

Lloret-Fillol Research Group



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Abstract

Our research group is devoted to develop and perform mechanistic investigations of first row transition metal mediated transformations. Currently we are focusing our attention in multi proton-electron transformations, such as water oxidation, water and CO₂ reduction, oxidation and reduction of organic compounds and C-H activation based on earth abundant elements. Nature employs fascinating single and multi proton-electron transformations to sustain all life, where many fundamental chemical questions with incredible technological potential are unsolved.

From a conceptual point of view we are interested in transferring concepts from artificial photosynthesis to the organic synthesis to carry out endergonic transformations using sun-light

as a driving force. We envision that these studies will trigger the development of new and greener methodologies for the transformation of organic molecules. Our approach implies the combination of photoredox and transition metal catalysis.

Our approach implies the use of *in-situ* spectroscopic and spectrometric techniques, photochemical and electrochemical studies, kinetic and labelling studies and theoretical modelling to gain fundamental information about the operative mechanism. We would also like to develop and use high-throughput screening techniques to explore and expand new methodologies.

Nevertheless, the major aim of our research is gain insight in the understanding of the chemical reactivity.

Multi Proton-Electron Transformations

Nature employs single and multi-electron redox transformations implemented in crucial metabolic routes that sustain all life. Metalloenzymes are the responsible to execute these challenging redox reactions. They have defined active sites bearing one or more redox active metals such as Mn, Fe, Ni, Co and Cu. Representative examples of those transformations such as the light-driven water oxidation to O₂, protons and exited electrons (CaMn₄O₄) for the storage of sunlight into chemical bonds *via* CO₂ reduction, the H₂ oxidation and proton reduction by hydrogenase enzymes (Fe and Ni), the methane hydroxylation by the soluble methane monooxygenase (sMMO) using O₂ as the oxidant (Fe and Cu), the biological activity of the vitamin B₁₂ (Co), the C-H oxidation by heme and non-heme enzymes (Fe) and the dinitrogen fixation to ammonia (Fe, V, Mo), illustrate its great potential. However, our knowledge about the role of the metal center, biological mechanisms and our capacity of mimicking the reactivity and selectivity is limited. The preparation and study of model systems to emulate this fascinating reactivity is linked with basic chemical fundaments.

To emulate them with synthetic model systems that perform efficient and selective transformations we need to consider all aspects present in the metallozymes that enhance the reactivity towards the desired transformations. For instance we need to manage single electron, proton or all versions of proton-couple-electron-transfer (PCET) events. Likewise, we need to understand how to tune and control the metal ion oxidation states, the relationship between oxidation state, electron density, spin state and reactivity, how the first coordination sphere through electronic and geometric modifications and the second coordination sphere through secondary interactions impacts in the reactivity and selectivity. In order to get some insights on those questions we are working in the understanding of the water oxidation and water and CO₂ reduction reactions.

Water Oxidation

Water is the most appealing source of electrons that can be used in global scale in order to store energy into chemical bonds. However, the oxidation of the water molecule is an energetically uphill multi-proton-electron transformation identified as one of the bottlenecks for the development of artificial photosynthesis. Water oxidation needs to be

catalysed in order to proceed at low energy barriers and practical reaction rates. Intermediates involved in water oxidation are highly unstable and their characterization is very challenging. Indeed, despite the large quantity of work carried out to elucidate the mechanism that operates in the oxygen evolving center (CaMnO₄) located in the photosystem II (PSII) it is not fully understood. Several proposals are still under debate about the O-O formation mechanism and the role of the calcium. Well-defined molecular complexes offer the possibility to study the fundamental aspects of the water oxidation reaction, shedding light on the principles for a PSII understanding and efficient catalyst design.

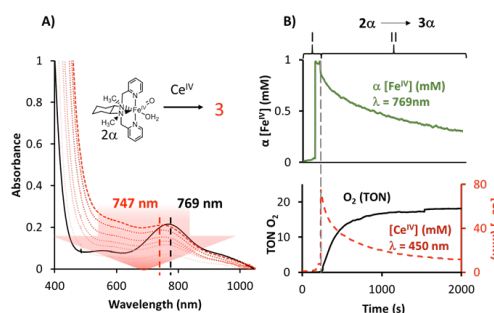


Fig. 1 UV-Vis spectra of [Fe^{IV}(O)(bpmcn)](OTf)₂ (solid line) and its evolution to the Fe^{IV}-O-Ce^{IV} complex upon addition of 75 eq. of CAN (dotted lines). Time courses for the reaction of B) 1-α with 75 eq. CAN monitoring [Fe^{IV}=O] formation and decay (top), [Ce^{IV}] decay (bottom, right axis, dotted line), and O₂ evolution (bottom, left axis, solid line).

On the other hand, catalysts based on earth-abundant metals are particularly desirable because of the cost and availability of these metals, being iron among the most attractive candidates.

Further studies of our well-defined water oxidation complexes led us identify a unique intermediate in water oxidation chemistry. We have spectroscopically characterized a Fe^{IV}-O-Ce^{IV} complex which is the last intermediate prior to the rate determining step. Although similar intermediates have been previously postulated for ruthenium complexes they have never been spectroscopically characterized.

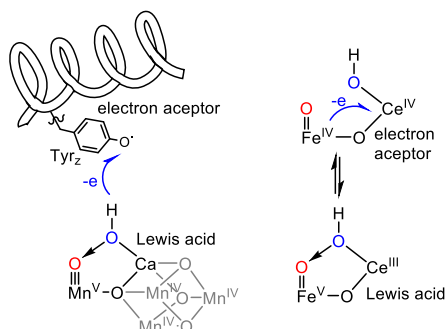


Fig. 2 – Parallels between the OEC and the iron–cerium complex.

The intermediate $\text{Fe}^{\text{IV}}\text{-O-Ce}^{\text{IV}}$ allows the detailed study of the elemental step of the O-O bond formation. Based on kinetic studies we determined that the rate determining step is the O-O bond formation. Now, for the first time we can study if the O-O bond is formed directly at the $\text{Fe}^{\text{IV}}\text{-O-Ce}^{\text{IV}}$ intermediate or there is first an electron transfer forming $\text{Fe}^{\text{V}}\text{-O-Ce}^{\text{III}}$ prior the O-O bond. The later situation is reminiscent to one of the postulated intermediates in the water oxidation mechanism for the OEC.

Water and CO_2 Reduction

Metal complexes have shown to be very efficient in the catalytic water and CO_2 reduction under electro- and photocatalytic conditions. However, the operating mechanisms are still not fully understood and efficiencies do not meet the requirements for real world applications yet. Therefore, there is still a need for developing new systems to extract mechanistic information, and studying new ideas and concepts to enhance their reactivity and selectivity. Indeed, selectivity is a key issue in CO_2 reduction. Also, new reactivity could be envisioned from the intermediates involved in these reactions. Transition metal hydride complexes (M-H) are intermediates in hydrogen evolution catalysis. Therefore, their control could lead to selective transformations of organic molecules, via controlling the M-H heterolytic (H^- transfer) or homolytic (H^\bullet transfer) cleavage.

Since the first report by the group of C. Chang and J. Long showing that aminopyridine complexes are active for the electrocatalytic reduction of protons to H_2 , the family of compounds has notably grown. These cobalt systems have several advantages i) they are water soluble, ii) they are based on abundant metals in the earth crust, iii) their electronic and steric properties are easily tuneable, and as expected iv) their basicity favours the heterolytic water reduction mechanism. This is one of prerequisites for the immobilization of the

catalysts onto an electrode or a semiconductor, since the homolytic mechanism requires a bimetallic pathway to produce H_2 . Altogether suggests that they are very appealing catalysts to study the water reduction mechanism.

In 2014, we reported the efficiency of $[\text{M}(\text{Py}_2^{\text{Ts}}\text{tacn})(\text{OTf})](\text{OTf})$ (M: Fe, Co, Ni; Figure 3) to catalyse the electrochemical proton reduction to H_2 , even in pure water which is still very difficult to achieve. The cobalt complex is also very active in the photocatalytic hydrogen reduction. In addition, we have done preliminary work on the synthesis, characterization and catalytic tests of robust tetradentate aminopyridine cobalt complexes (Figure 1). These complexes share the same 1,3,5-triazacyclononane (tacn) moiety as a basic structure which has been modified with different electronically modified pyridine arms. The modification of electronic properties of the ligand is done by introducing a range of substituents at the pyridine ring with different electronic properties.

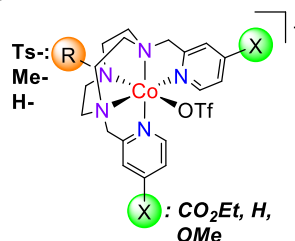


Fig. 3 line drawing structure of the developed cobalt complexes with the general formula $[\text{Co}(\text{X}^{\text{R}}\text{Py}_2^{\text{R}}\text{tacn})(\text{OTf})](\text{OTf})$.

The catalysts show high activity in both electrochemical (overpotentials 150-500 mV) and photochemical reduction of water to H_2 . Up to TON >8500, TOF >14 s^{-1} were obtained in $\text{CH}_3\text{CN}:\text{H}_2\text{O}:\text{Et}_3\text{N}$ (6:4:0.2 mL) in combination with a photoredox catalyst at 25 °C.

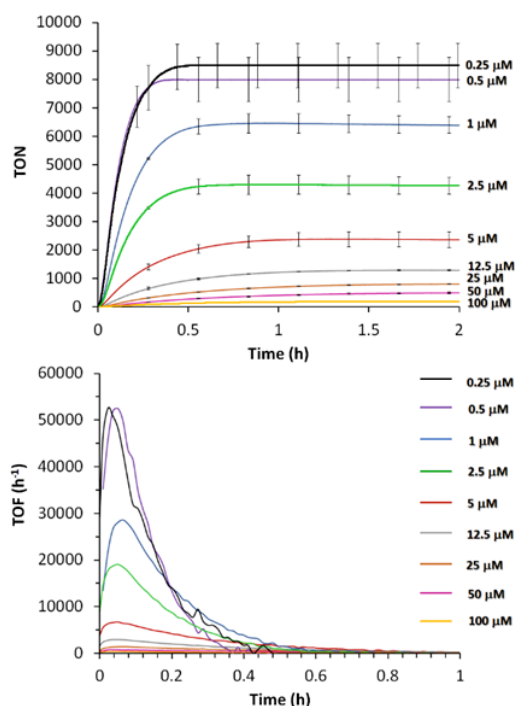


Fig. 4 Top) On-line hydrogen evolution traces with different concentrations of cobalt catalyst. Bottom) TOF vs time.

Moreover the easy functionalization of the catalysts allows us to obtain metalloenzymes based on the formation of biotin-streptavidin adduct. Interestingly, the cobalt complex is more active as photo- and electrocatalyst for water reduction inside of the cavity of the protein.

Preliminary results show that they are active CO₂ reduction electrocatalysts.

Beyond Artificial Photosynthesis

Mimicking Natural photosynthesis has the potential to provide greener and light-driven methodologies for sustainable fuel production but also synthetic products. In both cases endergonic reactions can be carried out. Added value chemicals have less scaling and economic restrictions than the production of energy carriers. Therefore, the use of concepts derived from Natural and artificial photosynthesis to perform selective transformations can provide the development of greener chemical transformations.

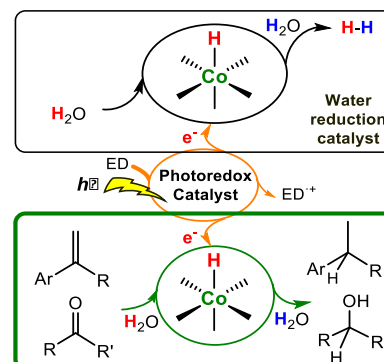


Fig. 5 – General scheme of reactivity.

Currently, we are expanding this concept by employing our readily available cobalt complexes, based on aminopyridine ligands developed for water reduction to hydrogen, in combination with a photoredox catalyst to reduce organic molecules.

Mechanistic investigations suggested that molecular cobalt-hydride intermediates are involved in the H₂ formation when using aminopyridine-based cobalt complexes. Based on these findings, we envisioned that the photochemically-obtained [Co]-H species could be a potential catalytic intermediate for the reduction of organic functionalities using the combination of light, H₂O and an electron donor as formal hydrogen source.

We have developed a methodology for the light-driven reduction of ketones, aldehydes and olefins. We have also obtained the homocoupling of olefins. The reduction of those organic substrates in aqueous media is very remarkable since the putative cobalt-hydride intermediates are highly reactive towards protons.

Our mechanistic investigations suggest that the reduction mechanism is substrate dependent, being both active the hydride transference and the hydrogen atom transfer.

High-throughput experimental techniques: In order to accelerate the development of light-driven methodologies we have developed parallel screening platforms of 24 and 48 reactions under temperature (-80 to 120 °C) and light intensity control. High-throughput screening photoreactors (HTSP) are a convenient tool to quickly take into account all the different variables that affect the reactions.



Fig. 6 - High-throughput screening photoreactors (HTSP)

Organometallic Reactivity

Currently we are exploring new organometallic complexes to activate small molecules. Our studies involve the development of highly modular mono, bi and tridentate phosphine ligands with an accessible $C_{sp^3}-H$ to produce P-C, P-C-P and CP_3 metal complexes.

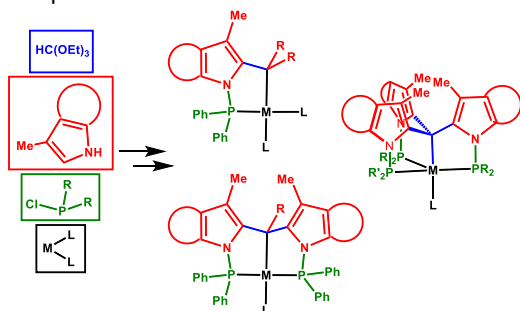


Fig. 7 – Modular approach for the synthesis of P-C, P-C-P and CP_3 metal complexes.

The readily available tris[(diphenylphosphino)-3-methyl-1H-indol-2-yl] methane ligand ($DPMI_3CH$) provides a highly rigid and well-defined coordination geometry that has been successfully applied for the synthesis of C_3 -symmetric second and third row transition metal complexes where the apical $C_{sp^3}-H$ is activated. We are interested into expanding their reactivity to first row transition metal complexes and to study with detail the $C_{sp^3}-H$ activation and $C_{sp^3}-H \cdots M$ interactions which have an extraordinary relevance in inorganic, organometallic and synthetic chemistry.

First we have explored the $C_{sp^3}-H \cdots M$ interactions with transition metals (Ag(I), Cu(I), Ni(II), Co(II)) with $DPMI_3CH$ and with the analogous *i*Pr-phosphine substituted.