

“Green” Catalytic Systems for Solvent-Free Alcohol Oxidations

Background

Catalysts for organic chemical transformations, in particular those used for alcohol oxidations, are considered to be valuable commodities for the bulk, fine chemical as well as pharmaceutical industries as they are utilized in some of the most vital reactions that yield aldehydes and ketones. These products in turn are often useful as intermediates for other synthetic targets of economic significance. The majority of oxidation methodologies currently in use rely on catalysts containing expensive precious metals, require harmful and toxic oxidants, and involve the use of organic solvents. As such there is a growing demand for the development of ‘green’ catalytic methods that function in conjunction with environmentally benign oxidants and cost effective, easy to use catalysts that function either under solvent free conditions or in aqueous solution. In addition, the ability to produce desired products from a wide variety of substrates with good catalytic performance is also highly desired.

Technology

Research from the University of Wisconsin-La Crosse has led to the discovery and development of a novel suite of catalytic systems for industrially-relevant green oxidations including the oxidative conversion of primary and secondary alcohols to value-added aldehydes and ketones. Similar systems have been developed for the oxidation of olefins to produce important epoxides, and for the oxidation of alkanes to produce alcohols.

Specifically the team has developed a series of iron-based catalysts known as ‘helmet’ phthalocyaninato complexes of iron(III). Preliminary studies have focused on a formulation commonly known as the ‘diiPc’ iron(III) system. Notably, the team has shown that this system is capable of catalytically oxidizing a diverse array of substrates including five non-benzylic alcohols (1-pentanol, 2-pentanol and cyclohexanol as well as 2,4-dimethyl-3-pentanol and 5-hydroxymethylfurfural) in the absence of added organic solvent. The presence of water as the monodentate axial ligand in the diiPc complex allows for markedly increased solubility in non-aromatic alcohols, making it an ideal catalyst for use with a much wider and more diverse range of substrates under solvent free conditions. It is envisaged that modification of the diiPc and related ligands will be undertaken to impart further enhancements to catalyst solubility in substrates or water, and/or superior stability in substrate alcohols.

In addition to the diiPc system, the team have also developed a means of forming derivatized catalysts utilizing what is commonly referred to as a “helmet naphthalocyaninato” iron(III) complex. Specifically, a sulfonated version has been produced that possesses excellent solubility in water due to the added hydrophilic groups. To date, the sulfonated helmet naphthalocyaninato complex has been shown to provide for efficient formation of acetone from isopropanol as well as conversion of 2-pentanol to 2-pentanone using hydrogen peroxide as the primary oxidant. As such we anticipate that the same system would also be effective in the oxidation of 2-butanol to produce methyl ethyl ketone (MEK), an important commodity scale industrial chemical, and in many other commercially important transformations. Furthermore, preliminary studies have shown this molecule can be immobilized on various solid supports including anion-exchange resins, thereby resulting in a heterogeneous catalyst that can be utilized in the development of catalytic transformations that occur under flow conditions. Additionally, we now know that the sulfonated catalyst efficiently catalyzes the oxidation of phenol with hydrogen peroxide to produce para-benzoquinone. This transformation, along with other related reactions, is very important in the treatment of wastewater.

Research and Development Status and Commercialization Needs

A suite of novel catalysts and associated techniques have been developed and characterized with reactions validated for a diverse array of substrates using batch methodology. Further work is currently being undertaken to develop a flow

reactor system that could be scaled up for industrial/commercial applications. In addition, it is anticipated that further derivatization can be undertaken to yield more efficient catalysts. WiSys is currently seeking a strategic partner interested in providing a route to market for the commercialization and wide dissemination of its novel catalyst systems.

Applications and Key Benefits

- Iron based catalyst, hence cost competitive to those containing precious metals;
- Catalyst systems exhibit strong performance and versatility under environmentally benign 'solvent free' reaction conditions, further reducing costs and environmental impact;
- Select derivatives are soluble in water thereby providing for an aqueous phase catalytic system;
- Catalysts are capable of promoting a diverse array of alcohol oxidations producing ketones and aldehydes that can be used to produce pharmaceuticals, fine chemicals, pigments, disinfectants and more;
- Primary catalyst shows high selectivity and efficiency, and reactions proceed with high turnover numbers (TON) and turnover frequency (TOF) relative to related catalytic systems.
- Selectivity for the expected aldehyde and ketone products is excellent with no observable over-oxidation to carboxylic acids, thereby demonstrating excellent chemoselectivity.

Intellectual Property

A U.S. Patent Application (US10065980) has been allowed for this technology. A further patent application is pending for applications outside of alcohol oxidation. For more information, please contact WiSys at licensing@wisys.org.

Publications

Peterson, B.M., Herried, M.E., Neve, R.L. and McGaff, R.W., 2014. Oxidation of primary and secondary benzylic alcohols with hydrogen peroxide and tert-butyl hydroperoxide catalyzed by a "helmet" phthalocyaninato iron complex in the absence of added organic solvent. *Dalton Transactions*, 43(48), pp.17899-17903.

Robinson, J.R., Bahr, K.A., Bierman, M.J., Guzei, I.A., Kieler-Ferguson, H.M., McCoy, A.M. and McGaff, R.W., 2011. Resolution of enantiomers of a series of chiral alkoxy-modified phthalocyaninato nickel (ii) complexes by enantioselective HPLC. *Dalton Transactions*, 40(44), pp.11809-11814.

Brown, E.S., Robinson, J.R., McCoy, A.M. and McGaff, R.W., 2011. Efficient catalytic cycloalkane oxidation employing a "helmet" phthalocyaninato iron (III) complex. *Dalton Transactions*, 40(22), pp.5921-5925.

Supplemental Information

In addition to alcohol oxidations, the above novel catalysts have recently been shown to have utility in the catalytic oxidation of sulfur-containing compounds using hydrogen peroxide or ambient air as the primary oxidant at room temperature.

Preliminary data generated via a recently funded WiSys Innovation Grant has demonstrated proof of concept with two sulfur-containing substrates, 2-mercaptoethanol (1) and dibenzothiophene (2) to produce 2-hydroxyethyl disulfide (3) and dibenzothiophene 5,5-dioxide (4), respectively, as the sole final products.

Briefly, and in regard to reaction 1 (Figure 1 below), the reaction has been catalyzed in a solution of ethanol/water at room temperature using WiSys' novel catalysts. The reaction shows complete conversion to the product shown below with both hydrogen peroxide and ambient air as the oxidant. In addition, the team have also validated air oxidation employing a supported catalyst.

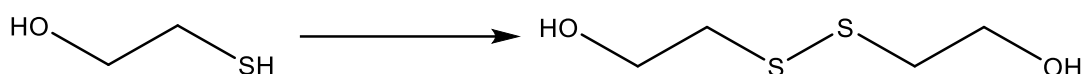


Figure 1. Reaction 1 - Oxidation of 2-mercaptoethanol

Catalysts have also demonstrated utility in a second reaction shown in Figure 2 using an acetonitrile, dichloromethane solution with hydrogen peroxide as the oxidant. Once again, complete conversion in as little as 30 minutes at room temperature was observed with turnover numbers up to 700 overnight. Preliminary data does not support use of ambient air, however, it is anticipated that pure O₂ may provide optimized results.

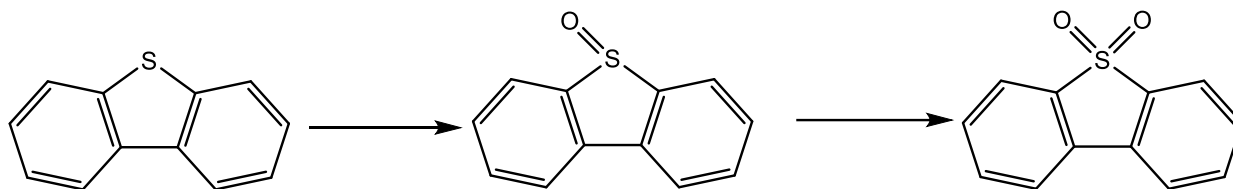


Figure 2. Reaction 2 – Oxidation of dibenzothiophene

Further studies are proposed to optimize performance of the catalysts in the above referenced transformations as well as to generalize these reactions by demonstrating oxidation of additional related sulfur-containing substrates. Further work is also proposed around heterogeneous reactions and investigations of other solid support systems.

The above data provides direct evidence that WiSys' novel catalysts have potential to provide an effective means for the removal of undesirable sulfur-containing compounds from crude oil, natural gas, and/or aqueous waste streams, and to do so without the need for elevated temperatures, pure oxygen, or high pressures. The team anticipates that in some cases only ambient air will be required for the catalytic transformation of undesirable chemical species.