

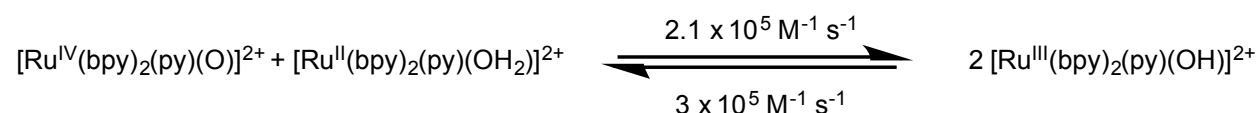
**Selection of reviews/resources for topics beyond scope of this review:**

- Photochemical reactions, see: Hoffmann, N. *Eur. J. Org. Chem.* **2017**, 15, 1982.
- Biological systems, see: Reece, S. Y.; Nocera, D. G. *Annu. Rev. Biochem.* **2009**, 78, 673.
- High-level theory (Marcus-Type), see: Hammes-Schiffer, S. *Acc. Chem. Res.* **2009**, 42, 1859.

For general review, see: Huynh, M. H. V.; Meyer, T. J. *Chem. Rev.* **2007**, 107, 5004.

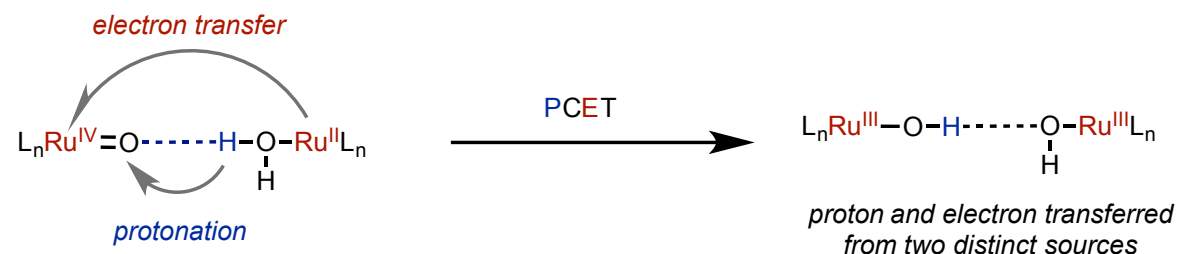
**History and Definitions of Proton-Coupled Electron Transfer (PCET)**

- In 1981, the term proton-coupled electron transfer (PCET) was first used to describe a process in which electrons and protons transferred together – specifically in a concerted  $e^- / H^+$  transfer process.
- Meyer and coworkers invented the term to distinguish the following process from a hydrogen atom transfer (HAT) mechanism, in which the proton and electron are delivered from the same bond.



*JACS* **1981**, 103, 2897.

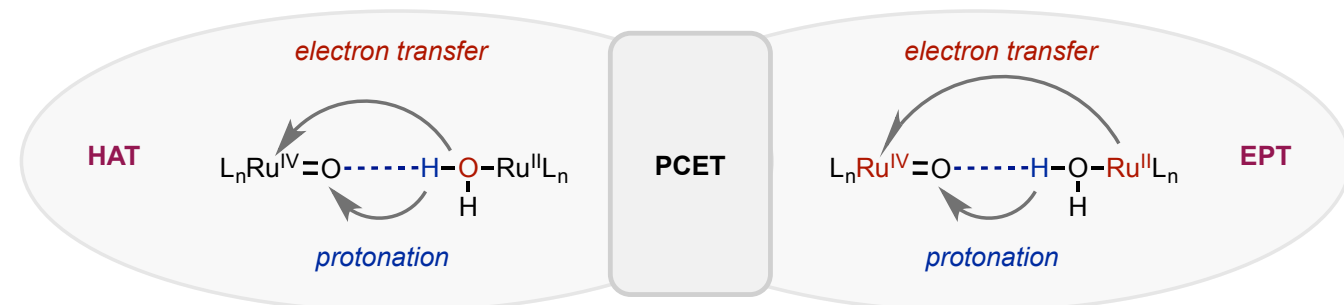
- The mechanism is thought to be simultaneous transfer of a proton from  $H_2O$  and an electron from  $Ru^{II}$  via a concerted process.



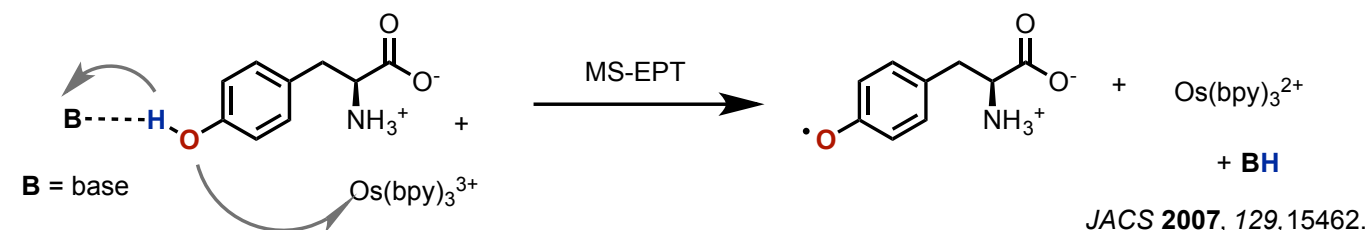
- Despite the original definition of PCET being born out of differentiating from HAT, the terminology has evolved to include the general reaction paradigm of transfer of protons and electrons. In general, PCET can occur through several processes/elementary steps defined accordingly in the context of this review, such as:

- Hydrogen atom transfer (HAT) - simultaneous proton/electron transfer from *same* underlying X-H  $\sigma$  orbital or bond
- Concerted electron-proton transfer (EPT) - simultaneous (relative to period of coupled vibration,  $\sim 10$  fs) proton/electron transfer from *different* and independent sources

Note: Other terms do exist, but for the purpose of this review will not be defined (i.e. concerted proton-electron transfer (CPET), electron transfer proton transfer (ET-PT), concerted electron-proton transfer (CEP)).



- In the example shown, EPT occurs at a single site – both the proton and electron are delivered from a single donor to a single acceptor (complex to complex transfer)
- Another class of EPT reactions are *multiple site* electron-proton transfer (MS-EPT) in which concerted electron-proton transfer occurs to different acceptors or from different donors.

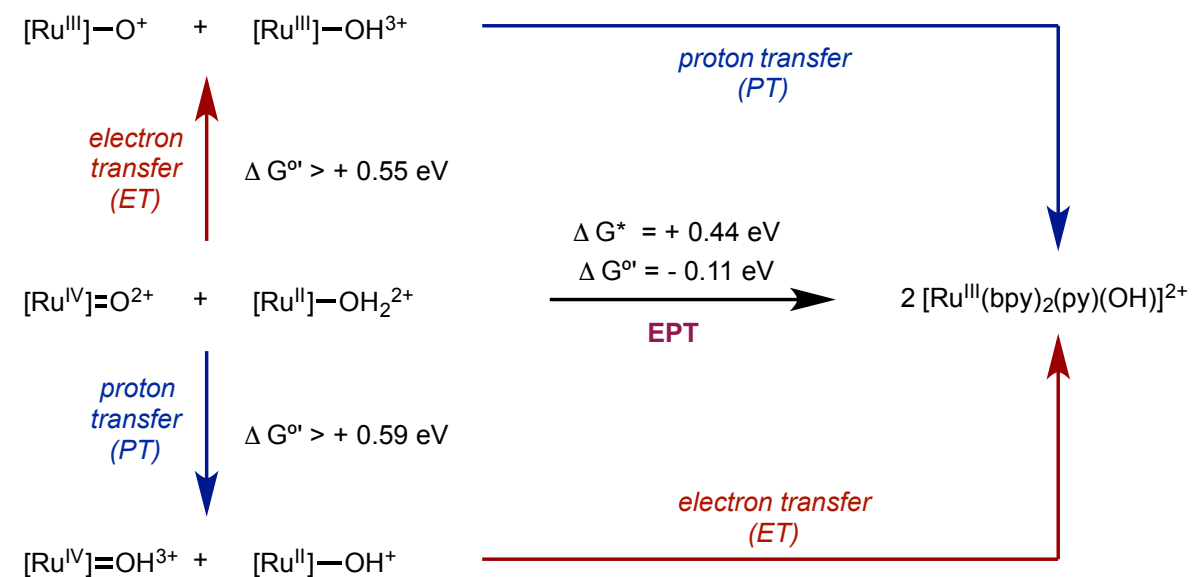


- MS-EPT is more common in biological systems involving enzymes or cofactors that can stabilize key reactive intermediates

**Mechanistic Insights - EPT**

- In general, the sequence of transfer events can occur in a variety of multistep mechanisms that are highly dependent on reaction conditions such as temperature or pH.

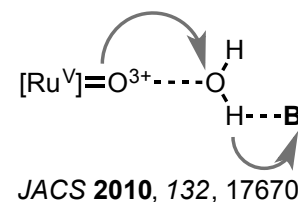
in pH = 7 (ligands are bpy + py)



- At a neutral pH, comproportionation via EPT dominates because it avoids high energy intermediates that would result from ET-PT or PT-ET – the energy required exceeds the experimental free energy of activation.
- At a low pH, PT-ET becomes more favorable through stabilization of  $[Ru]=OH^{3+}$ .

**Other related processes**

a) Atom-proton transfer (APT)



b) Hydride-proton transfer (HPT)

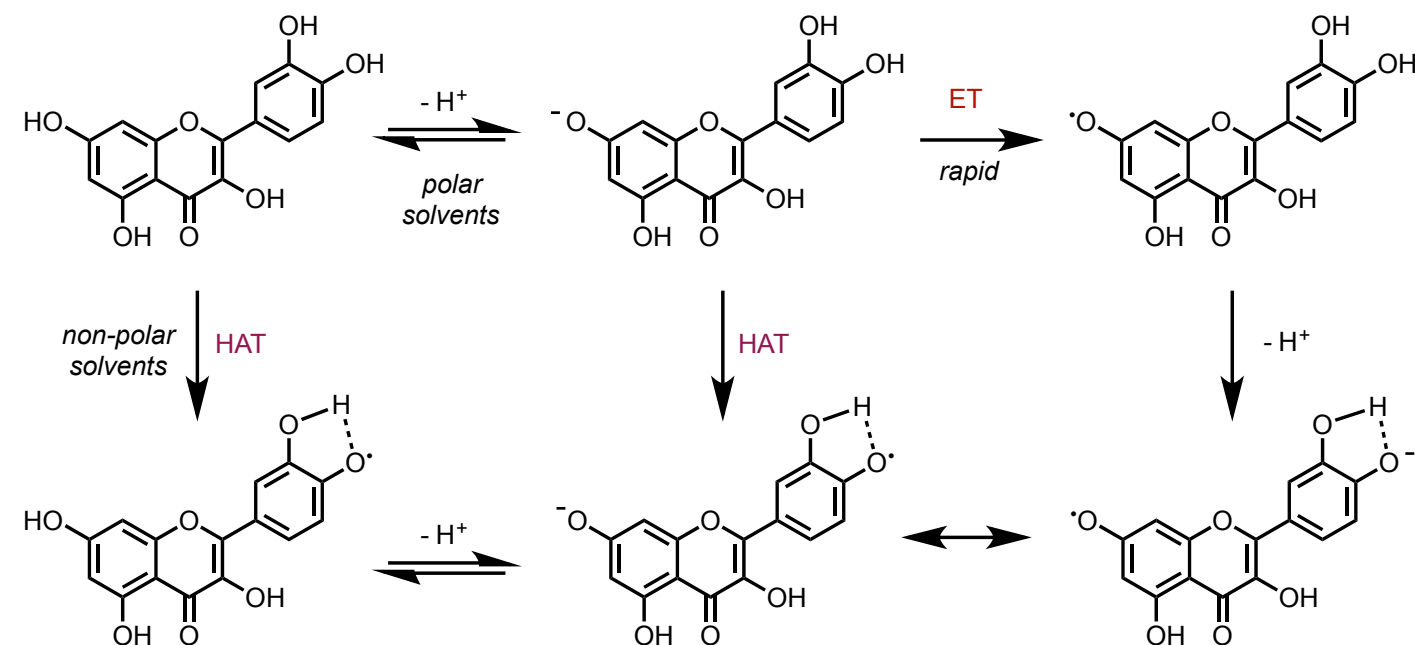
*Angew. Chem. Int. Ed.* **2002**, 41, 3870.

*JACS* **2010**, 132, 16318.

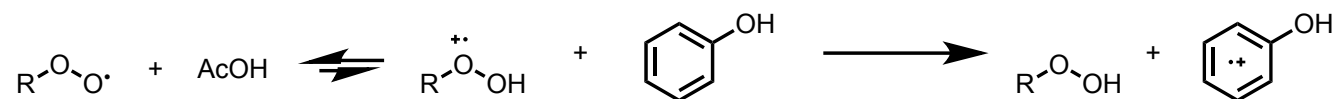
# Proton-Coupled Electron Transfer with Metal Complexes

## Organic PCET - Phenol Case Study

- Phenols are considered to be one of the more commonly encountered organic molecules that engages in PCET.
- Mechanistic studies have shown that three distinct PCET pathways can be viable for phenol-based reagents: HAT, EPT, and PT-ET.
- The precise mechanism of phenol-based PCET depends on: (a) hydrogen-bond-accepting and anion-solvating effects of solvent; (b) electron affinities and bond-dissociation enthalpies of initially formed radicals; (c) electronic influence of substituents on phenol ring.



- In addition to solvent polarity accelerating specific steps in the PCET of phenols, acids can be added with peroxides to generate highly reactive peroxy radical cations to facilitate 16 fold increase in the rate of the reaction.

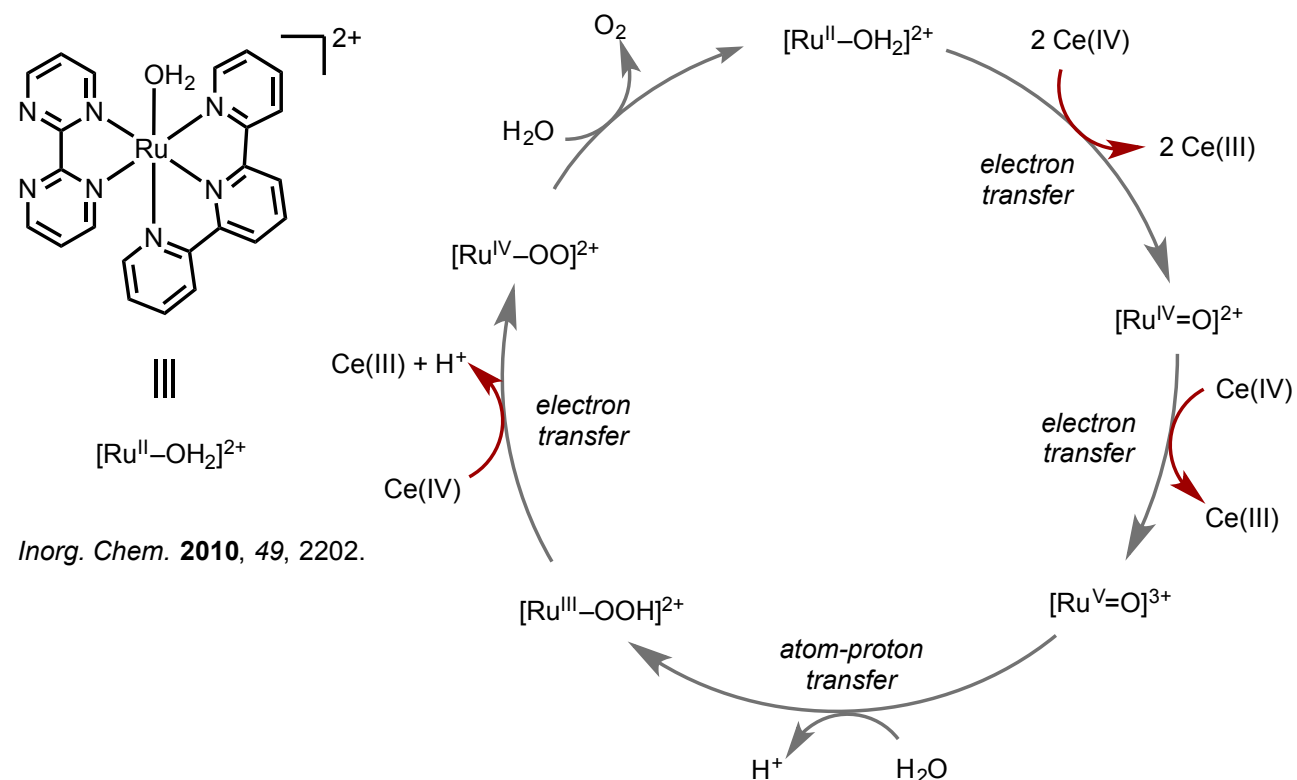


## Metal-mediated PCET Processes

- PCET mechanisms are important processes in the context of metal complex reactivity because of potential insights toward biochemically mediated processes.
- In general, harnessing PCET with metal-mediated paradigms is a powerful tool for studying fundamental mechanisms and enabling reactivity.

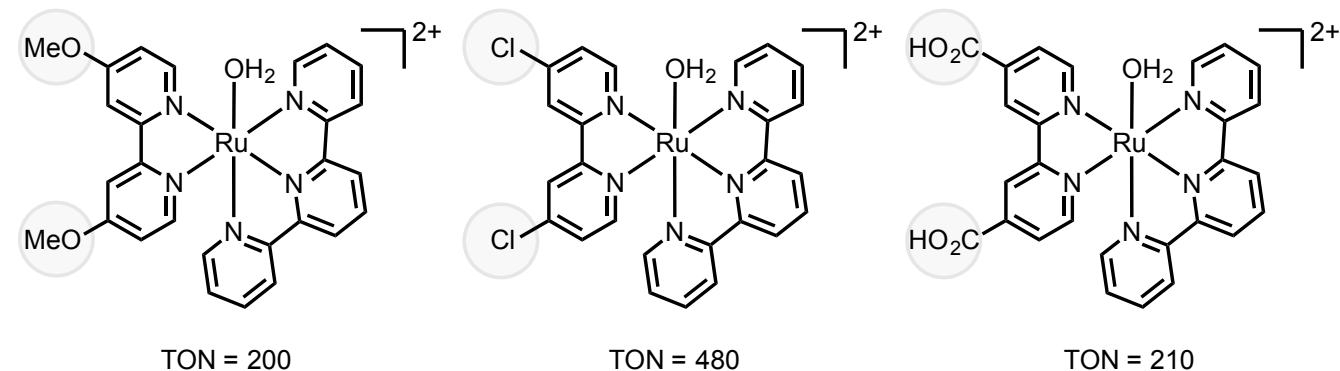
### a) Water oxidation

- Photosystem II is considered to be the active component in water oxidation, specifically the  $\text{Mn}_4\text{Ca}$  cluster that is a part of the oxygen-evolving complex.
- Most common approach toward a biomimetic Mn-cluster is photosensitized oxidation.
- Ru-based catalytic studies provide evidence for a synergistic PCET and APT sequence.

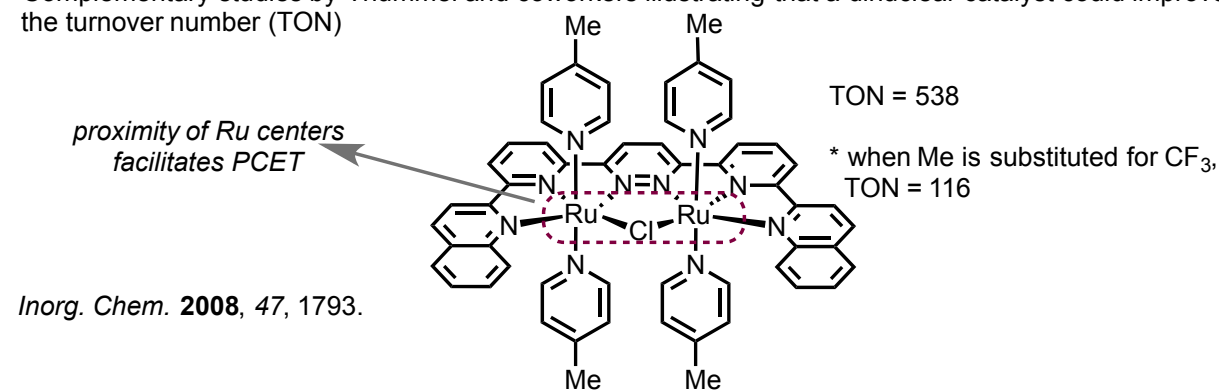


*Inorg. Chem.* **2010**, 49, 2202.

- Burlinguette and coworkers reported a series of electronically diverse complexes and measured the turnover number – both strongly electron-donating and -withdrawing substituents generally gave lower TN due to catalyst instability, while halide substituents performed the best.
- It is hypothesized that  $\text{O}_2$  evolution catalysts require a balance between electron density on the metal and  $\pi$ -back bonding to the most labile ligand



- Complementary studies by Thummel and coworkers illustrating that a dinuclear catalyst could improve the turnover number (TON)

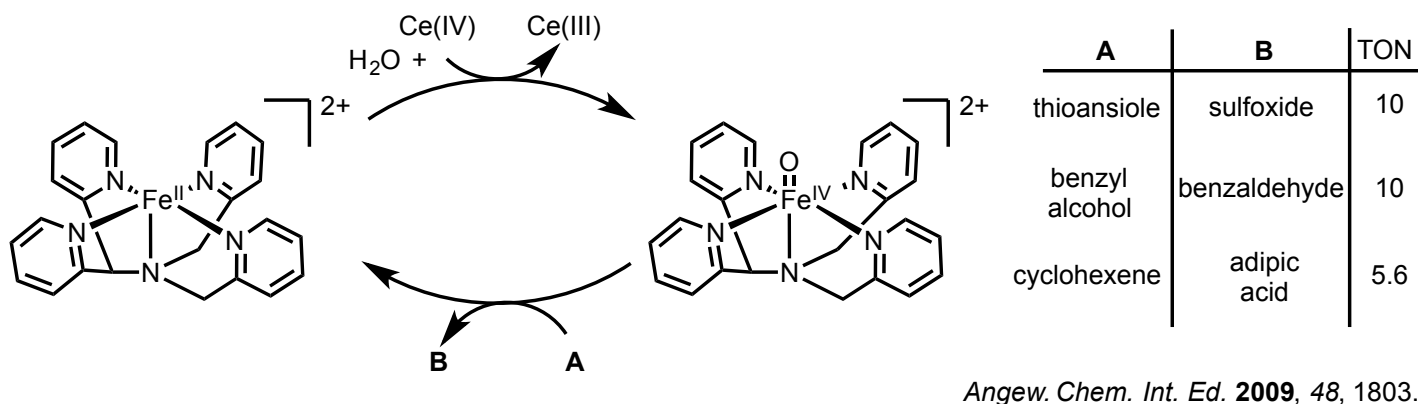


*Inorg. Chem.* **2008**, 47, 1793.

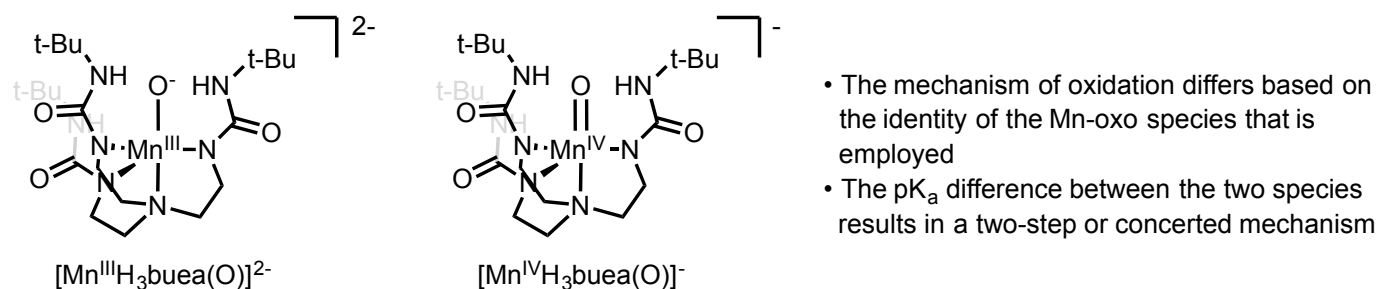
# Proton-Coupled Electron Transfer with Metal Complexes

## b) Oxidation of organic molecules

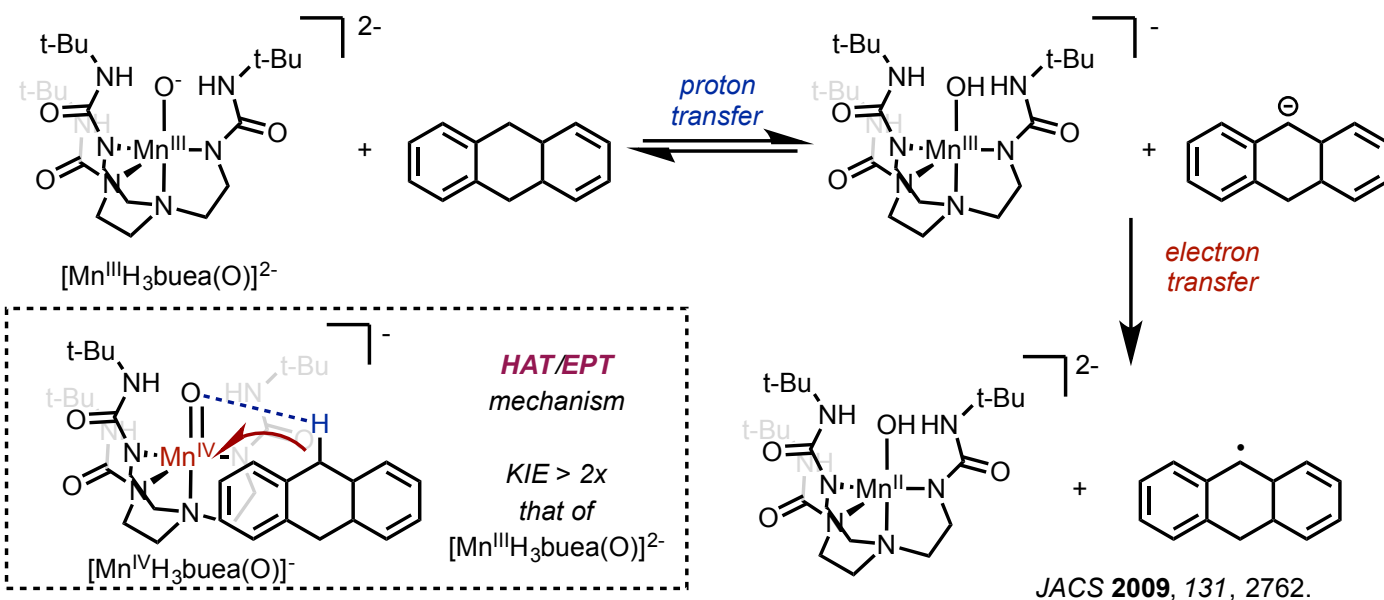
- Despite organic PCET processes being thermodynamically favored, the initially oxidized intermediates can often react unpredictably with the proton/electron donating reagents
- In the context of PCET involving organic oxidation reactions, metal oxo species can often serve as engines for oxygen atom transfer



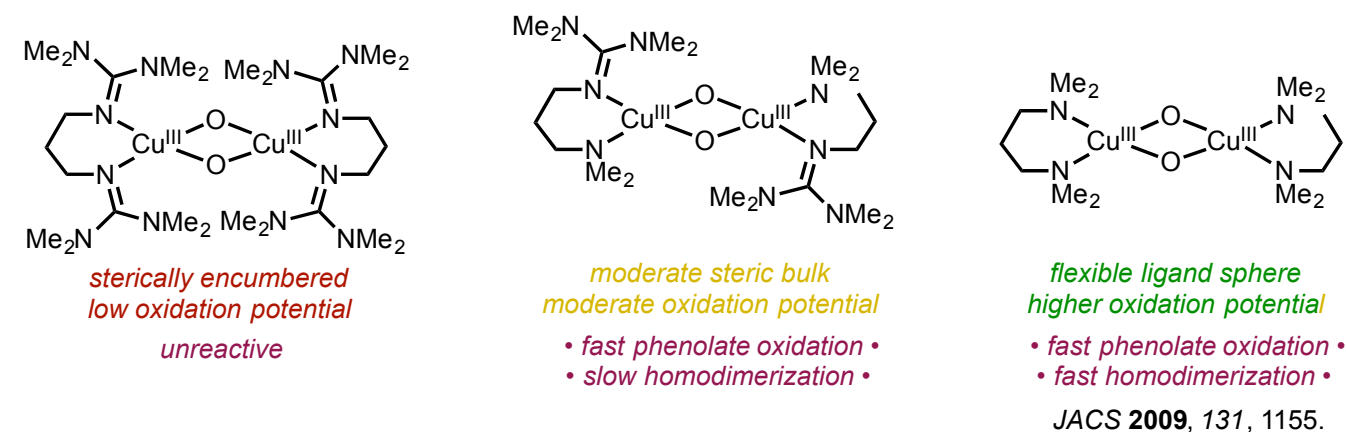
- In an interesting series of reports by Borovik and coworkers, Mn-oxo complexes were shown to act as bases in a PCET pathway to oxidize dihydroanthracene via C–H bond cleavage



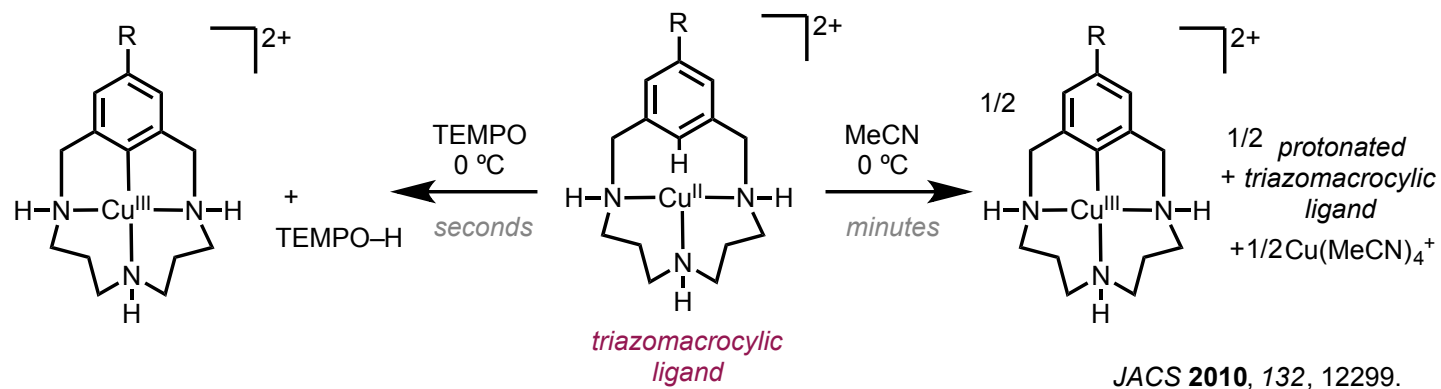
for preparation of complexes, see: JACS **2006**, 128, 8728.



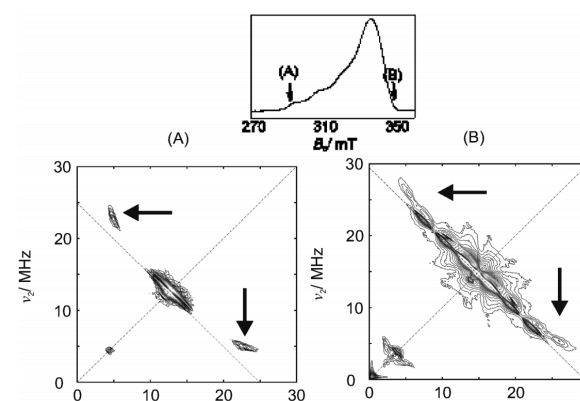
- Tuning of the ligand sphere can also influence the type of reactivity that is observed, including site-selectivity, chemoselectivity, and the transformation itself
- An assortment of hybrid guanidine ligands bound to a dimeric copper complex resulted in interesting divergent reactivity



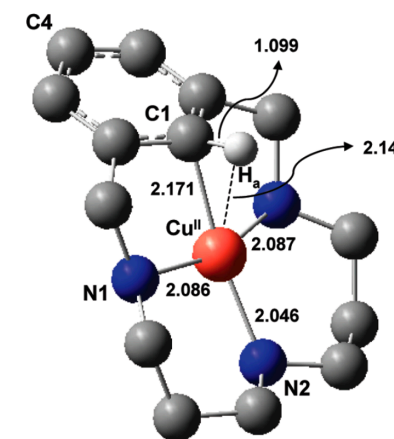
- Several studies have focused on the effect of PCET on relatively mild C–H bond activation pathways.



- In an effort to probe the mechanism of this C–H activation step, the authors carry out EPR, DFT, and UV-Vis kinetic data that supports a PCET pathway.

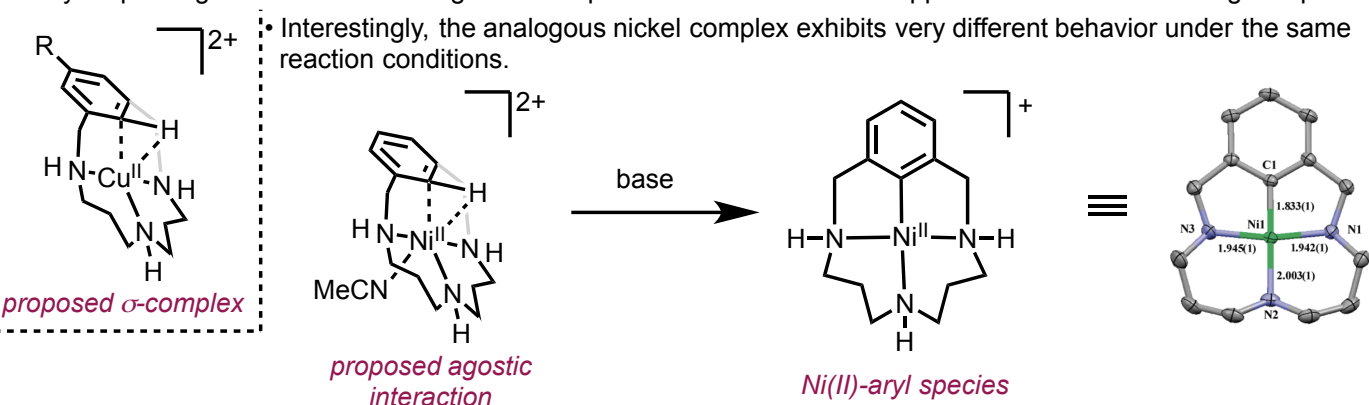


HYSCORE EPR pulse experiment consistent with complex having electronic ground state with unpaired electron localized in copper  $d_{x^2-y^2}$



# Proton-Coupled Electron Transfer with Metal Complexes

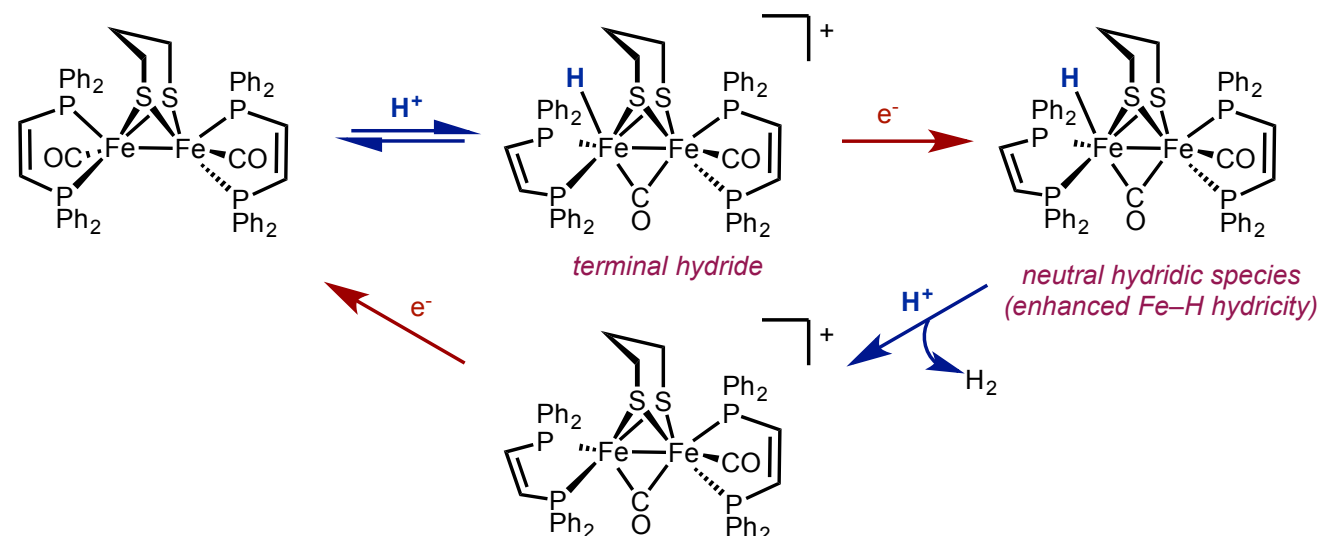
- Key step thought to be a rate-limiting PCET step involved in a binuclear copper-mediated C–H cleavage step.



- The precise mechanism of this C–Ni bond formation is still debated, as there is no evidence to support a simple base assisted deprotonation mechanism and Ni(II)/(IV) oxidative addition to a C–H bond of this class has no substantial precedence.

## c) Oxidation and Reduction of Hydrogen

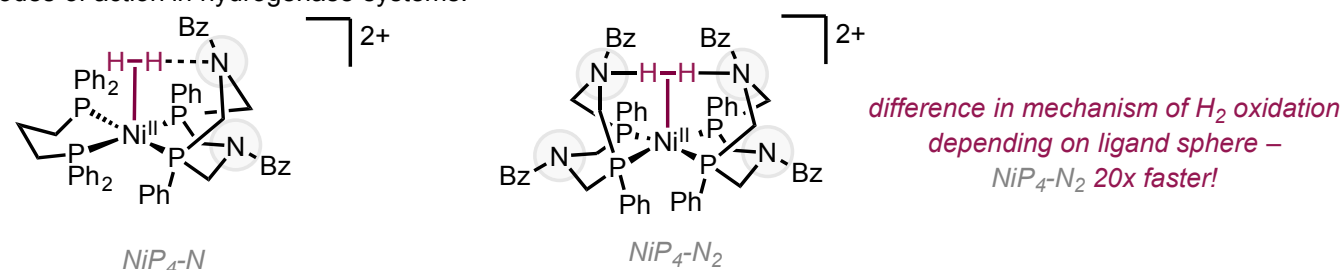
- Hydrogen oxidation and reduction is highly sought out because of the multifaceted utility of harnessing hydrogen in ammonia production, fuel cells, and organic synthesis.



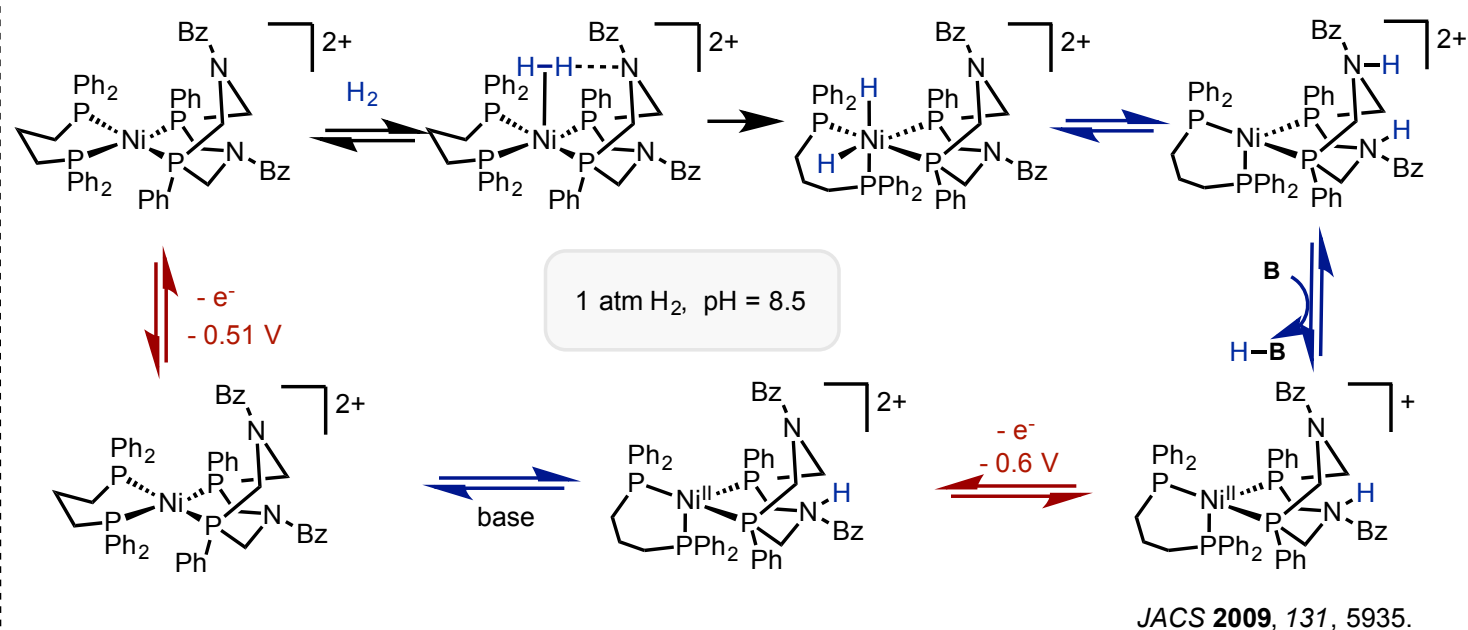
- Hydrogen evolution complex (HEC) is thought to utilize PCET to reduce a proton to hydrogen – model systems that invoke a terminal hydride can catalyze proton reduction at 200 mV less than isomeric bridging hydride.

*Coord. Chem. Rev.* **2009**, 253, 1476.

- The opposite process, dihydrogen oxidation, is also a fundamentally important sequence that sheds light on various modes of action in hydrogenase systems.

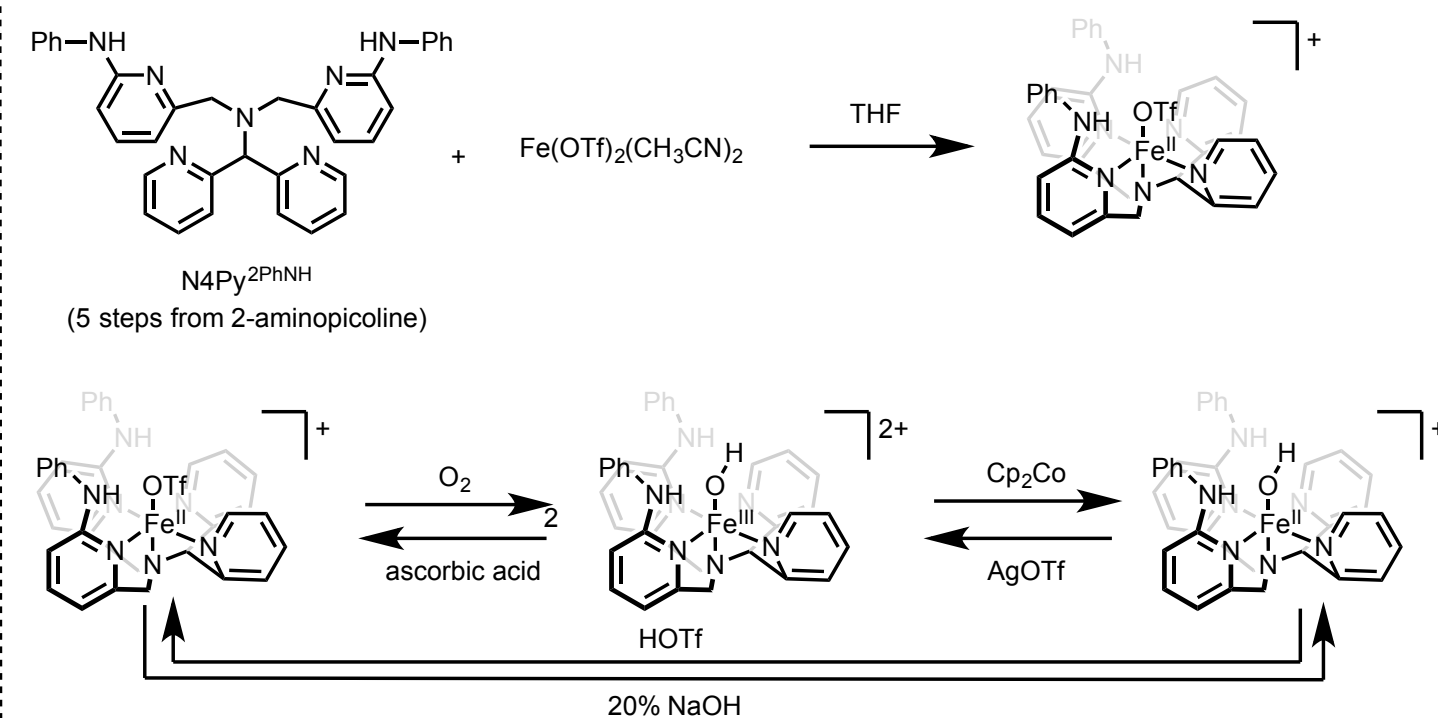


## Proposed PCET cycle:



## d) Reduction of Oxygen

- Strategies for reducing dioxygen include both primary- and secondary-sphere coordination involvement, particularly with iron, manganese, and copper catalysts.



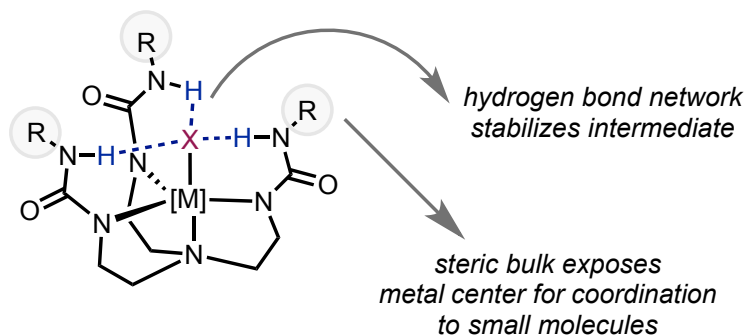
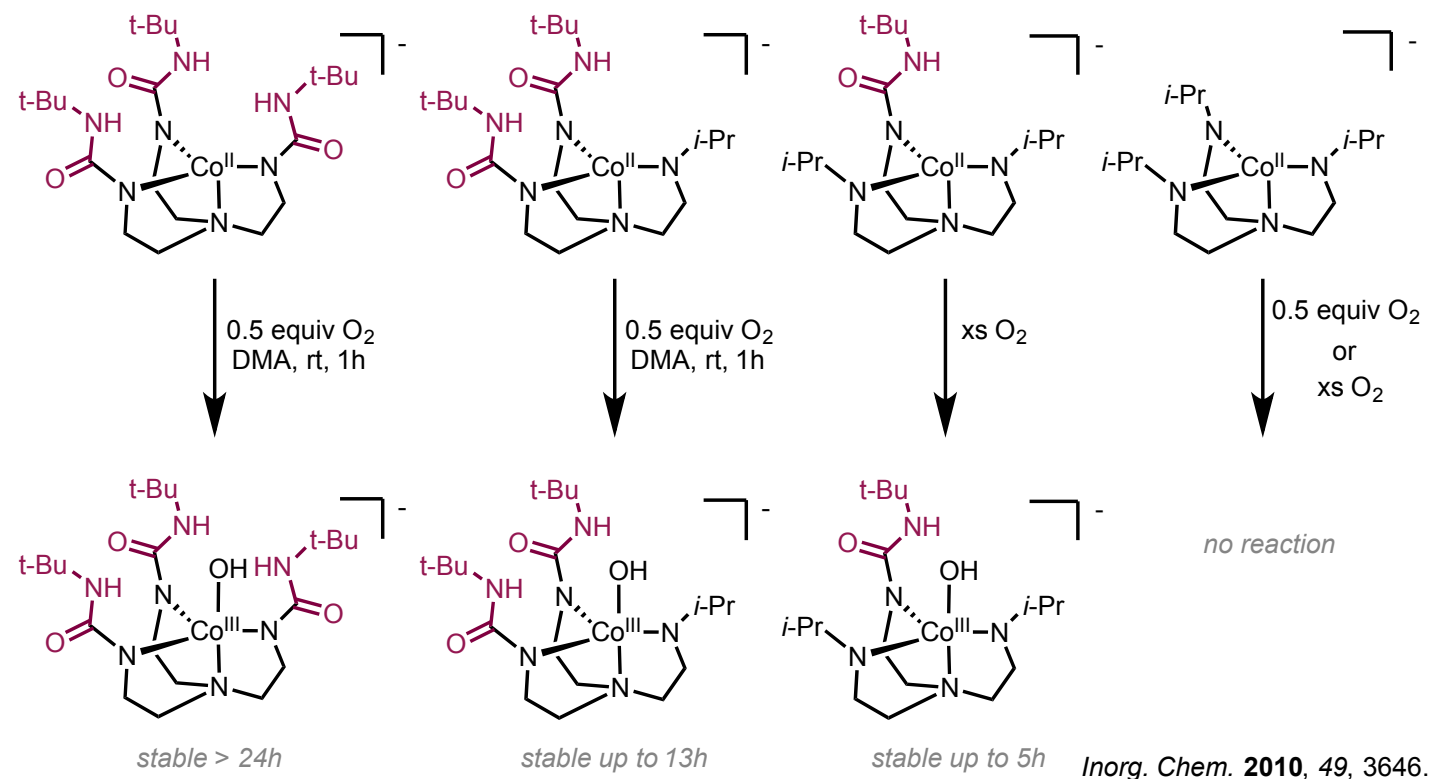
- Unique stability derived from significant hydrogen bond donor/acceptor potential – complex remains intact in presence of strong acids.
- Catalyst can be regenerated in many ways through a variety of redox manipulations and  $O_2$  can be reduced efficiently due to secondary sphere interactions.

*Inorg. Chem.* **2009**, 48, 10024.



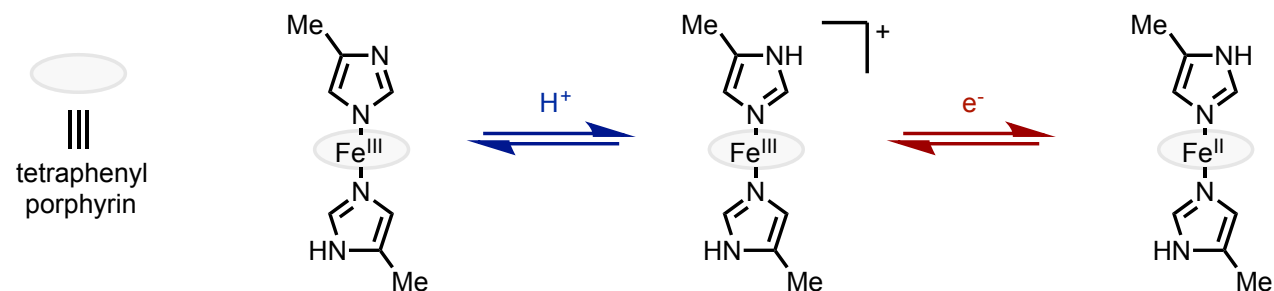
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- The stabilization effect of secondary-sphere hydrogen bond interactions in the context of oxygen reduction was qualitatively assessed in a series of cobalt oxo complexes.



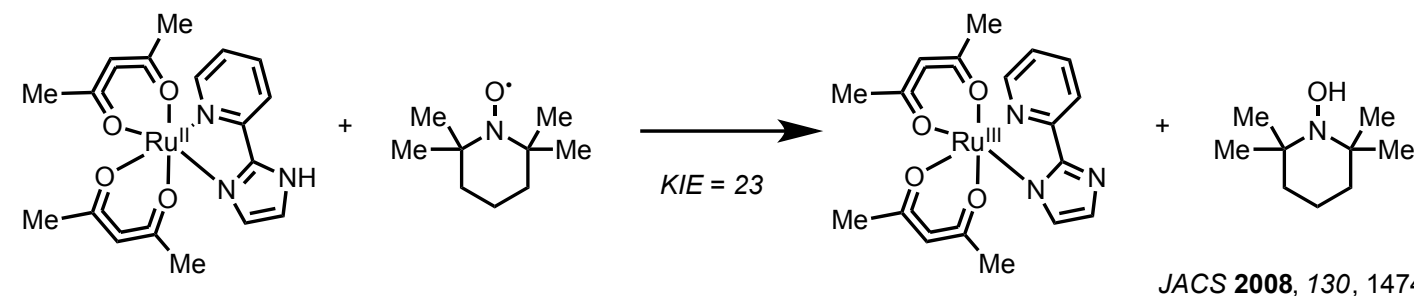
## e) Oxidation and Reduction of Metals

- In the context of small molecule activation, PCET is a powerful approach, but it can also be used to manipulate redox states of the metal complex itself in oxidation or reduction.
- This area is heavily mechanistic in nature and does not include many synthetic applications, but there could be space for developing robust redox cycling in an organometallic catalytic process.

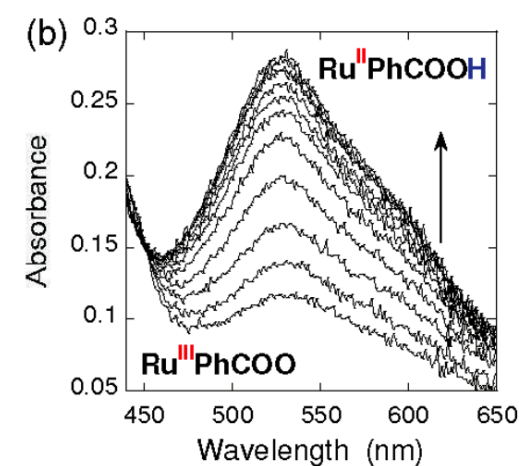
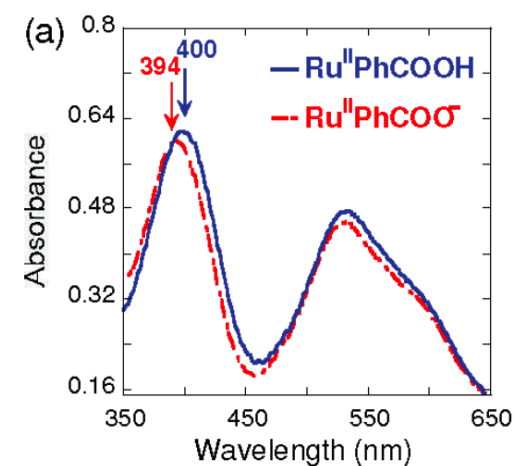
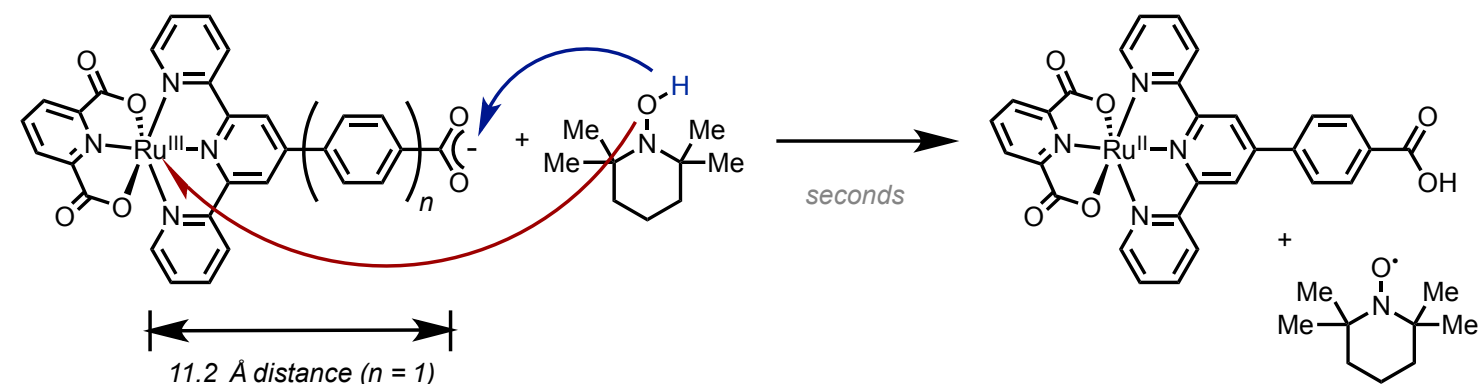


- This is another example of simple pH modularity in accessing various oxidation states of a metal species via PCET.

*JACS* **2008**, 130, 2774.



- Interesting mechanistic studies have been conducted regarding the effect of distance between electron and proton transfer sites in PCET systems.
- This line of inquiry has high impact on various subfields such as the understanding of complex biological systems (i.e. PSII or ribonucleotide reductases) and potential applications in charge injection semiconducting materials.



- Based on cyclic voltammetry measurements, the two species exhibit almost identical chemically reversible oxidations.
- Thermodynamic and spectroscopic measurements suggest that there is little to no interaction between redox and basic sites despite a CPET mechanism still being viable – reduction potentials of reactants can be used to calculate the energy barriers for PT and ET, thus ruling out a stepwise mechanism.

*JACS* **2009**, 131, 9874.

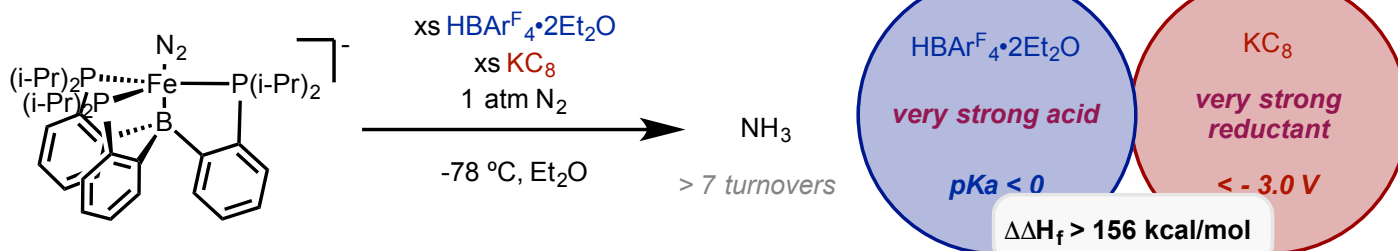
# Proton-Coupled Electron Transfer with Metal Complexes

## Applications of PCET in Other Processes

- Based on the operative mechanism of PCET, there are opportunities to discover new reactivity while also improving the energetic efficiency of existing processes.

### a) PCET as lower driving force for N<sub>2</sub> reduction

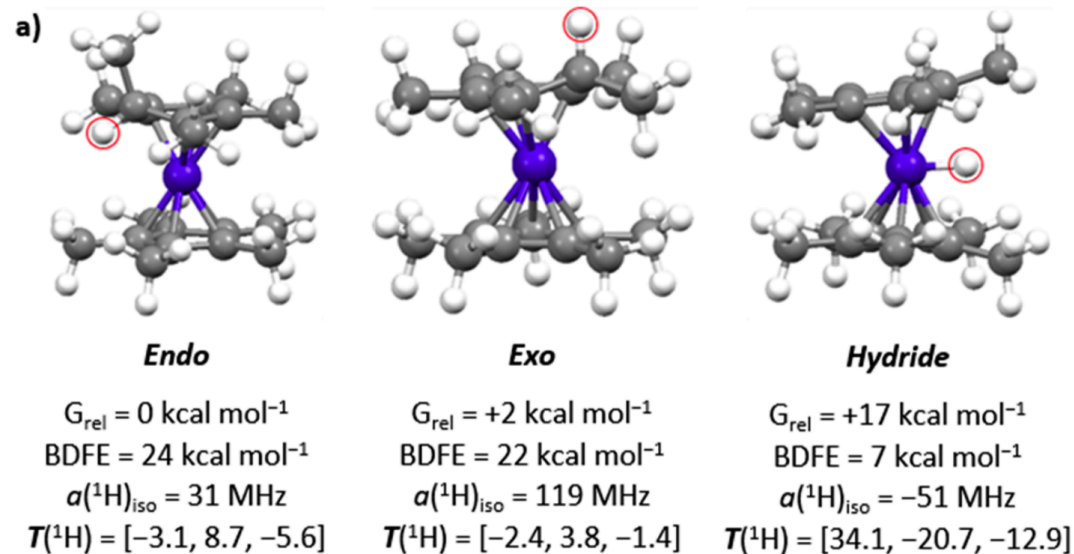
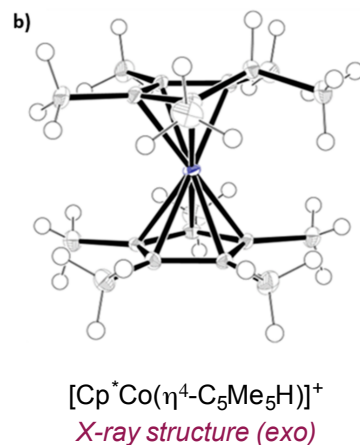
- Several groups have been interested in the catalytic reduction of  $N_2$  to  $NH_3$  using a combination of chemical oxidants and reductants



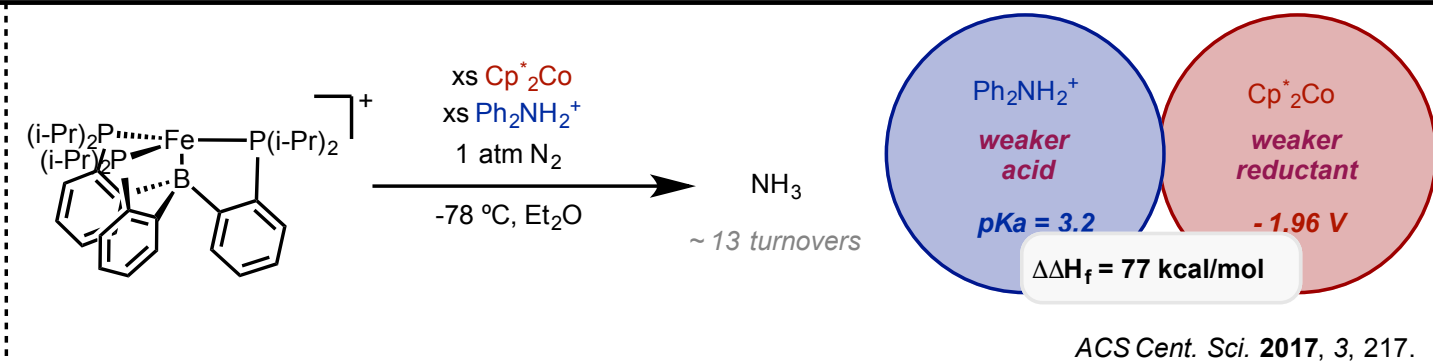
- Despite the elegance of achieving this process, the corresponding redox manifold is very harsh and has an extremely high enthalpic driving force.
- Peters and coworkers turned to the development of a novel PCET reagent for the direct reduction of  $\text{N}_2$  to  $\text{NH}_3$ .



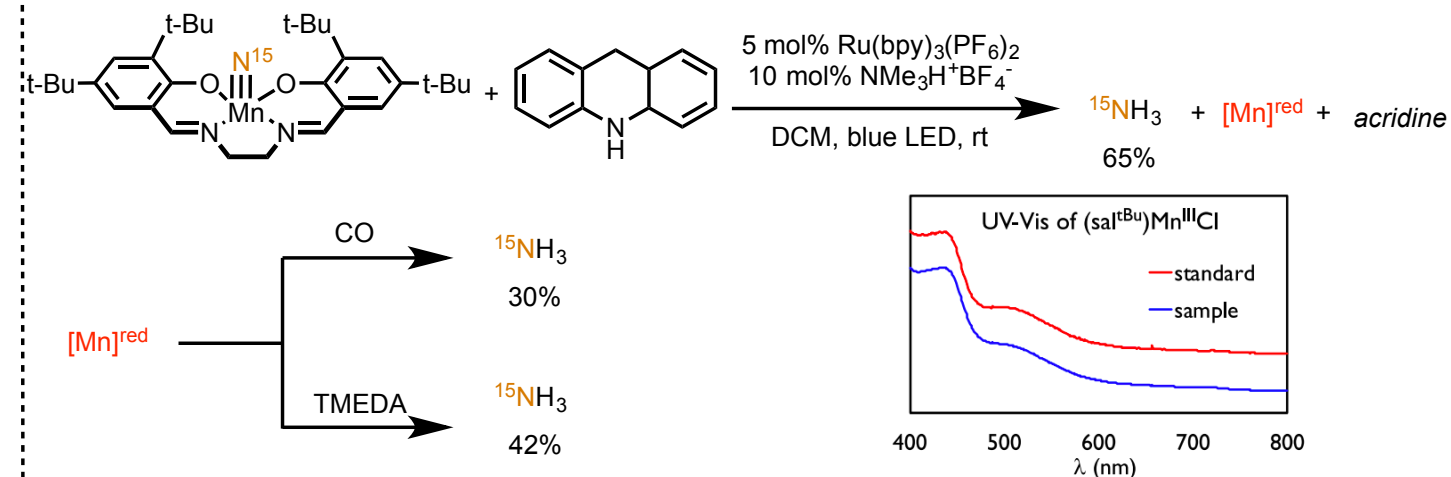
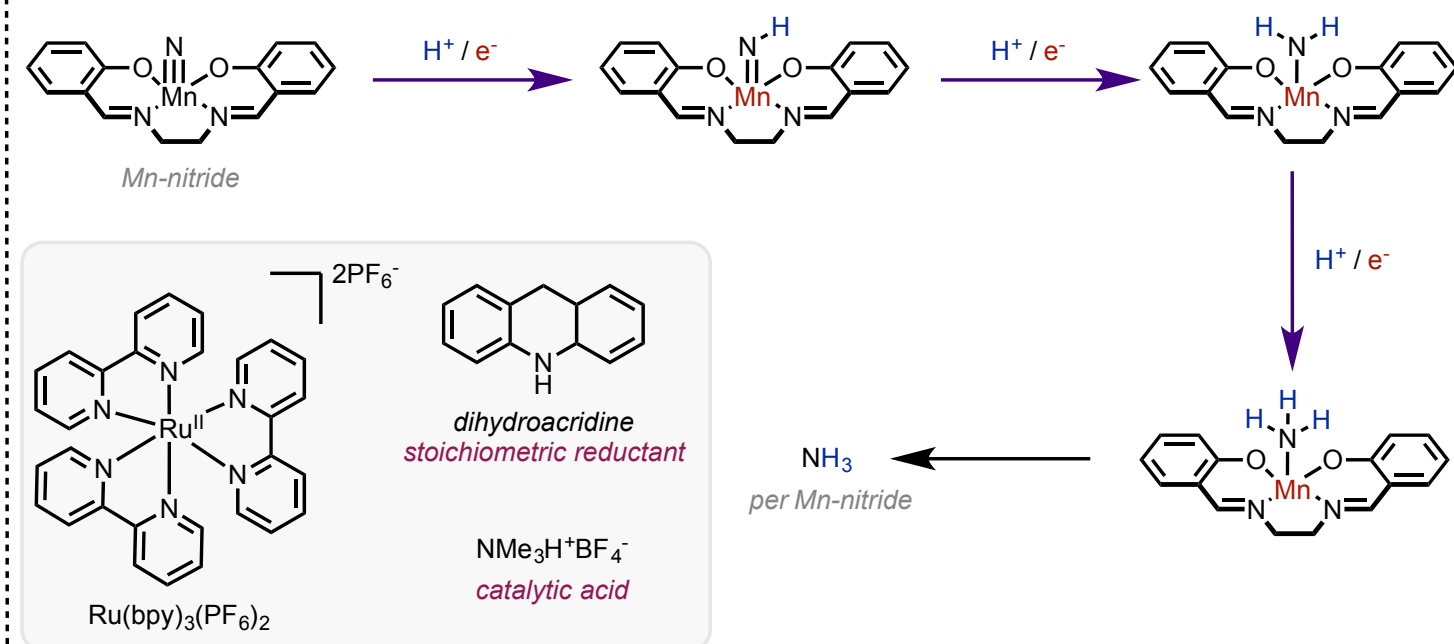
"H <sup>+</sup> "	$\Delta G_{\text{calc}}$
Ph <sub>2</sub> NH <sub>2</sub> <sup>+</sup>	-21 kcal/mol
PhNH <sub>3</sub> <sup>+</sup>	-13 kcal/mol



**JACS 2019, 141, 4721.**



- An alternative to PCET chemical redox is photochemical PCET, which will not be covered in detail in this review, but elegant work can be found in the following review: *Acc. Chem. Res.* **2016**, 49, 1546.



remaining mystery complex can still produce ammonia

**JACS 2019, 141, 4795.**

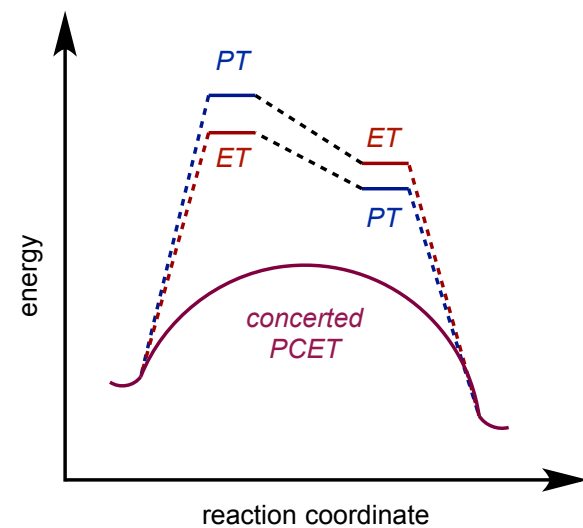
# Proton-Coupled Electron Transfer with Metal Complexes

## Summary of Key Concepts

General mechanism of PCET of metal complexes:

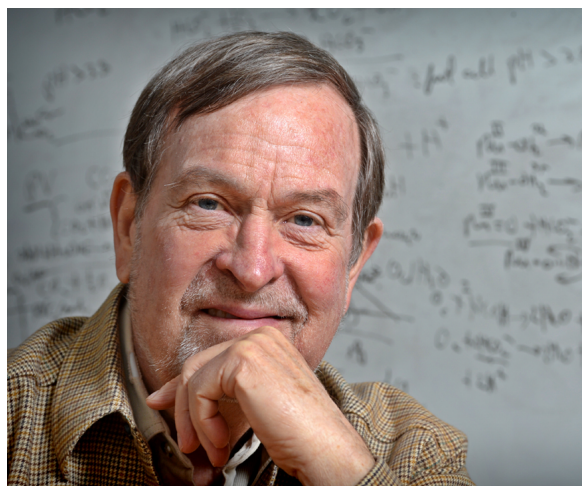


reaction mechanism can be modulated  
based on  $pK_a$ , ligand sphere (primary or secondary  
interactions), metal identity



concerted mechanism allows for milder  
reagents and effective, kinetically rapid  
redox events to occur

## Important Players in PCET Chemistry



Prof. Thomas J. Meyer



Prof. Jillian L. Dempsey



Prof. Daniel Nocera



Prof. Robert R. Knowles



Prof. James Mayer



Prof. Sharon Hammes-Schiffer