

# Enhanced Organocatalyzed Redox Processes for Sustainable Chemical Synthesis

Report for 2009

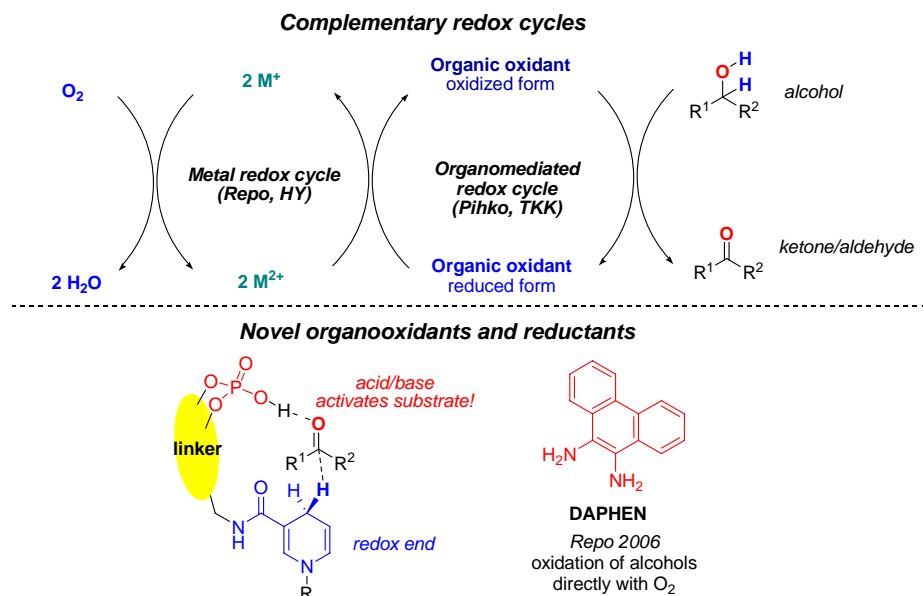
## Research team and Sites of Research:

Prof. Petri Pihko and Inkeri Majander, TKK, Laboratory of Organic Chemistry (until March 2008) /Dr Syam Krishnan, University of Jyväskylä (October 2008-December 2009, part-time)  
Prof. Timo Repo and Afnan Al-Hunaiti (full-time), University of Helsinki (HY), Department of Chemistry, Laboratory of Inorganic Chemistry

## Description of the project and goals

The chemical and the materials industry is facing several challenges in the society's drive towards a sustainable economy. One of the key challenges for the future is the effective utilization of readily available biomass-derived materials as raw materials. The main difficulty lies in the lack of suitable and sustainable methods for converting these highly oxygenated carbohydrate and ligninous materials into smaller, less functionalized but more valuable building blocks. Another, very serious challenge is to improve the poor energy and atom efficiency of a majority of chemical processes, especially in the pharmaceutical industry.

One of the sectors where green, sustainable methods are especially lacking are selective oxidation and reduction processes. At present, nearly all *selective* oxidations and reductions of organic and biomass-derived materials are performed by highly wasteful protocols, using large amounts of oxidants or reductants and generating equally large quantities of waste. The aim of this project is to develop **highly selective and recyclable organocatalytic redox catalysts that can be coupled with metal-based recycling methods, allowing oxidations with oxygen and reductions with hydrogen or alcohols**. We believe that our biosynthetically inspired organo/metal-catalyzed redox couple systems would be much more environmentally friendly and easier to adapt to the needs of the chemical industry than currently available solutions.

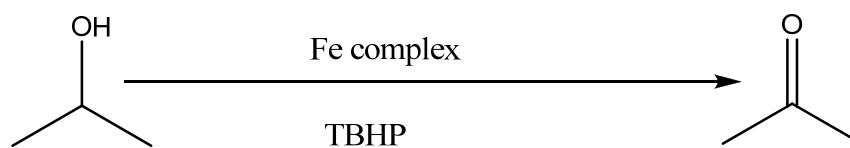


The project will pool the expertise of two research groups, both of them needed to accomplish the project target. The *Laboratory of Organic Chemistry (TKK -> JY)* will focus on development of organocatalytic redox mediators and *Laboratory of Inorganic Chemistry/ (HY)* is responsible for preparation of organometallic and inorganic complexes capable to regenerate organocatalytic species with molecular oxygen or hydrogen.

## Current status of research (Repo/HY)

During the reporting period we have identified a novel iron based oxidation catalyst which can be applied in the oxidation of primary and secondary alcohols (Scheme 1). In order to illustrate the oxidation potential of the catalytic system, catalytic activity with various alcohols have been studied. tert-Butyl hydrogen

peroxide (t-BHP) is used as an oxidant. As observed, the system is efficiently converting secondary alcohols to ketones and primary to corresponding acids.



**Scheme 1:** Selective oxidation of secondary alcohols using iron based catalyst occurs with high activity.

Research on organocatalytic redox-reaction has been also carried on. As for the oxidation of benzyl alcohols to carbonyl compounds alternatively metal-free oxidation, such as the Swern and Pfitzner-Moffat protocols, is based on, e.g. dimethylsulfoxide as oxidant in the presence of an activating reagent such as N,N-dicyclohexylcarbodiimide, an acid anhydride or acid halide. Although the latter methods avoid the use of heavy metals, they usually involve moisture-sensitive oxidants and environmentally undesirable reaction media, such as chlorinated solvents.

By using combinatorial chemistry as a tool in screening of novel organocatalysts in solvent free system new catalysts have been identified. From an environmental and cost-effective viewpoint, the discovered organocatalytic oxidation processes with benign oxidant such as O<sub>2</sub> and H<sub>2</sub>O<sub>2</sub> are extremely valuable and highly attractive.

Progress and future plans of the work:

- The research to find greener catalytic system for oxidation not only alcohols but also other functional group such as amines, sulphides and other challenging groups such as alkanes will be continued.
- The study of the reactions of benzyl alcohols oxidation using organocatalysis is almost completed. The manuscript is in preparation.
- The oxidation reaction of primary alcohols using iron metal complex is ready. The manuscript is in preparation.
- The electronic effect studies and reaction kinetics, mechanism and structure activity relationship will be further studied to obtain more detailed information about the nature of the rate-limiting step and to discover more active catalysts, this variation should provide evidence for whether an oxidation or the reduction step is rate-limiting. The mechanistic studies of new catalyst will be studied by using in situ FT-IR, ESI-MS and NMR methods.

### Current Status of Research (Pihko)

Since the research group moved to Jyväskylä in 2008, research has focused on Cu- and Ru-mediated oxidation catalysis. We have already established a Cu-catalyzed method for the oxidative coupling of indoles with β-keto esters (in collaboration with Tekes-funded project Enabling Synthesis Technologies). In addition, an aqueous method for enantioselective Ru-catalyzed transfer hydrogenation has been developed (in collaboration with PCAS Finland):

Evanno, L.; Ormala, J.; Pihko, P. M.\* 'A highly enantioselective access to tetrahydro-isoquinoline and β-carboline alkaloids with simple Noyori-type catalysts in aqueous media'. *Chem. Eur. J.* **2009**, 15, 12963-12967.

### Publications resulting from the project

1. Pihko, P. M.\*; Majander, I.; Erkkilä, A. 'Enamine Catalysis.' In: *Topics in Current Chemistry*, **2009**, 128, Chapter 21. DOI:10.1007/128\_2008\_21
2. Erkkilä, A.; Pihko, P. M.\*; Clarke, M.-R. 'Simple Primary Anilines as Organocatalysts for the Epoxidation of α-Substituted Acroleins.' *Adv. Synth. Catal.* **2007**, 349, 802-806.
3. Lahtinen, P.; Ahmad, J. U.; Lankinen, E. Pihko, P. M.; Leskelä, M.; Repo, T. 'Organocatalyzed Oxidation of Alcohols with Molecular Oxygen.' *J. Mol. Cat. A* **2007**, 275, 228-232.
4. Erkkilä, A.; Majander, I.; Pihko, P. M.\* 'Iminium Catalysis.' *Chem. Rev.* **2007**, 107, 5416-5470.

In addition, the following publications were generated in collaboration with this project on the subject of hydrogen activation:

5. Victor Sumerin, Felix Schulz, Michiko Atsumi, Cong Wang, Martin Nieger, Markku Leskelä, Timo Repo, Pekka Pyykkö and Bernhard Rieger, 'Molecular Tweezers for Hydrogen: Synthesis, Characterization, and Reactivity' *J. Am. Chem. Soc.*, **2008**, *130*, 14117–14119.

6. Sumerin, V., Schulz, F., Nieger, M., Leskelä, M., Repo, T., and Rieger, B. *Angew. Chem., Int. Ed.* **2008**, *47*, 6001-6003. This article was also highlighted in the Cover of the *Angewandte Chemie*.