

Lloret-Fillol Research Group



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Administrative support: Beatriz Martin

Abstract

Our research group is devoted to explore the reactivity of first row transition metal (1RTM) mediated transformations. We are inspired by Nature, which employs 1RTM to carry out single and multi-proton/-electron transformations to sustain life. Nevertheless, many fundamental chemical questions with incredible technologic potential still remain unsolved.

Currently our attention is focused on carrying out i) multi-proton/-electron reactions such as water oxidation and, water and CO₂ reduction and reductions of organic compounds as well as ii) electro- and photocatalytic C-X (X = H, Cl or Br) activations mediated by biomimetic complexes based on earth abundant elements.

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. To this end, we are developing and using high-throughput screening techniques (HST) to explore and expand these new methodologies.

To gain fundamental information about the operative mechanism we use *in-situ* spectroscopic and spectrometric techniques, photo- and electrochemical studies, kinetic and labelling studies and theoretical modelling. Nevertheless, the major aim of our research is to gain insight into 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 responsible to execute these challenging redox reactions in living organisms. Nature found highly efficient active sites bearing one or more redox active metals such as Mn, Fe, Ni, Co and Cu, which can carry out representative examples such as the light-driven water oxidation (CaMn_4O_4) and the final storage of sunlight into chemical bonds via CO_2 reduction, the H_2 oxidation and proton reduction by hydrogenase enzymes (Fe and Ni), the methane hydroxylation by the soluble methane monooxygenase (sMMO) using O_2 as the oxidant (Fe and Cu), the biological activity of the vitamin B_{12} (Co), the C-H oxidation by heme and non-heme enzymes (Fe) and the dinitrogen fixation to ammonia (Fe, V, Mo). These are only a part of the myriad transformations which illustrate the great potential. However, our knowledge about the role of the metal center, the biological mechanisms and our capacity of mimicking their reactivity and selectivity is limited. The preparation and study of model systems to emulate this fascinating reactivity is linked to the bases of the chemical fundamentals.

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 in 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 electronic and geometric modifications of the first coordination sphere and interactions of the second coordination sphere impact in the reactivity and selectivity. In order to get some insights into those questions we are working in the understanding of the water oxidation, water reduction and CO_2 reduction reactions by bio-inspired catalysts and the expansion to new organic transformations.

Water Oxidation

Water is the most appealing global-scale source of electrons that can be used in order to store energy into chemical bonds. However, the oxidation of the water molecule is an energetically uphill multi-proton-electron process 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 (CaMn_4O_4) 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.

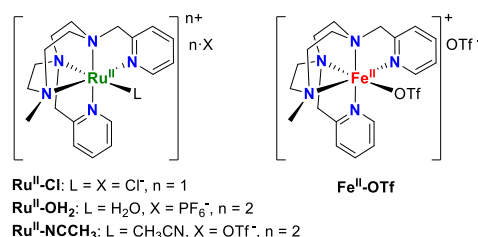
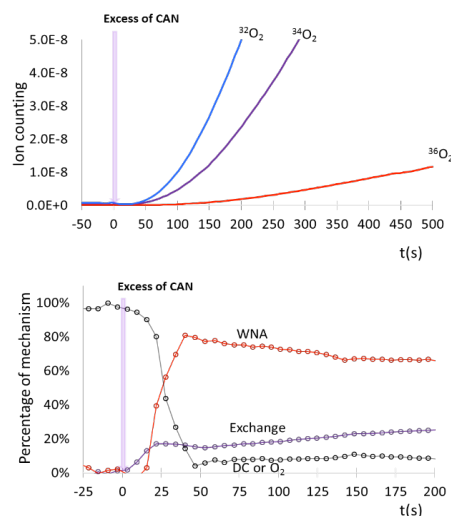


Fig. 1. Example of ruthenium and iron complexes studied.

On the other hand, catalysts based on earth-abundant metals are also particularly desirable because of the low cost and availability, being iron among the most attractive candidates. We have shown that iron complexes are highly efficient water oxidation catalysts. Nevertheless, the faster, most active and studied water oxidation catalyst are still based on ruthenium. Therefore, we would like to understand the relation between ruthenium and iron water oxidation catalysts. Since there was no direct comparison between iron and ruthenium we have designed and investigated homologous ruthenium and iron complexes.



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Fig. 2 On-line values and mechanism percentage obtained after analysis of the m/z 32 (blue), 34 (purple) and 36 (red) ion counting monitored after the addition of 100 eq of CAN dissolved in $H_2^{18}O$ to a solution of $Ru^{IV}(^{16}O)$ in $H_2^{16}O$.

The N -pentadentate ruthenium complex $Ru^{II}-OH_2$ exhibits a significant WO activity while $Fe^{II}-OTf$ resulted to be inactive. Our studies by means of catalytic, kinetics, spectroscopic, spectrometric and electrochemical techniques in combination with theoretical calculations, pointed that the water oxidation reaction follows a water nucleophilic attack mechanism. Our data suggest that the O-O bond formation is the rate determining step ($\Delta G^\ddagger = 25.5 \text{ kcal}\cdot\text{mol}^{-1}$) and it occurs at the $Ru^V(O)$ intermediate. This $Ru^V(O)$ intermediate is accessible under catalytic conditions through an ET process from $Ru^{IV}(O)$ ($E_{1/2} \sim 1.81 \text{ V}$ vs SHE).

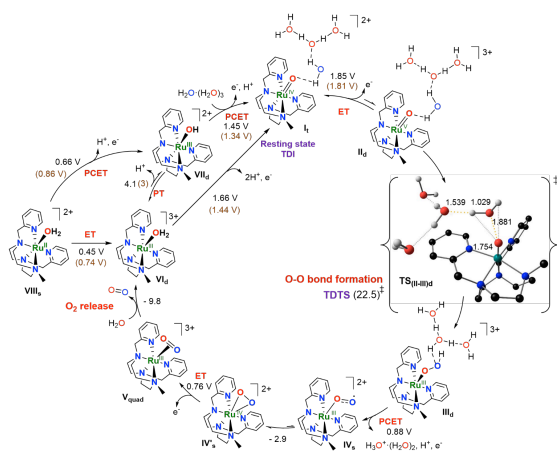


Fig. 3. Proposed WO catalytic cycle for complex $[Ru^{II}(OH_2)(Py_2^{Me_6}tacn)](PF_6)_2$ ($Ru^{II}-OH_2$) based on experimental and computational data.

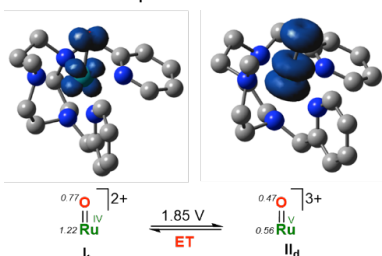


Fig.4. Spin densities calculated for $Ru^{IV}(O)$ (I_d) and $Ru^V(O)$ (II_a).

Additionally, our water evolution experiments indicate that the formation of a $[(Py_2^{Me_6}tacn)Ru^{IV}-O-Ce^{IV}]$ adduct is unlikely to be formed. On the other hand, the homologous iron complex follows a parallel mechanism to the ruthenium complex but its inactivity is linked with the

inaccessibility of $Fe^V(O)$ ($E_{1/2} = 2.15 \text{ V}$ vs SHE) under reaction conditions rather than other scenarios. These serve as an iron - ruthenium link and they will aid in the future development of new and more effective WO catalysts.

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 exploring new concepts to enhance their reactivity and selectivity. Indeed, selectivity is a key issue in CO_2 reduction that can be controlled by molecular complexes. In addition, new reactivity could be envisioned from intermediates involved in these transformations. For example metal complexes in low oxidation state and transition metal hydride complexes ($M-H$) are intermediates in hydrogen evolution catalysis. Therefore, new selectivities of reduction of organic molecules can be envisioned by following reaction pathways via $M-H$ heterolytic (H^- transfer) or homolytic (H^\bullet transfer) cleavage.

Since the first report on water reduction with aminopyridine complexes the family of compounds has notably grown. These cobalt systems have several advantages i) are water soluble, ii) are based on abundant metals in the earth crust and iii) their electronic and steric properties are easily tuneable. Moreover, the high basicity of the ligands favours the heterolytic water reduction mechanism, which is highly desirable for the immobilization of the catalysts onto an electrode or a semiconductor, since the homolytic mechanism follows a bimetallic coupling pathway. Altogether suggests that they are very appealing catalysts to study the water reduction mechanism.

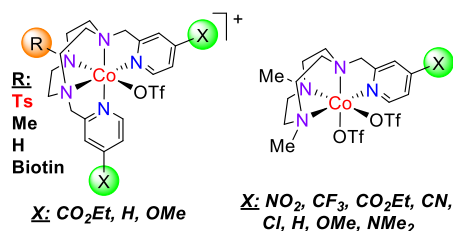


Fig.5. Cobalt aminopyridine complexes active in electro- and photocatalytic proton and CO_2 reduction.

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In 2014, we reported an new family of very efficient electro- and photochemical water reduction catalysts (WRC) $[\text{Co}(\text{Py}_2^{\text{Ts}}\text{tacn})(\text{OTf})](\text{OTf})$ (Figure 5), even in pure water which is still very difficult to achieve. The system based 1,3,5-triazacyclononane (tacn), a very basic moiety, which confer unique properties among WRC. In this line we have expanded the family of cobalt catalysts $([\text{Co}^{\text{II}}(\text{OTf})_2(\text{Y}^{\text{X}}\text{PyMetacn})])$ to the readily available family of tetradentate ligands 1,4-dimethyl-7-[2'-(4 β ,6 γ -pyridyl)methyl]-1,4,7-triazanone (Figure 5). The modification of electronic properties of the ligand is done by introducing a range of substituents at the pyridine ring. The catalysts obtained 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) at 25 $^\circ\text{C}$. Moreover, we provided evidences of the key intermediates in the photocatalytic water reduction and identified the protonation of the cobalt as the rate-determining step by combination of stoichiometric, kinetics, deuterium labelling and computational modelling. Moreover, we provided a unified scheme to rationalize the electronic effects. This information will be of value for the design of more active water reduction catalysis.

Moreover the easy functionalization of the catalysts allows us to obtain metalloenzymes based on the biotin-streptavidin adduct. Interestingly, the cobalt complex is more active as photo- and electrocatalyst for water reduction inside of the protein cavity. We rationalized this effect with the help of computational dynamics due to the proximity of protonated aminoacids of the cavity and the metal center.

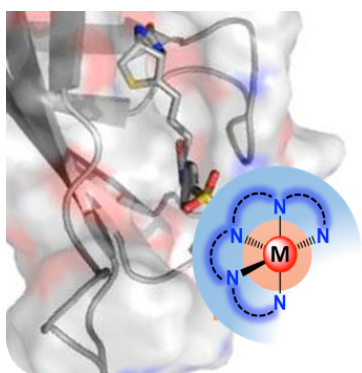


Fig. 6 line drawing structure of the developed cobalt complexes with the general formula $[\text{Co}^{\text{X}}(\text{Py}_2^{\text{R}}\text{tacn})(\text{OTf})](\text{OTf})$.

Our results also show that both families of complexes are active as catalysts for both photo- and electro CO_2 reduction to CO with an exquisite selectivity.

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 must be carried out. Nevertheless, 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.

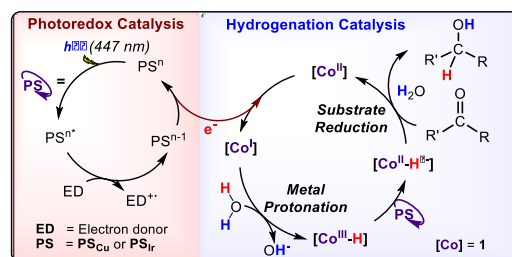


Fig. 7 – General scheme of reactivity.

Currently, we are expanding this concept by employing our designed cobalt complexes, based on aminopyridine ligands and initially 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 H_2 formation when using aminopyridine-based cobalt complexes. Based on these findings, we envisioned that the photochemically-obtained $[\text{Co}]\text{-H}$ species could be a potential catalytic intermediate for the reduction of organic functionalities using the combination of light, H_2O 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

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dependent, being both active the hydride transference and the hydrogen atom transfer.

More interestingly, the system presents an exquisite selectivity for the reduction of acetophenone versus aliphatic aldehydes. Indeed, this selectivity is unprecedented for previous metal catalyzed transformations. The present system benefits from avoiding the use of protecting-deprotecting steps and the use of stoichiometric amounts of lanthanides, which are required in other reduction methods of ketones and aldehydes.

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. The irradiation is homogeneous in all reaction positions with a standard deviation lower than 2.5 %.

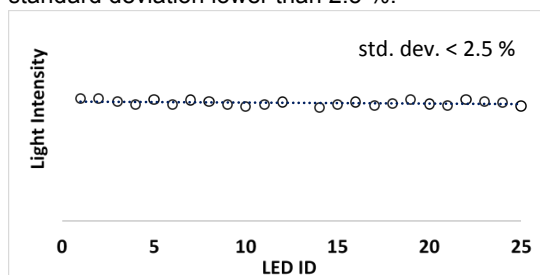


Fig 8. Comparison of the light intensity between all positions of the photoreactor at 700 mA.

Importantly, we have developed a system to calibrate the light-intensity. With the calibration, the High-throughput screening photoreactors (HTSP) designed are a convenient toolkit to precisely control all different variables that affect the reactions.

Organometallic Reactivity

We are developing new organometallic complexes to activate small molecules. Our studies involve 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.

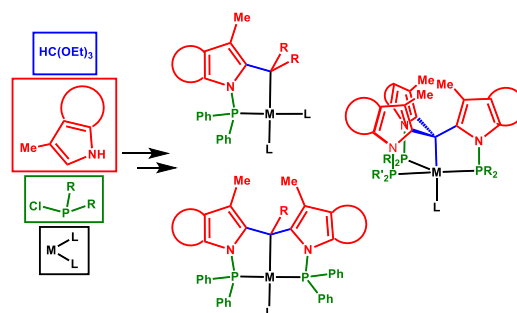


Fig. 9 – Modular approach for the synthesis of P-C, P-C-P and CP_3 metal complexes.

The readily available tris[(diphenylphosphino)-3-methyl-1H-indol-2-yl] methane ligand ($TPMI_3CH$) 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. However, although desirable the homologous first row transition metal complexes resulted to be challenging. Therefore, we became interested in expanding their reactivity to first row transition metal complexes and studying 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. In this regard we have found that the $C_{sp^3}-H$ is activated obtaining the nickel(II) halogenated complex. Now we are exploring their potential as catalysts for reduction of challenging substrates.

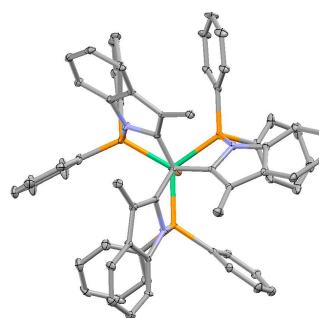


Fig. 10 $[Ni^{II}(TPMI_3C)Cl]$ metal complexes.

Articles

“Nuevas estrategias para la conversión de la energía solar en enlaces químicos”

Anales (2016), 112, 133

Zoel Codolà, Arnau Call, Ferran Acuña-Parés, Carla Casadevall, Julio Lloret Fillol*

“Water oxidation: High five iron”

Nature Energy (2015) 10.1038/nenergy.2016.23

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“Spectroscopic, electrochemical and computational characterization of Ru species involved in catalytic water oxidation. Evidence for $[\text{Ru}^{\text{V}}(\text{O})(\text{Py}_2\text{Metacn})]$ intermediate”

Chemistry–A European Journal (2016) 22, 10111

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