fogeron, T.; Retailleau, P.; Chamoreau, L.-M.; Li, Y.; Fontecave, M. Pyranopterin Related Dithiolene Molybdenum Complexes as Homogeneous Catalysts for $CO_2$ Photoreduction. *Angew. Chem. Int. Ed.* **2018**, 57, 17033–17037[2]. This paper reports the synthesis of dithiolenes mimicking molybdopterin and the first bis-ditholene Mo-based complex mimicking the active site of formate dehydrogenase catalytically active for the reduction of $CO_2$.
- Fogeron, T.; Retailleau, P.; Gomez-Mingot, M.; Yun, L.; Fontecave, M. Nickel Complexes Based on Molybdopterin-like Dithiolenes: Catalysts for $CO_2$ Electroreduction. *Organometallics* **2018**, 38, 1344–1350[3]. This paper reports the synthesis and the $CO_2$ reduction catalytic properties of $NiS_4$ complexes based on molybdopterin mimics, as bioinspired versions of the active site of [NiFe]CO-dehydrogenases.
- Mouchfiq, A.; Todorova, T. K.; Dey, S.; Fontecave, M.; Mougel, V. A Bioinspired Molybdenum–Copper Molecular Catalyst for $CO_2$ Electroreduction. *Chem. Sci.* **2020**, 11, 5503–5510[4]. This paper reports for the first time the catalytic potential of dinuclear Mo-Cu complexes, mimicking the active site of [MoCu]CO-dehydrogenases, for the electroreduction of $CO_2$.

## 1. INTRODUCTION

One of the central questions of chemical sciences, fundamentally challenging and potentially rich in applications, regards the activation of the small, abundant, thermodynamically and kinetically stable, molecules from our environment, such as water ($H_2O$), oxygen ($O_2$), nitrogen ($N_2$), carbon dioxide ($CO_2$). This question is also obviously central to life chemistry: life evolved and developed thanks to the fantastic enzymatic power used by all living organisms to derive their chemical repertoire (the biomass) from these molecular precursors. Thus, biological chemistry is a unique source of inspiration for "inventing" new reactions based on such building blocks in order to generate cheap synthetic compounds useful to the chemical industry. The bioinspired chemistry approach specifically applied to $CO_2$ photo- and electro-reduction catalysis has, surprisingly, been only very rarely exploited until now, in contrast to the case of water oxidation, proton reduction and $O_2$ activation. Our efforts in this direction are discussed here.

A single living cell contains thousands of active and selective metalloenzymes that achieve complex metabolic and biosynthetic reactions, occurring within an active site, where the substrate binds close to reactive amino acids, cofactors or prosthetic groups (organic or inorganic) and is transformed. Resulting from 4 billion years of evolution under very soft conditions (water as the solvent, low temperature, atmospheric pressure) the solution selected by Nature for a given reaction is anticipated to be highly relevant, in terms of activity, selectivity and stability. Thus, it might be greatly rewarding, when searching for a catalyst for that reaction, to carefully identify and analyze the biochemical version, and then design, synthesize and characterize a chemical mimic of the active site. This so-called biomimetic or bioinspired catalysis approach is highly demanding, as it requires combining biochemical studies and chemical synthesis, in order to adequately translate our understanding of the structure and function of an enzyme active site into a synthetic catalytic system.

Reduction of $CO_2$ implies multiple proton and electron transfers and is thus kinetically limited (large energy barriers). Catalysts are absolutely needed to bind and activate $CO_2$ thus reducing the high overpotentials typically encountered. In addition, they have to be selective (a challenging issue considering the large number of possible reactions occurring at comparable potentials, including proton reduction into $H_2$ since protons are needed for $CO_2$ reduction), stable and cheap (thus driving research to focus on catalysts based on non-noble abundant metals). While appreciating the importance of heterogeneous catalysts, the potential of homogeneous molecular catalysts is obvious. These have several benefits: (i) they are easily tunable and optimizable via synthetic modifications of the ligands and variations in metal ions, giving the opportunity to identify key stereo-electronic effects on mechanism, selectivity, and efficiency; (ii) they often display quite high product selectivity. On the

other hand, they often suffer from low activity (current densities, turnover frequencies) and low stability (turnover numbers) and past research has been limited to a very small number of complexes, often based on noble metals (Re, Ru, Rh and Ir), and, for the greatest part, discovered more than 30 years ago, with very little innovation since then (Figure 1). Few exceptions use non-noble metals such as Fe-porphyrins, among the most efficient molecular catalysts, and [Mn(bpy)(CO)$_3$Br], for example (Figure 1). A recent article reviewed this class of catalysts thoroughly[5].

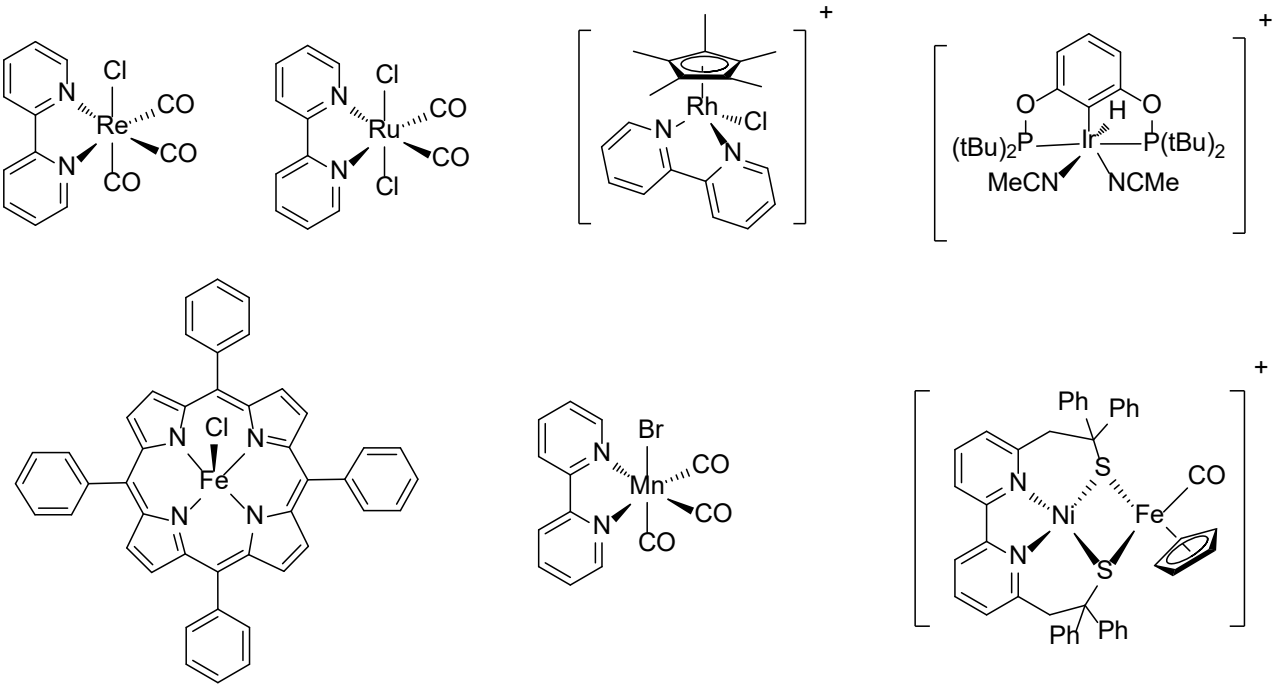



**Figure 1.** Molecular catalysts for $CO_2$ reduction.

## 2. $CO_2$ REDUCTASES: THE NATURAL CATALYTIC SOLUTIONS FOR $CO_2$ REDUCTION

Early during evolution, living organisms had to deal with $CO_2$ reduction and to find appropriate catalytic solutions. As a matter of fact, a number of fascinating metalloenzymes, named here "$CO_2$ reductases ($CO_2$Rases)", use intriguing active sites, based on non-noble metals, displaying remarkable catalytic efficiency and selectivity, under mild conditions and in water. Formate dehydrogenases (FDHs) and CO dehydrogenases (CODHs) catalyze the reversible transformation of $CO_2$ to HCOOH and to CO, respectively. FDHs use a mononuclear metal complex (Mo or W)[6] while CODHs use polynuclear active sites, either a Mo-S-Cu center[7] or a Ni center bound to a unique $Fe_4S_4$ cluster[8] (Figure 2). While reaction mechanisms are still incompletely understood and the reason why these active sites have been selected by microorganisms is unclear, recent structural investigations provide enough information to allow mimicking these active sites.

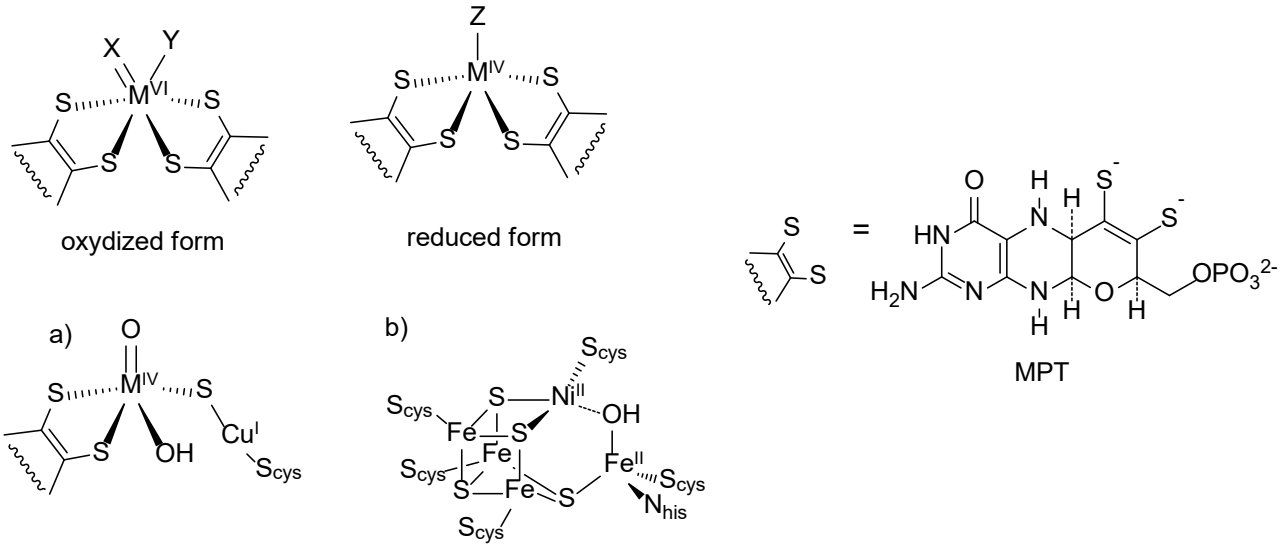



**Figure 2.** Top: active site of FDHs; M = Mo/W, X = S/O, Y = S-Cys/Se-Cys, Z = SH. Bottom: active site of CODHs; (a) [MoCu]CODHs with M = Mo and (b) [NiFe]CODHs. MPT = molybdopterin.

A few three-dimensional crystal structures provide a rather clear description of the active sites of FDHs[9]. For interconverting $CO_2$/$HCO_2H$, Nature has made a unique choice: a mononuclear metal center (exclusively Mo or W) coordinated by two molybdopterin (MPT) ligands (Figure 2). This natural cofactor contains a chelating dithiolene group and, thus, 4 sulfur atoms coordinate the metal ion. Additional apical ligands, proposed to be of crucial functional importance, are present, however their exact coordination configuration have remained ill-defined. It is generally thought that the coordination sphere in the oxidized $Mo^{VI}$ resting state is completed by a selenocysteine (in a few cases a cysteine) residue and a sulfide group (Mo=S or Mo-SH) in a distorted trigonal prismatic coordination geometry while, in the reduced active $Mo^{IV}$ intermediate state, the selenocysteine is seemingly no longer present and the Mo center is pentacoordinated presumably with a SH ligand. While extensively investigated, biochemically and via DFT calculations, the exact mechanism of the reaction is still a matter of discussion. However, it is assumed that the system is designed to generate an active metal-hydride species which upon reaction with $CO_2$ produces formic acid[10].

$CO_2$ reduction in [NiFe]CODHs occurs at the Ni center with the assistance of a dangling redox-inactive Fe ion. The two ions are bridged by a $Fe_3S_4$ cluster and a OH group (Figure 2). Spectroscopic and crystallographic studies have provided key mechanistic insights into $CO_2$ reduction catalysis[8]. It is proposed that $CO_2$ binds to Ni, after reduction, in a $\eta 1-$ $CO_2$ mode to form a Ni-C bond and interacts with Fe in a $\eta 1$-OCO mode. One O atom is also H-bonded to a lysine residue and the other is within H-bonding distance to a protonated histidine. C-O cleavage occurs with the assistance of a proton to generate and release CO. It thus appears that the enzyme mainly involves a dinuclear NiFe center in which Ni is redox-active, transferring electrons to $CO_2$, while Fe serves as a Lewis acid to facilitate electron transfer to $CO_2$ and heterolytic cleavage of the C-O bond.

While characterized crystallographically, much less is known regarding the mechanism of CO oxidation catalyzed by [MoCu]CODHs[11]. Mo is in a $Mo^{VI}S_3O_2$ square pyramidal coordination with one bidentate molybdopterin dithiolene ligand, one sulfide connecting Mo to Cu and two oxygen ligands (presumably one oxo and one hydroxo), while $Cu^I$ completes its coordination sphere only with a cysteine ligand (Figure 2). It is proposed (but not clearly established) that only Mo enjoys redox changes while Cu remains in the $Cu^I$ state. It should be noted that [MoCu]CODHs have been only shown to function for CO oxidation and not for $CO_2$ reduction, so far.

## 3. MIMICKING $CO_2$ REDUCTASES: NEW CATALYSTS FOR $CO_2$ PHOTO- AND ELECTRO-REDUCTION

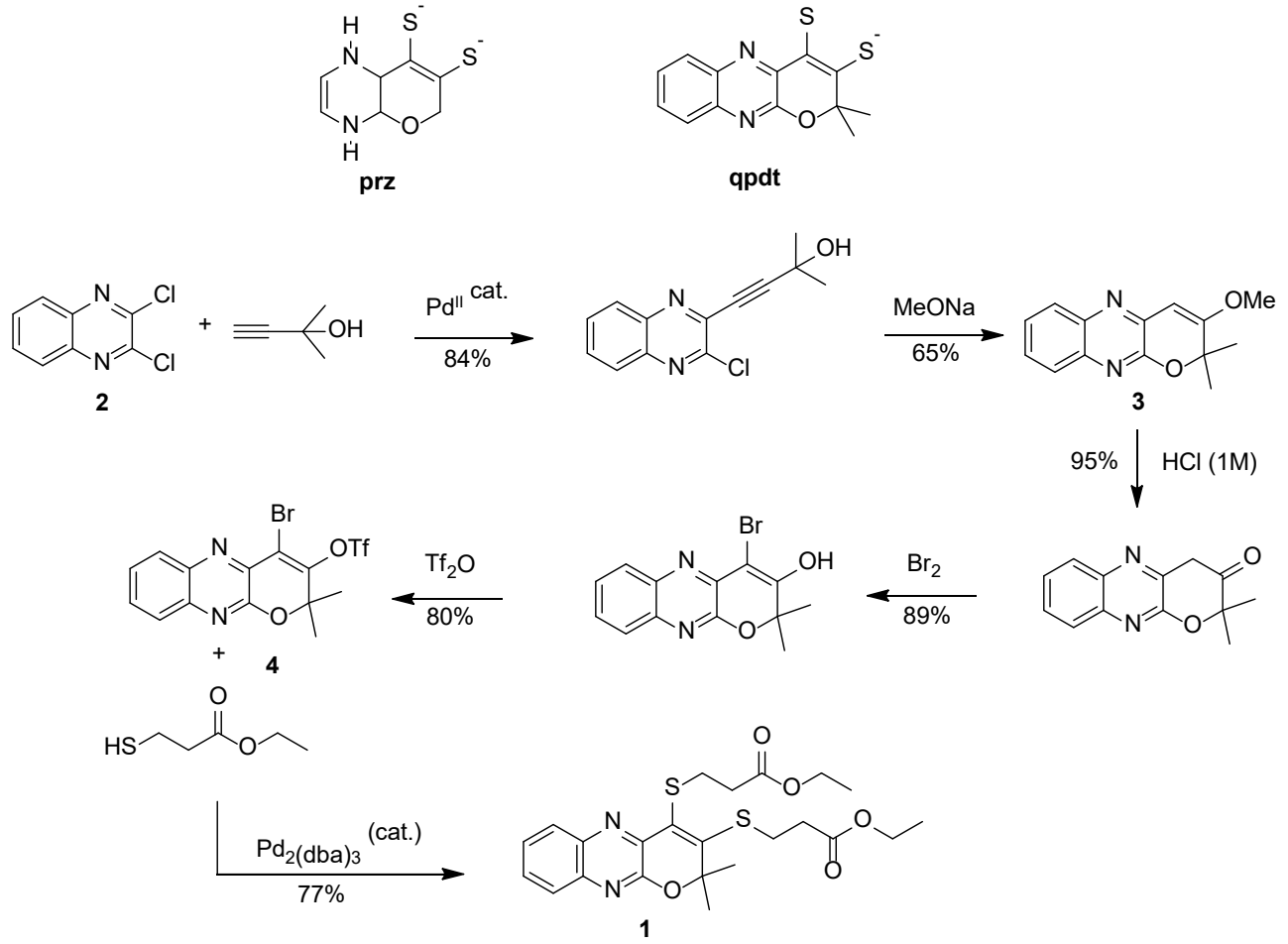
At the beginning of our project, no bioinspired molecular complex, mimicking CODH and FDH active sites, was reported to be functional for $CO_2$ reduction catalysis. [M(bipyridine)$(CO)_4$ (M= Mo/W) complexes, however not bioinspired, were the only Mo- or W-based ones reported to be active[12,13].Only two, very interesting, examples of sulfur-bridged Mo-S-Cu complexes, mimicking CODH active sites, had been prepared but not functionally characterized [14–16]. The $NiFe_4$ cluster of CODH had not been mimicked yet but an exquisite biomimetic dinuclear Ni-OH-Fe complex had been prepared, with no evaluation for catalysis[17]. A wide series of Mo or W complexes using simple dithiolene ligands had also been synthesized and characterized, thanks to the outstanding contribution of R. Holm, S. Sarkar and S.J.N. Burgmayer, but again none of them had been studied for their $CO_2$ reduction catalytic activity[18–22].

### 3.1. $CO_2$ Conversion to Formic Acid: Mimics of FDHs.

Our first approach implied the synthesis and functional characterization of a series of complexes containing a mononuclear metallic ion, Mo or W, and very simple dithiolene, easily accessible by synthesis. A large amount of such ligands and complexes were already reported and their preparation could be nicely reproduced[18,23,24]. The novelty could have come from the systematic evaluation of their activity for both electroreduction and photoreduction of $CO_2$. In the former case, cyclic voltammetry and controlled-potential electrolysis (CPE), classically with the complex dissolved in $CO_2$-saturated organic solvents complemented with a supporting electrolyte and a source of protons, were routinely used for assessing catalysis (electrocatalytic waves and onset potentials) and selectivity (faradic yields, FY). In the second case, we routinely used a reaction mixture containing $[Ru(bpy)_3]^{2+}$ as a photosensitizer, a source of protons, and a sacrificial electron donor in a $CO_2$-saturated organic solvent. These preliminary studies proved unsuccessful as, while catalytically

active, all investigated complexes were selective for proton reduction, yielding $H_2$ as the only reaction product under both conditions and could thus not convert $CO_2$ into CO or HCOOH. As an example, we reported the excellent $H^+$ reduction catalytic activity of bis(dithiolene)W complexes, $W^{VI}O_2L_2$ and $W^{IV}OL_2$, with L= dithiolene, a class of molecular catalysts rarely characterized before, and DFT calculations allowed to nicely understand why such metal-oxo systems are so selective for proton versus $CO_2$ reduction, as discussed below[25].

It thus appeared that more complex systems, better mimicking the natural MPT ligand, were required. Specifically, a theoretical study showed that, in view of accurately reproducing the molecular, not only structural (bond lengths and angles) but also charge distribution and redox potentials which might be critical for activity, properties of MPT, a simple dithiolene ligand was not appropriate even within a pyran ring carrying the dithiolene moiety and that the minimal ligand should be a fused pyran-pyrazine dithiolene (**prz**, Scheme 1)[26]. Guided by this study, we succeeded in preparing large amounts of an original quinoxaline-pyran-fused dithiolene ligand (**qpdt**, Scheme 1), closely related to MPT[1,27]. Garner *et al*. synthesized a tricyclic pyranopterin dithiolene ligand system (containing the pyrimidine ring) and used it to prepare a Co complex[28]. Burgmayer *et al*. have also reported the synthesis, via a solvent-dependent spontaneous cyclization process, of pyrano-$S_2$BMOPP, a tricyclic pyranopterin dithiolene ligand[29,30].




**Scheme 1.** Structures of **prz**, **qpdt** (top) and synthetic route to **qpdt** in a protected form **1** (bottom). dba=*trans,trans*-dibenzylideneacetone.

One difficulty, as far as synthesis of **qpdt** is concerned, resides in the pyran ring-closure step. To circumvent this problem, we chose to first prepare the tricyclic skeleton and to introduce the dithiolene moiety in a second step. Another concern regards the high sensitivity of dithiolene species with respect to air. This thus requests that the target ligand be synthesized in a protected form, preferentially under anaerobic conditions, and deprotection be realized only in the presence of the metal ion to be chelated *in situ*. Briefly, 2,3-dichloroquinoxaline (**2**) was submitted to Sonogashira coupling followed by a pyran ring-closure step with sodium methoxide to afford the methyl enol ether **3**. Hydrolysis, monobromination and triflation yielded the bromovinyl triflate **4** with high yield (Scheme 1). Then a double palladium-catalyzed cross-coupling reaction, using 5 % [$Pd_2(dba)_3$] (dba=*trans,trans*-dibenzylideneacetone) and Xantphos (10 %) in dioxane, with two equivalents of $HSCH_2CH_2CO_2Et$ and three equivalents of $iPr_2NEt$ at 110 °C gave rise to the protected dithiolene ligand **1**. This synthetic strategy was inspired by the work of Itoh *et al*. who developed a general carbon–sulfur bond formation method by palladium-catalyzed coupling of aryl bromides/triflates with thiols[31,32]. Here, we thus showed for the first time that this reaction can be extended to aryl bromides/triflates.

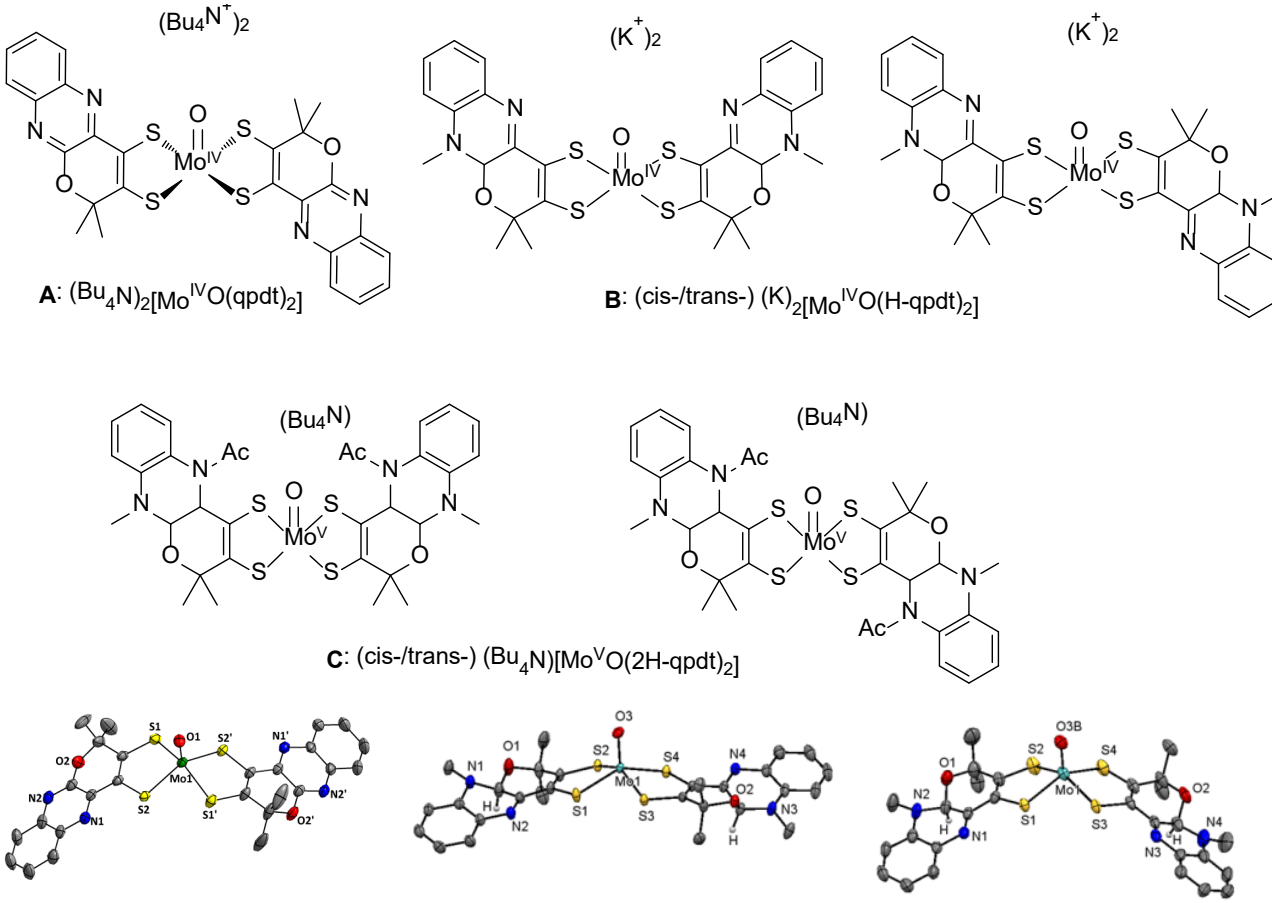
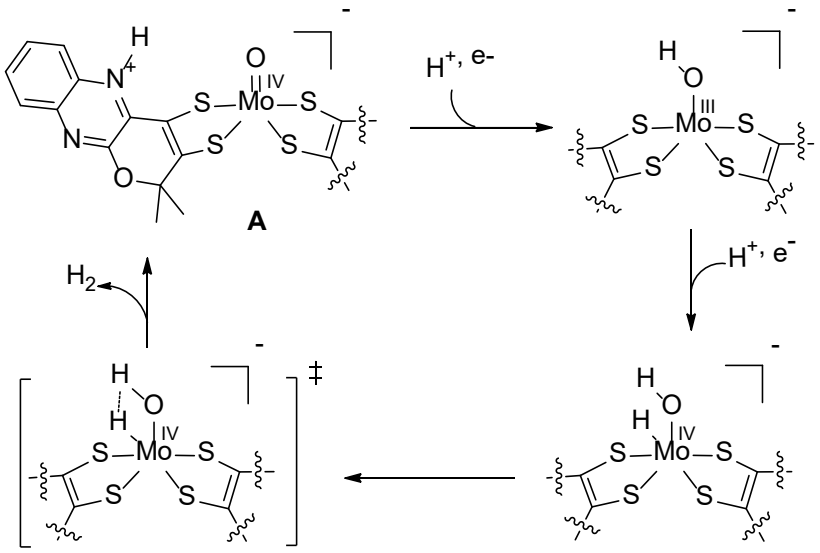



**Figure 3.** Structures of complexes **A**, **B** and **C.** Bottom: ORTEP views of the anion component of **A** (left) and **B (**trans: middle; cis: right**)**[2].

The availability of compound **1** allowed us investigating its reactivity as a chelating agent, after deprotection leading to **qpdt**, in order to prepare original metal-dithiolene complexes with a biomimetic MPT-like ligand. The first example of such a **qpdt**-based complex was $(Bu_4N)_2[Mo^{IV}O(qpdt)_2]$, complex **A**, obtained by treatment of **1** with tBuOK under anaerobic conditions to generate **qpdt** which was directly reacted with $K_3Na[MoO_2(CN)_4]$ under alkaline conditions and then with $Bu_4NBr$ for cation exchange (Figure 3)[1]. The crystal structure of complex **A** shows that the $Mo^{IV}$ cation is penta-coordinated in a $S_4O$ environment with a distorted square based pyramidal geometry. The four dithiolene sulfur atoms originate from two *trans*-oriented **qpdt** ligands and the coordination sphere is completed with one terminal oxo ligand. This makes **A** a unique biomimetic complex, sharing a number of structural properties with the active site of FDHs. Unfortunately, in the presence of $CO_2$ and protons, complex **A** selectively reduces $H^+$ into $H_2$ under both electrochemical and photochemical conditions, with no evidence for $CO_2$ reduction products. In fact, it proved an excellent and stable catalyst for electroreduction of $H^+$, provided by trifluoroacetic acid (TFA), in acetonitrile, with an intense catalytic wave developing at potentials more cathodic than -0.55 V *vs*. Ag/AgCl, the onset potential, and a remarkable TOF value of 1030 $s^{-1}$ at -1.3 V *vs*. Ag/AgCl using 0.1 M TFA. Electrolysis at a controlled potential (-1.3 V *vs*. Ag/AgCl) confirmed the

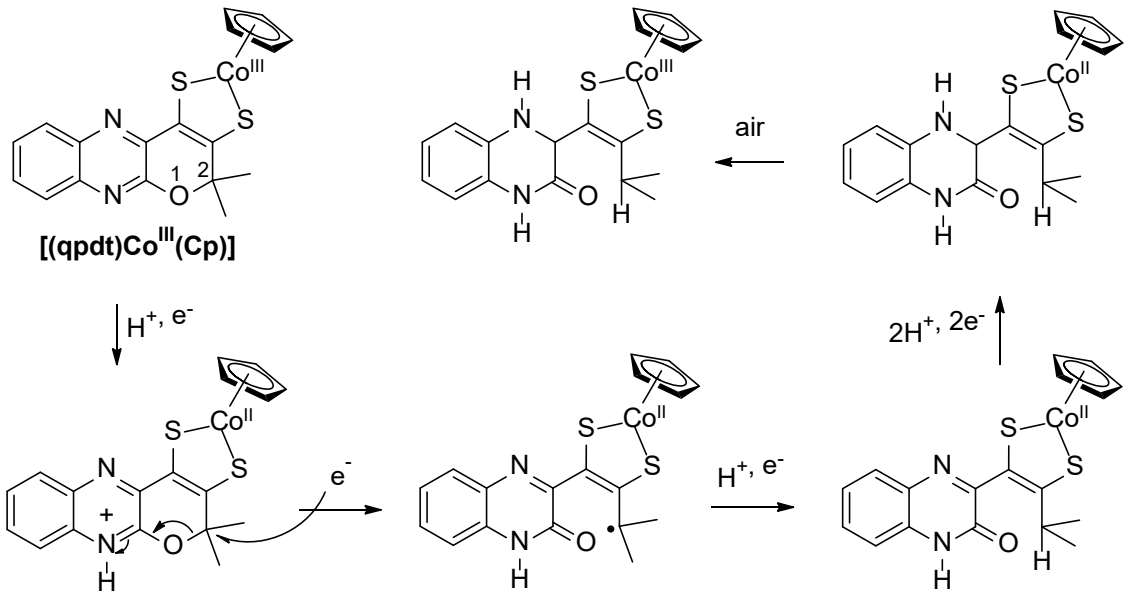
formation of $H_2$ exclusively[1]. Complex **A** was also studied for its catalytic light-assisted proton reduction activity under conditions comparable to those used in the case of the Mo-dithiolene complex, $[Mo(bdt)_2(tBuNC)_2]$ (bdt = benzene-1,2-dithiolate), previously reported as a HER catalyst[33]: $[Ru(bpy)_3]^{2+}$ served as the photosensitizer and 0.1 M ascorbic acid (pH 4.0) as the sacrificial electron donor in $CH_3CN:H_2O$ (1:1). Under visible light irradiation a remarkable initial TOF value of 203 $h^{-1}$ was obtained and the catalyst was found to be relatively stable under these conditions[1].

DFT calculations provided clear insights into the mechanism of the reaction (Scheme 2). A first one-electron reduction of $Mo^{IV}$ coupled to protonation at the oxo group followed by a second one-electron reduction generates a hydride species upon protonation. Intramolecular protonation of the hydride by the O-bound proton affords $H_2$. A similar mechanism was supported by DFT calculations in the case of bis(dithiolene)W complexes, $W^{IV}OL_2$, with L being a simple dithiolene such as bdt (benzene-dithiolate)[25]. Thus, all these M-oxo complexes (M=Mo or W) are exquisitely designed to catalyze proton reduction to $H_2$, via a reactive M−hydroxo−hydride species: the oxygen ligand plays a key role in binding a proton in the vicinity of the reactive metal-bound hydride thus facilitating protonation of the hydride generating $H_2$. We also used the **qpdt** ligand to prepare a homodinuclear cobalt $(Et_4N)_2[Co^{III}(qpdt)_2]_2$ complex, which could be structurally characterized[34]. While inactive for electro- or photo-reduction of $CO_2$, it proved efficient for catalyzing proton reduction, in agreement with previous results using Co-dithiolene complexes[23,24]. The mechanism, based on DFT calculations, implies the formation of a Co-H hydride intermediate and a key role of the adjacent S atoms of the dithiolene ligand, as proton-exchange sites, thus facilitating protonation of the hydride species to generate $H_2$.




**Scheme 2.** Proposed mechanism of proton reduction catalyzed by complex **A**, as supported by DFT calculations.

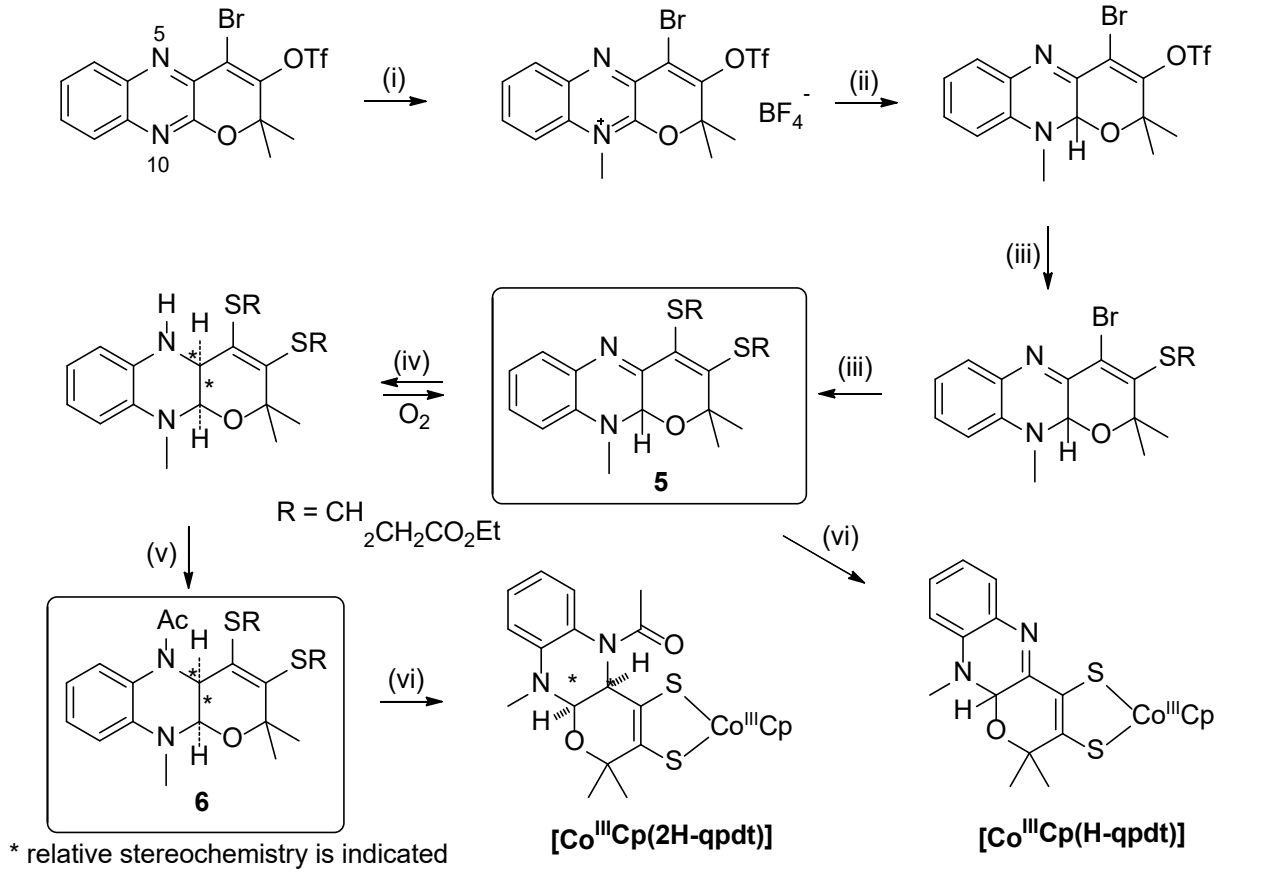
In fact, later on, we realized that complex **A** was not the actual catalyst. Indeed, at cathodic potentials required for $H^+$ reduction, the central pyrazine ring of the dithiolene ligand enjoys a double hydrogenation that results in the opening of the pyran ring[35]. Complex **A** is thus converted into another $Mo^{IV}O(L)_2$ complex, L being a dithiolene ligand derived from **qpdt** by hydrogenation and pyran ring opening (Scheme 3). This was exquisitely shown using a (cyclopentadienyl=Cp)cobalt$^{III}$ derivative, $[Co^{III}(Cp)(qpdt)]$. Its cyclic voltammogram (CV) in $CH_3CN$ displays a reversible redox couple at -0.53 V assigned to the $Co^{III}/Co^{II}$ couple. Upon addition of acetic acid, a new irreversible wave appeared at -1.0 V and shifted towards positive potentials upon increasing addition of acid, with constant current intensity, assigned to a proton-assisted reduction of the ligand. By chance, the product of the reaction could be isolated in a pure form after electrolysis at a controlled potential of -1.1 V, crystallized and characterized by 1D and 2D NMR, MS, FT-IR spectroscopies and by X-ray crystallography. The structure of the final dithiolene-Co complex, with a novel dithiolene ligand containing a 4-dihydro-1H-quinoxalin-2-one group, resulting from hydrogenation of **qpdt** and O1-C2 bond cleavage, and the mechanism of its formation are shown in Scheme 3. In the case of complex **A** the appearance of an irreversible signal in the CV at potentials more anodic than the catalytic wave upon addition of acid was, as in the case of $[Co^{III}(Cp)(qpdt)]$, the signature of the same dithiolene ligand transformation.




**Scheme 3.** Pyran ring-opening under reduction conditions.

The first study of a Mo-dithiolene complex with catalytic activities for $CO_2$ reduction was reported in 2018[2], nicely illustrating the power of the biomimetic approach. In fact, we soon were concerned by the fact that the first model system described above had a number of major differences with the natural active site of FDHs. First, the axial ligand in complex **A** is an oxo atom, while it is likely to

be sulfur-based within the enzyme, even though there is still some uncertainty regarding the nature of that ligand in both oxidized and reduced states of the enzyme. Second, the **qpdt** biomimetic ligand had its central pyrazine ring fully oxidized, while that in the natural MPT ligand is fully reduced. As discussed above, these characteristics were shown as sources of increased selectivity for proton reduction and instability (pyran ring opening during catalysis), respectively. Both are difficult issues to address. While, thanks notably to R. Holm work, some examples have been reported[18,19], the preparation of Mo/W-dithiolene complexes with biologically relevant axial S- (sulfido, thiolato) or Se-based ligands is highly challenging[36], and furthermore direct reduction of **qpdt** without pyran ring opening proved unsuccessful in our laboratory.




**Scheme 4.** Synthesis of protected H-qpdt (**5**), 2H-qpdt (**6**) and complexes [$Co^{III}$Cp(H-qpdt)], [$Co^{III}$Cp(2H-qpdt)]. Conditions: i) $(Me_3O)(BF_4)$; ii) $(Me_4N)BH(OAc)_3$; iii) $Pd(dba)_2$ (cat.), $HSCH_2CH_2CO_2Et$; iv) $NaBH_3(CN)$; v) AcCl; vi) $CoCpI_2(CO)$.

Following an original synthetic strategy, starting from **qpdt** and involving methylation at N-10 and acylation at N-5 to protect the molecule from pyran ring opening, we succeeded to prepare two, more biomimetic, dithiolenes with the central pyrazine ring in either the two-electron or the four-electron reduced state, named H-qpdt and 2H-qpdt (compounds **5** and **6** in the protected form, respectively) (Scheme 4). 2H-qpdt is particularly appealing as it is the closest to the structure of MPT. Interestingly, the two protons of the junction of the pyrazine and pyran cycles adopt a *cis* configuration, as it is the

case, with R, R absolute configuration, in MPT[35]. H-qpdt and 2H-qpdt were successfully used to prepare the corresponding (bis-dithiolene)Mo-oxo complexes, **B** and **C** (Figure 3).

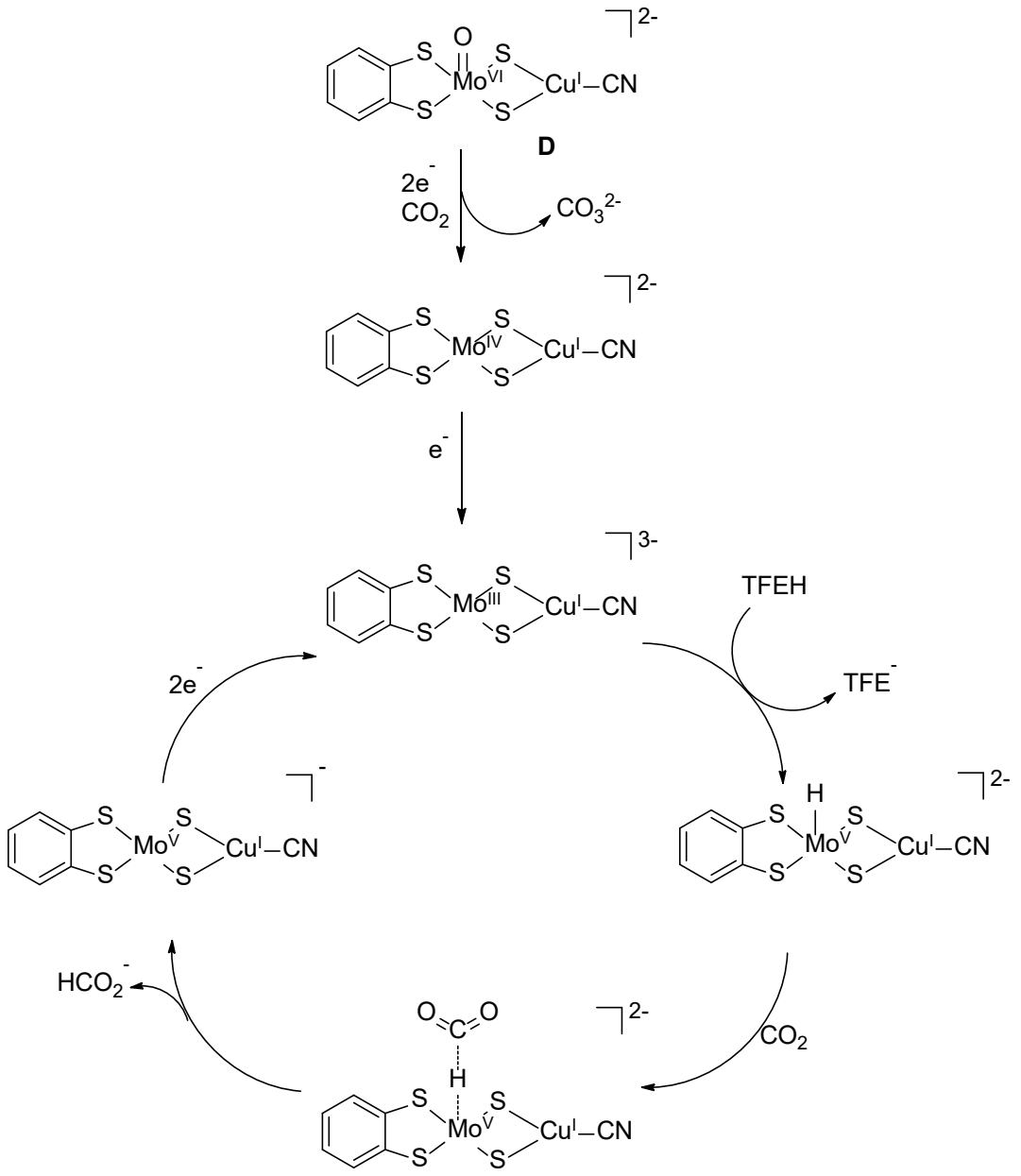
Complex **B**, $K_2[Mo^{IV}O(H\text{-}qpdt)_2]$, could be characterized structurally. The molecular structures of the anion component $[Mo^{IV}O(H\text{-}qpdt)_2]^{2-}$ are shown in Figure 3[2]. Three isomers were isolated: *trans*-S,S, *trans*-R,R and *cis*-S,R. In the two first enantiomers, the two dithiolene ligands are in a *trans* orientation with respect to the $MoS_4$ core. In the third one, the two ligands are *cis*-oriented. The same ligand was used to prepare the neutral complex $[Co^{III}Cp(H\text{-}qpdt)]$, also structurally characterized[2]. Unfortunately, we failed to obtain single crystals of complex **C**, $[Mo^{V}O(2H\text{-}qpdt)_2]^-$, suitable for X-ray diffraction. This might be due to the presence of many stereoisomers. Indeed, since 2H-qpdt exists in the form of a mixture of two enantiomers and the two ligands could be *cis*- or *trans*-oriented with respect to the $MoS_4$ core, a mixture of seven stereoisomers was expected. We had thus to rely on a combination of different spectroscopic techniques and the crystal structure of $[Co^{III}Cp(2H\text{-}qpdt)]$[2] to confirm the structure shown in Figure 3. As $[Mo^{V}O(2H\text{-}qpdt)_2]^-$ contains two dithiolene ligands, one cannot conclude whether the two dithiolenes are *cis*- or *trans*-oriented.

Thanks to these ligand modifications driven by biomimetic considerations, we finally reported for the first time synthetic (bis-dithiolene)Mo complexes as catalysts for $CO_2$ reduction[2]. Catalytic $CO_2$ reduction activity was assessed under photochemical conditions, using $[Ru(bpy)_3]_2^+$ as a photosensitizer (PS), BIH (1,3-dimethyl-2-phenyl-2,3-dihydro-1H-benzoimidazole) as the sacrificial electron donor and $CH_3CN$/TEOA (triethanolamine) in a 5:1 ratio as the solvent, saturated with $CO_2$ ([cat.] = 0.05 mM , [PS] = 0.5 mM, [BIH] = 0.1 M). This study revealed the importance of the redox state of the central pyrazine ring since, under the same conditions, while complex **A** was highly selective for proton reduction into $H_2$, complexes **B** and **C** showed ability to catalyze $CO_2$ reduction into a mixture of formic acid and carbon monoxide, even in the presence of protons. The most active complex was complex **C**, with a total TON of 210 after 15 hours, a much larger proportion of $CO_2$-derived products accounting for almost 60 % (with 39 % formate and 19 % CO). Complex **B** was less active (TON= 95) and less selective (53 % $H_2$). Complex **C** is one of the very rare molecular catalysts generating formate as the major $CO_2$ reduction product under photoactivation conditions, together with $[Mn(bpy)(CO)_3X]$, $[Ru(bpy)_2(CO)_2]X_2$ and $[Rh(Cp)(bpy)X]$ complexes[37–41]. While the superiority of complex **C** is uncompletely understood, it is likely that a fully reduced pyrazine ring increases the hydridic nature of the Mo-H intermediate thus facilitating hydride transfer to $CO_2$.

### 3.2. $CO_2$ Conversion to Carbon Monoxide: Mimics of CODHs.

### 3.2. A) Mimics of [MoCu]CODHs

CODHs from *Oligotropha carboxidovorans* contains a heterobimetallic Mo-Cu active site in which the two ions are bridged by a sulfide ion, the Mo ion also being coordinated by the MPT ligand and an oxo/hydroxo moiety[7] (Figure 2). This fascinating and unique metal cofactor has led to the synthesis of a number of interesting biomimetic Mo/W-Cu complexes, over the years, but none of them had been reported to show catalytic activity for $CO_2$ reduction[14,15,42–45]. Exploration of this class of complexes led us to discover that complex **D**, $[Mo^{VI}(O)(bdt)S_2Cu^{I}CN]^{2-}$ (Scheme 5), previously synthesized by Tatsumi and col.[14], in which Mo and Cu ions are connected by two μ2-sulfido ligands and the MPT ligand is mimicked by the bdt ligand chelating the Mo ion, was able to catalyze the electroreduction of $CO_2$, however selectively to formate and not to CO[4]. CPE in $CO_2$-saturated $CH_3CN$ on a GC electrode at -2.62 V *vs.* $Fc^+/Fc$ in the presence of $[(bdt)Mo^{VI}(O)S_2Cu^{I}CN]^{2-}$ and 0.1 M of trifluoroethanol (TFEH) as a source of protons led to the formation of formic acid as the major product (70 – 75 %), together with $H_2$ (20 %) and very small amounts of CO. Thanks to IR spectroelectrochemical methods, coupled to DFT calculations, we have proposed the reaction mechanism shown in Scheme 5. We established that the starting complex was in fact a pre-catalyst, leading to the catalytic species, $[Mo^{IV}S_2(bdt)Cu^{I}CN]^{3-}$, via a 2-electron reduction followed by transfer of the nucleophilic oxo group to $CO_2$ forming $CO_3^{2-}$, and liberating a coordination site, and finally by a further one-electron reduction. Then, protonation yields a $Mo^{V}$-H hydride intermediate, which reacts either with $CO_2$ to produce formate or with a second proton to form $H_2$, however with a higher transition state barrier. While the catalyst operates at quite high overpotential, this first functional mimic opens a new direction regarding the design of molecular catalysts for $CO_2$ reduction and raises specific questions to be addressed such as: (i) which parameter makes the enzyme selective for CO and the mimic selective for formate? (ii) how does the $Cu^{I}$ site function synergistically with Mo as it is essential for catalytic activity?




**Scheme 5.** Proposed mechanism of $CO_2$ electroreduction catalyzed by $[Mo^{VI}(O)S_2(bdt)\ Cu^{I}CN]^{2-}$ (complex **D**), based on spectroscopic studies and DFT calculations. TFEH= Trifluoroethanol.

### 3.2. B) Mimics of [NiFe]CODHs

While a number of metal sulfur clusters have been prepared, the $NiFe_4$ cluster of CODH has not been synthetically mimicked yet. However, since $CO_2$ reduction by [NiFe]CODHs seems to use the Ni atom and only one Fe atom of the cluster, it is reasonable to consider simpler heterodinuclear NiFe mimics for $CO_2$ reduction. It is only in 2020 that the first catalytically active NiFe complex, namely $[L^{N2S2}Ni^{II}Fe^{II}Cp(CO)]^+$ ($L^{N2S2}$ = 2,2′-(2,2′-bipryridine-6,6′-diyl)bis(1,1′-diphenylethanethiolate), NiFeCp in the following (Figure 1), was reported[46]. NiFeCp was initially designed as a mimic of [NiFe]-hydrogenases[47,48] and shown to be an active and stable catalyst for $H^+$ electroreduction[49]. CPE at −1.3 V *vs*. SHE in phosphate buffer, pH 4, saturated with $CO_2$, using a graphite electrode modified with NiFeCp, led to the production of only two gaseous products, $H_2$ and $CH_4$ (with a $H_2/CH_4$ molar

ratio of 23:1 and FY for $CH_4$ evolution of 12 %), with no evidence for the formation of formic acid or CO[46]. The formation of $CH_4$, reflecting the ability of NiFeCp to catalyze a challenging 8 $e^-$/8 $H^+$ reduction, is intriguing and more mechanistic investigations are required. Nevertheless, this breakthrough again opens perspectives regarding the development of bioinspired NiFe species as electrocatalysts for $CO_2$ reduction.

Considering that Ni is the only redox active metal in the cluster of [NiFe]CODHs, a further simplification for the design of bioinspired catalysts results in mononuclear $NiS_n$ sites, a configuration present in the enzyme active site. Few Ni complexes, such as $[Ni(cyclam)]^{2+}$ [50–54], Ni-polypyridine complexes[41] or Ni complexes supported by N-heterocyclic carbene-amine ligands[55], but no $NiS_n$, had been studied as catalysts for $CO_2$ electroreduction or photoreduction. In 2017, a Ni complex bearing a $S_2N_2$–type tetradentate ligand was found to selectively catalyze $CO_2$ photoreduction to CO[56]. The availability of the **qpdt** ligand afforded the possibility to prepare a (bis-dithiolene)Ni complex, $(Bu_4N)[Ni^{III}(qpdt)_2]$, complex **E**, in which the Ni ion is tetracoordinated in a $S_4$ environment with a square planar geometry (Figure 4)[57]. For the first time, a $NiS_4$ complex was shown to catalyze $CO_2$ electroreduction into HCOOH as the major product (60 %) together with small amounts of CO and $H_2$, in acetonitrile in the presence of TFEH as a source of protons, however only on a mercury electrode. The same electrode is required in the case of $[Ni(cyclam)]^{2+}$ and this might originate from favourable transient interactions between the complex and the Hg surface, encouraging $CO_2$ binding and facilitating CO desorption[53,56,58]. This catalyst is remarkably stable since sustained reduction of $CO_2$ was achieved during an electrolysis experiment of 23 h. As supported by DFT calculations, formic acid likely derives from the reaction of $CO_2$ with a catalytically competent Ni-H hydride intermediate.

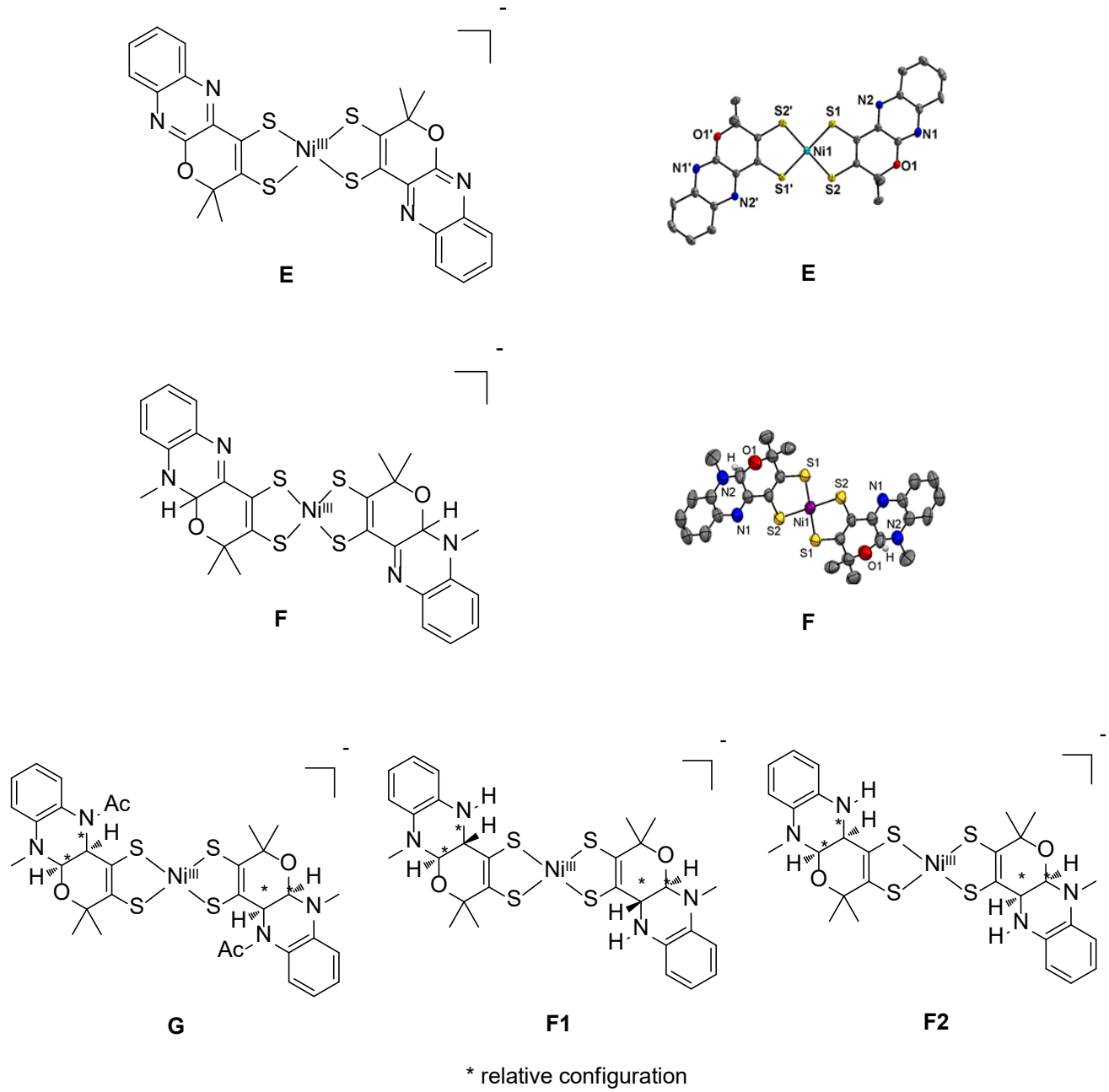



**Figure 4.** Structures of complexes $[Ni^{III}(qpdt)_2]^-$ (**E**), $[Ni^{III}(H\text{-}qpdt)_2]^-$ (**F**) and the ORTEP views of their anion component; $[Ni^{III}(2H\text{-}qpdt)_2]^-$ (**G**) and reduced **F**: *trans*-**F1** and *cis*-**F2**.

Finally, we compared the catalytic activity of three novel $NiS_4$ complexes, with dithiolene versions having a fully reduced pyrazine ring (Figure 4)[3]. **F1** and **F2** were obtained via chemical and electrochemical reduction of $(Bu_4N)[Ni^{III}(H\text{-}qpdt)_2]$ (**F**), respectively, while $(Bu_4N)[Ni^{III}(2H\text{-}qpdt)_2]$ (**G**) was obtained using the ligand 2H-qpdt. Intriguingly, while the only difference between **F1** and **F2** resided in the configuration of the ring junction, *cis* or *trans*, large differences in activity and selectivity were observed. It is very likely that this is also the consequence of using a Hg electrode. Thus, we postulate that noncovalent interactions between the complexes and the Hg surface are strong enough to affect the activity of stereoisomers differentially. **F1** proved the most active (larger TONs) and the most selective (FY for formate 70 %) among all studied (bis-dithiolene)Ni complexes.

## 4. CONCLUSIONS

While challenging, closely mimicking the complex active sites of FDHs and CODHs has been possible and has finally resulted in active catalysts for $CO_2$ reduction. With such structural and functional similarities to the inspiring metalloenzymes, these synthetic molecular complexes provides a novel perspective for: (i) better understanding the functional specificity of the biological active centers themselves; (ii) for making further progress towards even more biomimetic catalysts (for example mimicking the axial ligation in FDH model compounds, the $NiFe_4$ cluster of [NiFe]CODH or implementing the **qpdt** ligand and derivatives within a Mo-Cu dinuclear complex of [MoCu]CODH); (iii) for understanding reaction mechanisms in greater detail (in particular the respective roles of the metal ions in heteropolynuclear sites); (iv) for discovering more selective and active bioinspired catalysts for $CO_2$ reduction.

## AUTHOR INFORMATION


### Corresponding Author

**Marc Fontecave:** *Laboratoire de Chimie des Processus Biologiques, UMR CNRS 8229, Collège de France, Sorbonne Université, PSL Research University, 11 Place Marcelin Berthelot, 75005 Paris, France.* ORCID: 0000-0002-8016-4747, E-mail: marc.fontecave@college-de-france.fr

### Authors

**Yun Li:** *Laboratoire de Chimie des Processus Biologiques, UMR CNRS 8229, Collège de France, Sorbonne Université, PSL Research University, 11 Place Marcelin Berthelot, 75005 Paris, France.* ORCID: 0000-0003-4805-7156.

**Maria Gomez-Mingot:** *Laboratoire de Chimie des Processus Biologiques, UMR CNRS 8229, Collège de France, Sorbonne Université, PSL Research University, 11 Place Marcelin Berthelot, 75005 Paris, France.* ORCID: 0000-0002-1557-2648.

**Thibault Fogeron:** *Laboratoire de Chimie des Processus Biologiques, UMR CNRS 8229, Collège de France, Sorbonne Université, PSL Research University, 11 Place Marcelin Berthelot, 75005 Paris, France.* Present Address: *Laboratoire de Chimie, Ecole Normale Supérieure de Lyon, Université de Lyon, CNRS UMR 5182, 46 allée d'Italie, 69364 Lyon, France*. ORCID: 0000-0002-5646-2824.


### Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

**FUNDING SOURCES**

This work was supported by the French National Research Agency (PhotoCarb ANR-16-CE05-0025-01 and ANR JCJC project NitroCOCa ANR-17-CE05-0021).

**BIOGRAPHIES**

**Yun Li** graduated in Pharmaceutical Chemistry at the East China University of Science and Technology in Shanghai. She obtained her PhD degree in Organic Chemistry in Paris at the Pierre et Marie Curie University (Paris 6). She then moved to Geneva (Switzerland) and Columbus (Ohio, USA) as a post-doctoral fellow working in Medicinal Chemistry. She is now a permanent researcher of the French National Center for Scientific Research (CNRS) at the Collège de France / Paris Sorbonne University in Prof. Fontecave's group. Her research interests focus on the design and synthesis of biomimetic complexes for carbon dioxide reduction.

**Maria Gomez-Mingot** holds a PhD in Chemistry from the University of Alicante (Spain, 2013), where she worked at the Institute of Electrochemistry under the supervision of Prof. Montiel. In 2013, she moved to the Nano-electrochemistry group at the Nano-electrochemistry group at *ITODYS* as a Postdoctoral fellow with Dr. Ghilane. In 2014 she undertook further postdoctoral studies in Prof. Fontecave's group at the Laboratory of Chemistry of Biological Processes at *Collège de France* where she subsequently became permanent Research Engineer. Presently, she leads efforts to study homogeneous and heterogeneous catalysts for energy storage applications, in particularly hydrogen production, oxidation of water and $CO_2$ reduction.

**Thibault Fogeron** graduated from the ENS (Paris) in molecular chemistry (2015). In 2018, he obtained his PhD degree with a thesis on the development of bioinspired catalysts for the reduction of $CO_2$ at the Collège de France (supervisors: Prof. Fontecave and Dr. Li). In 2019, he joined the team of Prof. Hasserodt at ENS Lyon as a postdoc to work on the development of magnetogenic probes. His interests focus on bioinorganic chemistry.

**Marc Fontecave** became Docteur d'Etat in 1984 from the University P. et M. Curie, Paris. He went as a post-doctoral fellow to the Department of Biochemistry at Karolinska Institute (1985-1986) and then spent 20 years as Professor of Chemistry at University Joseph Fourier, Grenoble, France (1989-2009). He is Professor at Collège de France, Paris, and Director of the Laboratory of Chemistry of Biological Processes. He is a member of the French Academy of Sciences and of the Royal Swedish Academy of Sciences. His research interests cover catalysis and biocatalysis, bioinorganic and bioinspired chemistry, artificial photosynthesis and energy storage technologies (water splitting and $CO_2$ valorization).

## REFERENCES


(1) Porcher, J.-P.; Fogeron, T.; Gomez-Mingot, M.; Derat, E.; Chamoreau, L.-M.; Li, Y.; Fontecave, M. A Bioinspired Molybdenum Complex as a Catalyst for the Photo- and Electroreduction of Protons. *Angew. Chem. Int. Ed.* **2015**, *54*, 14090–14093.

(2) Fogeron, T.; Retailleau, P.; Chamoreau, L.-M.; Li, Y.; Fontecave, M. Pyranopterin Related Dithiolene Molybdenum Complexes as Homogeneous Catalysts for $CO_2$ Photoreduction. *Angew. Chem. Int. Ed.* **2018**, *57*, 17033–17037.

(3) Fogeron, T.; Retailleau, P.; Gomez-Mingot, M.; Yun, L.; Fontecave, M. Nickel Complexes Based on Molybdopterin-like Dithiolenes: Catalysts for $CO_2$ Electroreduction. *Organometallics* **2018**, *38*, 1344–1350.

(4) Mouchfiq, A.; Todorova, T. K.; Dey, S.; Fontecave, M.; Mougel, V. A Bioinspired Molybdenum–Copper Molecular Catalyst for $CO_2$ Electroreduction. *Chem. Sci.* **2020**, *11*, 5503–5510.

(5) Kinzel, N. W.; Werlé, C.; Leitner, W. Transition Metal Complexes as Catalysts for the Electroconversion of $CO_2$: An Organometallic Perspective. *Angew. Chem. Int. Ed.* **2021**, *60*, 11628–11686.

(6) Raaijmakers, H. C. A.; Romão, M. J. Formate-Reduced E. Coli Formate Dehydrogenase H: The Reinterpretation of the Crystal Structure Suggests a New Reaction Mechanism. *J. Biol. Inorg. Chem.* **2006**, *11*, 849–854.

(7) Dobbek, H.; Gremer, L.; Kiefersauer, R.; Huber, R.; Meyer, O. Catalysis at a Dinuclear [CuSMo(O)OH] Cluster in a CO Dehydrogenase Resolved at 1.1-Å Resolution. *Proc. Natl. Acad. Sci.* **2002**, *99*, 15971–15976.

(8) Jeoung, J.-H.; Dobbek, H. Carbon Dioxide Activation at the Ni,Fe-Cluster of Anaerobic Carbon Monoxide Dehydrogenase. *Science* **2007**, *318*, 1461–1464.

(9) Schulzke, C. Molybdenum and Tungsten Oxidoreductase Models. *Eur. J. Inorg. Chem.* **2011**, *2011*, 1189–1199.

(10) Maia, L. B.; Fonseca, L.; Moura, I.; Moura, J. J. G. Reduction of Carbon Dioxide by a Molybdenum-Containing Formate Dehydrogenase: A Kinetic and Mechanistic Study. *J. Am. Chem. Soc.* **2016**, *138*, 8834–8846.

(11) Shanmugam, M.; Wilcoxen, J.; Habel-Rodriguez, D.; Cutsail III, G. E.; Kirk, M. L.; Hoffman, B. M.; Hille, R. 13C and 63,65Cu ENDOR Studies of CO Dehydrogenase from Oligotropha Carboxidovorans. Experimental Evidence in Support of a Copper–Carbonyl Intermediate. *J. Am. Chem. Soc.* **2013**, *135*, 17775–17782.

(12) Tory, J.; Setterfield-Price, B.; Dryfe, R. A. W.; Hartl, F. [$M(CO)_4$(2,2′-Bipyridine)] (M=Cr, Mo, W) Complexes as Efficient Catalysts for Electrochemical Reduction of $CO_2$ at a Gold Electrode. *ChemElectroChem* **2015**, *2*, 213–217.

(13) Clark, M. L.; Grice, K. A.; Moore, C. E.; Rheingold, A. L.; Kubiak, C. P. Electrocatalytic $CO_2$ Reduction by M(Bpy-R)(CO)4 (M = Mo, W; R = H, TBu) Complexes. Electrochemical, Spectroscopic, and Computational Studies and Comparison with Group 7 Catalysts. *Chem. Sci.* **2014**, *5*, 1894–1900.

(14) Takuma, M.; Ohki, Y.; Tatsumi, K. Sulfido-Bridged Dinuclear Molybdenum−Copper Complexes Related to the Active Site of CO Dehydrogenase: $[(Dithiolate)Mo(O)S_2Cu(SAr)]^{2-}$ (Dithiolate = 1,2-$S_2C_6H_4$, 1,2-$S_2C_6H_2$-3,6-$Cl_2$, 1,2-$S_2C_2H_4$). *Inorg. Chem.* **2005**, *44*, 6034–6043.

(15) Gourlay, C.; Nielsen, D. J.; White, J. M.; Knottenbelt, S. Z.; Kirk, M. L.; Young, C. G. Paramagnetic Active Site Models for the Molybdenum−Copper Carbon Monoxide Dehydrogenase. *J. Am. Chem. Soc.* **2006**, *128*, 2164–2165.

(16) Niks, D.; Hille, R. Molybdenum- and Tungsten-Containing Formate Dehydrogenases and Formylmethanofuran Dehydrogenases: Structure, Mechanism, and Cofactor Insertion. *Protein Sci.* **2019**, *28*, 111–122.

(17) Huang, D.; Holm, R. H. Reactions of the Terminal NiII−OH Group in Substitution and Electrophilic Reactions with Carbon Dioxide and Other Substrates: Structural Definition of Binding Modes in an Intramolecular NiII···FeII Bridged Site. *J. Am. Chem. Soc.* **2010**, *132*, 4693–4701.
(18) Enemark, J. H.; Cooney, J. J. A.; Wang, J.-J.; Holm, R. H. Synthetic Analogues and Reaction Systems Relevant to the Molybdenum and Tungsten Oxotransferases. *Chem. Rev.* **2004**, *104*, 1175–1200.
(19) Groysman, S.; Holm, R. H. Biomimetic Chemistry of Iron, Nickel, Molybdenum, and Tungsten in Sulfur-Ligated Protein Sites. *Biochemistry* **2009**, *48*, 2310–2320.
(20) Majumdar, A.; Sarkar, S. Bioinorganic Chemistry of Molybdenum and Tungsten Enzymes: A Structural–Functional Modeling Approach. *Coord. Chem. Rev.* **2011**, *255*, 1039–1054.
(21) Basu, P.; Burgmayer, S. J. N. Recent Developments in the Study of Molybdoenzyme Models. *JBIC J. Biol. Inorg. Chem.* **2015**, *20*, 373–383.
(22) Williams, B. R.; Fu, Y.; Yap, G. P. A.; Burgmayer, S. J. N. Structure and Reversible Pyran Formation in Molybdenum Pyranopterin Dithiolene Models of the Molybdenum Cofactor. *J. Am. Chem. Soc.* **2012**, *134*, 19584–19587.
(23) McNamara, W. R.; Han, Z.; Yin, C.-J. M.; Brennessel, W. W.; Holland, P. L.; Eisenberg, R. Cobalt-Dithiolene Complexes for the Photocatalytic and Electrocatalytic Reduction of Protons in Aqueous Solutions. *Proc. Natl. Acad. Sci.* **2012**, *109*, 15594–15599.
(24) McNamara, W. R.; Han, Z.; Alperin, P. J.; Brennessel, W. W.; Holland, P. L.; Eisenberg, R. A Cobalt–Dithiolene Complex for the Photocatalytic and Electrocatalytic Reduction of Protons. *J. Am. Chem. Soc.* **2011**, *133*, 15368–15371.
(25) Gomez-Mingot, M.; Porcher, J.-P.; Todorova, T. K.; Fogeron, T.; Mellot-Draznieks, C.; Li, Y.; Fontecave, M. Bioinspired Tungsten Dithiolene Catalysts for Hydrogen Evolution: A Combined Electrochemical, Photochemical, and Computational Study. *J. Phys. Chem. B* **2015**, *119*, 13524–13533.
(26) Ryde, U.; Schulzke, C.; Starke, K. Which Functional Groups of the Molybdopterin Ligand Should Be Considered When Modeling the Active Sites of the Molybdenum and Tungsten Cofactors? A Density Functional Theory Study. *J. Biol. Inorg. Chem.* **2009**, *14*, 1053–1064.
(27) Porcher, J.-P.; Fogeron, T.; Gomez-Mingot, M.; Chamoreau, L.-M.; Li, Y.; Fontecave, M. Synthesis and Reactivity of a Bio-Inspired Dithiolene Ligand and Its Mo Oxo Complex. *Chem. – Eur. J.* **2016**, *22*, 4447–4453.
(28) Bradshaw, B.; Dinsmore, A.; Ajana, W.; Collison, D.; Garner, C. D.; Joule, J. A. Synthesis of the Organic Ligand of the Molybdenum Cofactor, in Protected Form. *J. Chem. Soc. Perkin 1* **2001**, *24*, 3239–3244.
(29) Williams, B. R.; Fu, Y.; Yap, G. P. A.; Burgmayer, S. J. N. Structure and Reversible Pyran Formation in Molybdenum Pyranopterin Dithiolene Models of the Molybdenum Cofactor. *J. Am. Chem. Soc.* **2012**, *134*, 19584–19587.
(30) Williams, B. R.; Gisewhite, D.; Kalinsky, A.; Esmail, A.; Burgmayer, S. J. N. Solvent-Dependent Pyranopterin Cyclization in Molybdenum Cofactor Model Complexes. *Inorg. Chem.* **2015**, *54*, 8214–8222.
(31) Itoh, T.; Mase, T. A General Palladium-Catalyzed Coupling of Aryl Bromides/Triflates and Thiols. *Org. Lett.* **2004**, *6*, 4587–4590.
(32) Itoh, T.; Mase, T. A Novel Practical Synthesis of Benzothiazoles via Pd-Catalyzed Thiol Cross-Coupling. *Org. Lett.* **2007**, *9*, 3687–3689.
(33) Eckenhoff, W. T.; Brennessel, W. W.; Eisenberg, R. Light-Driven Hydrogen Production from Aqueous Protons Using Molybdenum Catalysts. *Inorg. Chem.* **2014**, *53*, 9860–9869.
(34) Fogeron, T.; Porcher, J.-P.; Gomez-Mingot, M.; Todorova, T. K.; Chamoreau, L.-M.; Mellot-Draznieks, C.; Li, Y.; Fontecave, M. A Cobalt Complex with a Bioinspired Molybdopterin-like Ligand: A Catalyst for Hydrogen Evolution. *Dalton Trans.* **2016**, *45*, 14754–14763.
(35) Fogeron, T.; Retailleau, P.; Chamoreau, L.-M.; Fontecave, M.; Li, Y. The Unusual Ring Scission of a Quinoxaline-Pyran-Fused Dithiolene System Related to Molybdopterin. *Dalton Trans.* **2017**, *46*, 4161–4164.

(36) Groysman, S.; Holm, R. H. Synthesis and Structures of Bis(Dithiolene)Tungsten(IV,VI) Thiolate and Selenolate Complexes: Approaches to the Active Sites of Molybdenum and Tungsten Formate Dehydrogenases. *Inorg. Chem.* **2007**, *46*, 4090–4102.
(37) Takeda, H.; Koizumi, H.; Okamoto, K.; Ishitani, O. Photocatalytic $CO_2$ Reduction Using a Mn Complex as a Catalyst. *Chem. Commun.* **2014**, *50*, 1491–1493.
(38) Wang, X.; Thiel, I.; Fedorov, A.; Copéret, C.; Mougel, V.; Fontecave, M. Site-Isolated Manganese Carbonyl on Bipyridine-Functionalities of Periodic Mesoporous Organosilicas: Efficient $CO_2$ Photoreduction and Detection of Key Reaction Intermediates. *Chem. Sci.* **2017**, *8*, 8204–8213.
(39) Todorova, T. K.; Huan, T. N.; Wang, X.; Agarwala, H.; Fontecave, M. Controlling Hydrogen Evolution during Photoreduction of $CO_2$ to Formic Acid Using $[Rh(R\text{-}Bpy)(Cp^*)Cl]^+$ Catalysts: A Structure–Activity Study. *Inorg. Chem.* **2019**, *58*, 6893–6903.
(40) Ishida, H.; Terada, T.; Tanaka, K.; Tanaka, T. Photochemical Carbon Dioxide Reduction Catalyzed by Bis(2,2'-Bipyridine)Dicarbonylruthenium($^{2+}$) Using Triethanolamine and 1-Benzyl-1,4-Dihydronicotinamide as an Electron Donor. *Inorg. Chem.* **1990**, *29*, 905–911.
(41) Elgrishi, N.; Chambers, M. B.; Wang, X.; Fontecave, M. Molecular Polypyridine-Based Metal Complexes as Catalysts for the Reduction of $CO_2$. *Chem. Soc. Rev.* **2017**, *46*, 761–796.
(42) Gourlay, C.; Nielsen, D. J.; Evans, D. J.; White, J. M.; Young, C. G. Models for Aerobic Carbon Monoxide Dehydrogenase: Synthesis, Characterization and Reactivity of Paramagnetic MoVO(μ-S)CuI Complexes. *Chem. Sci.* **2018**, *9*, 876–888.
(43) Groysman, S.; Majumdar, A.; Zheng, S.-L.; Holm, R. H. Reactions of Monodithiolene Tungsten(VI) Sulfido Complexes with Copper(I) in Relation to the Structure of the Active Site of Carbon Monoxide Dehydrogenase. *Inorg. Chem.* **2010**, *49*, 1082–1089.
(44) Hollingsworth, T. S.; Hollingsworth, R. L.; Lord, R. L.; Groysman, S. Cooperative Bimetallic Reactivity of a Heterodinuclear Molybdenum–Copper Model of Mo–Cu CODH. *Dalton Trans.* **2018**, *47*, 10017–10024.
(45) Ghosh, D.; Sinhababu, S.; Santarsiero, B. D.; Mankad, N. P. A W/Cu Synthetic Model for the Mo/Cu Cofactor of Aerobic CODH Indicates That Biochemical CO Oxidation Requires a Frustrated Lewis Acid/Base Pair. *J. Am. Chem. Soc.* **2020**, *142*, 12635–12642.
(46) Ahmed, M. E.; Adam, S.; Saha, D.; Fize, J.; Artero, V.; Dey, A.; Duboc, C. Repurposing a Bio-Inspired NiFe Hydrogenase Model for $CO_2$ Reduction with Selective Production of Methane as the Unique C-Based Product. *ACS Energy Lett.* **2020**, *5*, 3837–3842.
(47) Lubitz, W.; Ogata, H.; Rüdiger, O.; Reijerse, E. Hydrogenases. *Chem. Rev.* **2014**, *114*, 4081–4148.
(48) Ahmed, M. E.; Dey, A. Recent Developments in Bioinspired Modelling of [NiFe]- and [FeFe]-Hydrogenases. *Curr. Opin. Electrochem.* **2019**, *15*, 155–164.
(49) Ahmed, M. E.; Chattopadhyay, S.; Wang, L.; Brazzolotto, D.; Pramanik, D.; Aldakov, D.; Fize, J.; Morozan, A.; Gennari, M.; Duboc, C.; Dey, A.; Artero, V. Hydrogen Evolution from Aqueous Solutions Mediated by a Heterogenized [NiFe]-Hydrogenase Model: Low PH Enables Catalysis through an Enzyme-Relevant Mechanism. *Angew. Chem. Int. Ed.* **2018**, *57*, 16001–16004.
(50) Beley, M.; Collin, J.-P.; Ruppert, R.; Sauvage, J.-P. Nickel(II)-Cyclam: An Extremely Selective Electrocatalyst for Reduction of $CO_2$ in Water. *J. Chem. Soc. Chem. Commun.* **1984**, *19*, 1315–1316.
(51) Beley, M.; Collin, J.-P.; Romain, R.; Sauvage, J.-P. Electrocatalytic Reduction of Carbon Dioxide by Nickel Cyclam$^{2+}$ in Water: Study of the Factors Affecting the Efficiency and the Selectivity of the Process. *J. Am. Chem. Soc.* **1986**, *108*, 7461–7467.
(52) Froehlich, J. D.; Kubiak, C. P. Homogeneous $CO_2$ Reduction by Ni(Cyclam) at a Glassy Carbon Electrode. *Inorg. Chem.* **2012**, *51*, 3932–3934.
(53) Froehlich, J. D.; Kubiak, C. P. The Homogeneous Reduction of $CO_2$ by $[Ni(Cyclam)]^+$: Increased Catalytic Rates with the Addition of a CO Scavenger. *J. Am. Chem. Soc.* **2015**, *137*, 3565–3573.
(54) Wu, Y.; Rudshteyn, B.; Zhanaidarova, A.; Froehlich, J. D.; Ding, W.; Kubiak, C. P.; Batista, V. S. Electrode-Ligand Interactions Dramatically Enhance $CO_2$ Conversion to CO by the [Ni(Cyclam)](PF6)2 Catalyst. *ACS Catal.* **2017**, *7*, 5282–5288.

(55) Thoi, V. S.; Kornienko, N.; Margarit, C. G.; Yang, P.; Chang, C. J. Visible-Light Photoredox Catalysis: Selective Reduction of Carbon Dioxide to Carbon Monoxide by a Nickel N-Heterocyclic Carbene–Isoquinoline Complex. *J. Am. Chem. Soc.* **2013**, *135*, 14413–14424.
(56) Hong, D.; Tsukakoshi, Y.; Kotani, H.; Ishizuka, T.; Kojima, T. Visible-Light-Driven Photocatalytic $CO_2$ Reduction by a Ni(II) Complex Bearing a Bioinspired Tetradentate Ligand for Selective CO Production. *J. Am. Chem. Soc.* **2017**, *139*, 6538–6541.
(57) Fogeron, T.; Todorova, T. K.; Porcher, J.-P.; Gomez-Mingot, M.; Chamoreau, L.-M.; Mellot-Draznieks, C.; Li, Y.; Fontecave, M. A Bioinspired Nickel(Bis-Dithiolene) Complex as a Homogeneous Catalyst for Carbon Dioxide Electroreduction. *ACS Catal.* **2018**, *8*, 2030–2038.
(58) Froehlich, J. D.; Kubiak, C. P. Homogeneous $CO_2$ Reduction by Ni(Cyclam) at a Glassy Carbon Electrode. *Inorg. Chem.* **2012**, *51*, 3932–3934.