

# **Copper di-imine complexes: Structures and catalytic activity in the oxidation of alcohols by dioxygen**

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**Academic Dissertation**

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## Abstract

Selective oxidation is one of the most important reactions in organic chemistry. Development of highly active catalysts instead of stoichiometric oxidants together with environmentally friendly oxidants such as molecular oxygen would provide means for greener processes and enhanced economics. In addition, water as a non-poisonous and easily available solvent could provide additional ecological safety. An excellent example of a large scale industry that would benefit from such development is the pulp and paper industry, where replacing the chlorine containing oxidising agents with oxygen activating catalyst would be highly preferable.

With a parallel screening method developed during this thesis, over 200 metal-ligand combinations were studied in the oxidation of the lignin model compound veratryl alcohol. In addition to catalyst screening, this simple and inexpensive system could also be used for the optimisation of the catalyst activity and for studying the catalytically active species and reaction mechanisms. In the screening of catalyst candidates copper compounds with nitrogen coordinating ligands such as 2,2'-bipyridine, 1,10-phenanthroline, dimethylglyoxime, pyridine-2-carboxaldoxime, *N,N,N',N'*-tetramethyl ethylenediamine, 1,2-diaminocyclohexane and 9,10-diaminophenanthrene turned out active oxidation catalysts under alkaline aqueous conditions. To test the final purpose of these catalysts, the most active complexes (copper with 2,2'-bipyridine and 1,10-phenanthroline) were studied in pulp delignification. The catalysts increased the delignification reactions but also caused depolymerisation of cellulose.

*In situ* complexation of the catalysts in parallel study makes the reaction solution a sort of mystery. UV-Vis spectroscopy turned out to be highly useful for solving the catalyst structure in the solution under different conditions. For more detailed information of the copper coordination sphere, solid state structures of crystallised complexes were determined by X-ray diffraction. To monitor the oxidation reaction of veratryl alcohol, techniques such as UV-Vis and ATR-IR spectroscopy, GC-analysis and pH measurements were applied. With these measurements the structures of the active catalysts was determined and the main steps of the reaction mechanism could be elucidated.

## Preface

This work was done in the Laboratory of Inorganic Chemistry at the University of Helsinki between 2000 and 2004 as a part of the project “Catalytic bleaching of pulp” (SEKAVA). Financial support from the National Technology Agency of Finland (Tekes), M-real Oyj, UPM-Kymmene Oyj, Stora Enso Oyj, Andritz Oy and Kemira Oyj is gratefully acknowledged. Grants from the Association of Finnish Chemical Societies and Tekniikan edistämissäätiö (Foundation for Advancing Technology) are also gratefully acknowledged.

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My warmest thanks belong to my friends and colleagues in our research group. You made the laboratory more than just a work place. Special thanks go to Mika and Markku for guiding my first steps in the research work. I want to thank Mika also for carrying out the crystallographic measurements used in this work.

I would like to thank my parents for their support (also financial) during my student years. My brother is greatly acknowledged for strengthening both my physical and mental welfare. Finally, I wish to thank you Maria, for your love and being there for me.

Helsinki, September 2005

Heikki Korpi

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## List of Original Publications

This thesis is based on the following publications (**I-V**), where the experimental details can be found. The publications are referred to in the text by their Roman numerals.

- I** H. Korpi, P. Lahtinen, V. Sippola, O. Krause, M. Leskelä and T. Repo:  
An efficient method to investigate metal-ligand combinations for oxygen bleaching. *Appl. Catal.* **2004**, 268, 199-206.
- II** P. Lahtinen, H. Korpi, E. Haavisto, M. Leskelä and T. Repo:  
Parallel Screening of Homogenous Copper Catalysts for the Oxidation of Benzylic Alcohols with Molecular Oxygen in Aqueous Solutions. *J. Comb. Chem.* **2004**, 6, 967-973.
- III** H. Korpi, K. Kervinen, E. Lankinen, M. Leskelä and T. Repo:  
On in situ made Cu-phenanthroline complexes in aqueous alkaline solutions and in catalytic oxidation of veratryl alcohol, **2005**, submitted for publication.
- IV** H. Korpi, M. Polamo, M. Leskelä, T. Repo:  
Bis(pyridine-2-carboxaldehyde oxime)copper(II) sulphate as catalyst precursor in the oxidation of veratryl alcohol by dioxygen, **2005**, *Inorganic Chemistry Communications*, in press.
- V** H. Korpi, V. Sippola, I. Filpponen, J. Sipilä, O. Krause, M. Leskelä, T. Repo:  
Copper-2,2'-bipyridines: catalytic performance and structures in aqueous alkaline solutions. **2005**, submitted for publication.

## Abbreviations

ABTS	2,2'-azino-bis(3-ethylbenzthiazoline-6-sulfonic acid)
Ac	acetate
Ar	aryl
bipy	2,2'-bipyridine
dMebipy	4,4'-dimethyl-2,2'-bipyridine
DACH	1,2-diaminocyclohexane
DAPHEN	9,10-diaminophenanthrene
DBAD	di- <i>tert</i> -butyl azodicarboxylate
DEAD	diethyl azo-dicarboxylate
DMG	dimethylglyoxime (butane-2,3-dione dioxime)
dOHbipy	4,4'-dihydroxy-2,2'-bipyridine
dOMebipy	4,4'-dimethoxy-2,2'-bipyridine
EtOAc	ethylacetate
GC	gas chromatography
GO	galactose oxidase
HBT	1-hydroxybenzotriazole
HPA-5	heptamolybdopentavanadophosphate anion
HPI	N-hydroxyphthalimide
L	ligand (here usually diimine compound)
M	metal (here usually copper)
Me	methyl
MS	mass spectrometry
NHA	N-hydroxyacetanilide
NMI	N-methylimidazole
OMe	methoxy
PAO	pyridine-2-carboxaldehyde oxime
POM	polyoxometalate
phen	1,10-phenanthroline
py	pyridine
salen	N,N'-bis(salicylidene)ethylenediamine
<i>t</i> -Bu	<i>tert</i> -butyl
TEMPO	2,2,6,6-tetramethylpiperidin-1-oxyl
TMED	N,N,N',N'-tetramethyl ethylenediamine
TOF	turnover frequency, mole of oxidised product/mole of catalyst/h
TON	turnover number, mole of oxidised product/mole of catalyst
VLA	violuric acid

## 1 Introduction

Selective oxidation is of importance in the production of fuels and organic reagents, bleaching of pulp or textiles, raw material industry and environmental catalysis. Traditional oxidation of organic compounds involves the use of stoichiometric amounts of environmentally non-friendly inorganic compounds of chromium, cobalt and manganese. These reactions create high amounts metal waste and reactions are often carried out in halogenated organic solvents, which are environmentally undesirable. When developing new catalytic applications the use of aqueous solutions and molecular oxygen which is cheap, easily available and an environmentally friendly oxidant would be highly beneficial.<sup>1</sup> In addition, the use of water and dioxygen in large scale production would show significant progress towards “greener” chemistry.<sup>2</sup>

For activating dioxygen, copper based enzymes and metalloproteins are an excellent working models.<sup>3</sup> In enzymes such as laccase, galactose oxidase (GO), cytochrome c oxidase and superoxide dismutase, a copper atom activates molecular oxygen for a variety of reactions. For example, galactose oxidase catalyses the aerobic oxidation of primary alcohols to aldehydes. This kind of selective oxidation under mild reaction conditions is one of the most important reactions in the synthesis of fine chemicals as well as in the chemical industry. In order to understand these reactions, electron transfer<sup>4</sup> and dioxygen activation<sup>5, 6</sup> by copper complexes have been widely studied, and various organometallic compounds have been synthesised to mimic the structures of oxygen activating compounds found in nature.

The manufacture of pulp and paper is another example of a large-scale industry where efficient use of molecular oxygen would be highly beneficial. For example during 2003 over 7 million tons of chemical and about 4.6 million tons of mechanical pulp was produced in Finland (being 31% of the pulp production in Western Europe).<sup>7</sup> Although chlorine dioxide is a very efficient oxidation agent, its use in the pulp bleaching sequence should be decreased because of the noxious chlorine-containing compounds formed during bleaching. Processes based on successive oxygen and peroxide stages are already being used, but they are often compromised between yield and pulp quality. Enhancement of the delignification through the catalytic activation of molecular oxygen is an important option for the development of efficient and sustainable processes and appropriate catalysts have been under intensive study for the past decades.<sup>8</sup>

## 2 The Scope of the Thesis

The aim of the project “Catalytic bleaching of pulp”, which this thesis work was part of, was “increasing the lignin removal by catalysing the oxygen delignification”. In order to achieve this aim with the resources of our laboratories, an efficient catalyst development was set as a secondary aim. Due to screening nature of the applied methods, also the understanding of the active catalyst structures and catalytic reactions turned out to be considerably important for developing new highly active catalysts.

In chemical pulp bleaching, lignin is usually transformed to more soluble fragments by the oxidation of phenolic, alcoholic and unsaturated lignin substructures. To model the delignification reactions, work for this thesis was focused on the oxidation of veratryl alcohol, which is known as a model for lignin substructure. The first catalysts studied for this purpose were Co(salen) complexes<sup>9</sup> which are known to be able to activate dioxygen. However, the search for new catalysts by traditional methods through ligand synthesis, complexation, analysis and finally oxidation experiments turned out to be laborious and often of uncertain outcome. To enhance the catalyst research, a simple and efficient parallel screening method for studying active metal-ligand combinations was developed (publications **I** and **II**). By combining this method with selectivity testing (developed in our co-operation laboratory at Helsinki University of Technology) an extensive evaluation of the delignification capability of the catalysts was achieved with laboratory scale experiments.

The effect of different catalyst structures on the oxidation activity (publications **IV** and **V**) as well as the reaction mechanism itself (publication **III**) were under active investigation. In addition to the methodical development work undertaken during the project, the understanding of the catalyst structures and the oxidation reaction was increased by means of various complementary techniques for reaction analysis.

## 3 Background

### 3.1 Oxygen

Oxygen is the most abundant element in the Earth’s crust. Molecular oxygen, O<sub>2</sub>, is the result of continuous photosynthesis and fills about 21% of the atmosphere.<sup>10</sup> The electronic structure of oxygen atom is  $1s^2 2s^2 2p^4$ , which in oxygen molecule gives electronic structure with two unpaired electrons in the ground state (triplet state). Oxygen has the second

highest electronegativity of all the elements and it is a very strong oxidiser. However, the reaction of triplet state oxygen and singlet state organic molecule is usually favored thermodynamically but it is spin-forbidden and it has a very slow reaction rate.<sup>11</sup> This is also a reason for the stability between organic molecules in nature and oxygen in the atmosphere.

Exciting dioxygen to its singlet state increases its reactivity. Complete reduction of dioxygen is a four electron process, where two water molecules are formed. However, the reaction proceeds usually by one and two electron steps rather than by single four electron transfers.<sup>12</sup> Usual reactions between O<sub>2</sub> and metal complexes proceed irreversibly by cleavage of oxygen-oxygen bond producing oxides, hydroxides or water. With appropriate ligand configuration the reversible binding of dioxygen with transition metal complexes is also possible.<sup>13</sup>

## 3.2 Copper

Copper on its oxidation state I has a  $d^{10}$  electron configuration. In aqueous solutions, only a low concentration of Cu(I) ions can exist, as they are easily oxidised to Cu(II). When complexed with chelating ligands, a favourable geometry around the copper atom can stabilise the complex considerably. The most common coordination geometries of Cu(I) complexes are four-coordinated tetrahedral or trigonal-pyramidal but also three- and two-coordinated complexes have been reported. Five coordinated Cu(I) structures are rare and have at least one significantly elongated Cu-ligand bond.<sup>5, 14</sup>

Most of the copper(II) compounds dissolve in water and form an aqua complex  $[\text{Cu}(\text{H}_2\text{O})_6]^{2+}$ . Addition of coordinating ligands to such aqueous solution leads to the formation of complexes by successive displacement of water molecules. In copper(II) complexes the  $d^9$  configuration makes the structure subject to distortions in octahedral and tetrahedral symmetries (Jahn-Teller effect). The distortion is usually seen as axial elongation, consistent with the lability and geometric flexibility of the complex. Therefore, typical Cu(II) complexes have square-planar or squarepyramidal geometries with ligands weakly associated in the axial position(s). Trigonal-bipyramidal coordinations in Cu(II) complexes have also been determined. In some cases also bridged compounds in which two or more Cu(II) ions are linked by hydroxo or other anionic ligands are formed.<sup>5, 14</sup>

Copper(III) complexes are rare. Most simple compounds of Cu(III) are alkaline and alkaline earth mixed oxides, but coordination complexes with macrocyclic nitrogen coordinating ligands have also been reported.<sup>15</sup> Typically, coordination geometry of copper(III) complexes is square planar and they are usually stabilised by strongly basic anionic ligands.<sup>5, 16</sup>

### 3.3 Copper-oxygen species

Differences in the coordination modes between metal and molecular oxygen are due to the electron configuration and electron donation properties of the metal. These properties can be tuned by the structure, number and geometric arrangement of organic ligands around the metal centre. Generally one-electron donating metals react with dioxygen to form end-on coordination in molar ratios of 1:1 or 1:2 while two electron donors form complexes with side-on coordination. However, the electron transfer from metal to oxygen is generally incomplete for reversible oxygen carriers, so the electron count is more or less an approximation.<sup>12</sup> Copper-dioxygen bonding studies have usually been conducted on enzyme mimicking compounds with nitrogen coordinating ligands. Various Cu:O<sub>2</sub> intermediates have been characterised at low temperatures by spectroscopic and crystallographic methods (Figure 1).<sup>5, 6, 17</sup> The coordination modes of Cu:O<sub>2</sub> species can be classified on the basis of copper:dioxygen molar ratios into 1:1, 2:1, 3:1 and 4:1 cores.<sup>18</sup>

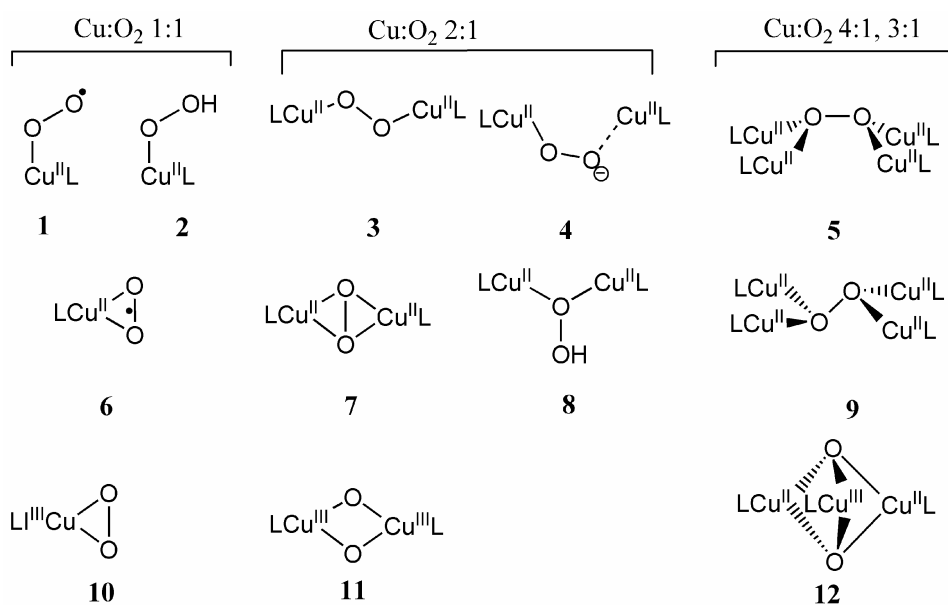


Figure 1. Different copper-oxygen coordination modes for Cu:O<sub>2</sub> species<sup>5</sup>. Complexes with (2)  $\eta^1$ -hydroperoxo<sup>19</sup>, (3) *trans*- $\mu$ -1,2-peroxo<sup>20</sup>, (5) *cis*-<sup>21, 22</sup> and (9) *trans*- $\mu_4$ - $\eta^2$ : $\eta^2$ -peroxo<sup>23</sup>, (6)  $\eta^2$ -superoxo<sup>24</sup>, (7)  $\mu$ - $\eta^2$ : $\eta^2$ -peroxo<sup>25, 26</sup>, (10)  $\eta^2$ -superoxo<sup>27</sup>, (11) bis( $\mu$ -oxo)<sup>28, 29</sup> and (12) bis( $\mu_3$ -oxo)<sup>30</sup> coordination have been crystallographically characterised.

### 3.4 Combinatorial Chemistry

Combinatorial methods have been developed to enhance organic synthesis for medical and biochemical applications.<sup>31</sup> The new methods gave the possibility to prepare simultaneously libraries of compounds instead of laborious synthesis targeting to prepare

one single molecule. Some examples of peptide libraries were reported in the 1980's, but in the 1990's the combinatorial methods became a more general tool for scientific research. During the last fifteen years, combinatorial technology has emerged from the product synthesis and drug discovery to agricultural chemistry, chemical biology, catalyst discovery and material science.<sup>32</sup>

The screening methods can be categorised into two classes. In the pool-split method every component in the library is combined together giving a very high-throughput of hundreds or thousands of experiments per day. However, effective analysis methods are also required.<sup>33</sup> In parallel screening, a set of discrete compounds are prepared simultaneously in arrays of physically separate reaction vessels.<sup>34</sup> This method gives medium to high throughput and analysis of the results is easier than for the pool-split method. Combinatorial study can also be divided into two working phases. Primary screening is designed for rapid evaluation of various combinations to find the positive leads/hits and to extend the library around these leads. In secondary screening the reaction for the hits is optimised and products are synthesised in sufficient quantities for detailed characterisation and evaluation.

In a search for new catalysts, the primary screening can be conducted as a search of large numbers of possible metal-ligand combinations. In the secondary screening the lead combinations can be further probed with different composition ratios or structural changes, and finally the most active catalysts are synthesised for more detailed study. In the search for homogenous catalysts by combinatorial methods, certain features should be noticed. First, the number of chosen ligands should be large enough to cover both electronic and structural variations. Second, suitable techniques and equipment for rapid screening should be available (catalyst preparation, reactor, reaction conditions, equipment for chemical analysis, etc.). Furthermore, sophisticated software to aid experimental design, screening, and the analysis of data is highly preferable.<sup>35</sup> The efficiency of these techniques in catalyst research has been widely acknowledged and numerous publications<sup>36</sup> and review<sup>37</sup> articles have been published.

### **3.5 Catalytic oxidation of alcohols with copper catalysts**

Selective oxidation of alcohols to carbonyl compounds is one of the most important reactions in organic chemistry.<sup>38</sup> Many of the transition metal catalysed oxidation reactions are troubled by the instability of the catalyst towards the water formed in the reaction or even as a solvent, and by the formation of hazardous mixture from oxygen and flammable solvents at high temperatures and pressures. In addition, the catalyst preparation is usually a result of tedious and expensive synthesis and sometimes the hard reaction conditions are fatal to catalyst stability. In nature, copper enzymes are known to activate dioxygen under

mild reaction conditions and in aqueous solutions. However, only a limited number of copper catalysed oxidation reactions of alcohols by dioxygen have been reported.

### 3.5.1 Copper-diimine catalysts

Copper-phenanthroline complexes were first time observed to react with methanol as early as 1966.<sup>39</sup> Ever since copper complexes of 1,10-phenanthroline (phen) and 2,2'-bipyridine (bipy) have been studied as catalysts in the oxidation of different alcohols.<sup>40</sup> In most of the studies, the catalyst is made by *in situ* addition of copper compound and ligand to the reaction solution. This type of catalyst synthesis raises questions about the structure of the active catalyst, because depending on the reaction conditions, the structure of the catalyst can change markedly. Garribba and co-workers recently reported how different species from copper(II) and bipyridine are formed by changing pH and L:Cu molar ratios.<sup>41</sup> The main species in aqueous solution were shown to be  $[\text{Cu}(\text{bipy})]^{2+}$ ,  $[\text{Cu}(\text{bipy})\text{OH}]^+$ ,  $[\text{Cu}(\text{bipy})(\text{OH})_2]$ ,  $[\text{Cu}(\text{bipy})_2]^{2+}$ ,  $[\text{Cu}(\text{bipy})_3]^{2+}$  and  $[\text{Cu}(\text{bipy})\text{OH}]_2^{2+}$ . In accordance with this, various structures for catalytically active Cu(I) and Cu(II) species have been reported (Figure 2). The first four (13<sup>42</sup>, 14<sup>43</sup>, 15<sup>44</sup>, 16<sup>45, 46</sup>) complexes have been presented as active species in alcohol oxidation reactions, while species 17<sup>47</sup> and 18<sup>48</sup> have been found in dioxygen activation experiments (these species also oxidised benzyl alcohol).

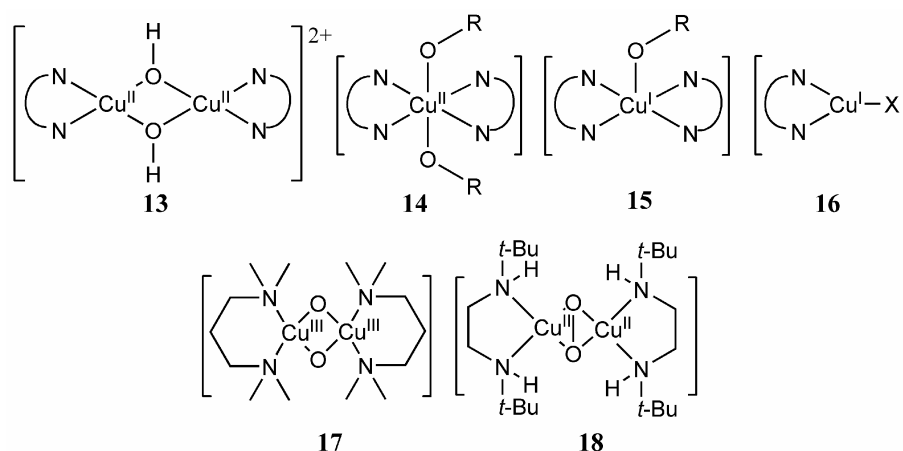


Figure 2. Structures of different active species in copper-diimine and -diamine catalysts, O-R = (benzyl)alcohol, X = Cl, OH.

Jallabert *et al.*<sup>42</sup> have studied Cu-phen catalyst in benzene solution and an almost equivalent amount of catalyst to alcohol. When the solvent was changed to toluene or acetonitrile, higher activities were achieved. Cu-diimine catalysed oxidation reactions have usually been done on benzylic alcohols, because the enhanced lability of  $\alpha$ -hydrogen atoms in these substrates increases the reactivity. There are also a few reports of oxidation of primary alcohols such as ethanol and propanol. For example, Munakata *et al.*<sup>40 b</sup> showed that ethanol as a solvent can be oxidised to acetaldehyde with Cu-bipy catalyst. In addition,

solvents such as acetonitrile<sup>43, 45</sup> and water-propanol mixture<sup>44</sup> have been used, but only a few studies using aqueous alkaline solutions have been reported.<sup>46</sup> Cu-diimine complexes have also been reported to catalyse the oxidation of some secondary alcohols to ketones, but with considerably lower reaction rates than primary alcohols to aldehydes.<sup>43, 45</sup>

In Cu-diimine catalysed reactions the primary alcohols are oxidised almost selectively to their corresponding aldehydes. However, it has also been reported that after all the alcohol has been oxidised, the aldehydes can be further oxidised to carboxylic acids.<sup>42, 43, 49</sup> Common to all mechanisms presented for these reactions is that no oxidation is observed without a base which is needed for the deprotonation of the alcohol. Usually the oxidation is presented by the reduction of Cu(II) and oxygen is needed to oxidise the Cu(I) complex back to Cu(II), but also mechanisms including Cu(III) intermediates have been elucidated (Figures 3 A and B). For example, in the mechanism presented by Capdevielle *et al.*<sup>45</sup> (3 A) the reaction is started with a Cu(I) complex, oxygen coordinates to the catalyst forming a  $\mu^2$ -peroxide bridge, and aldehyde and water are formed. In the mechanism by Sawyer *et al.*<sup>43</sup> (3 B), oxygen coordination forms a mononuclear intermediate with copper at oxidation state III, which then oxidises two alcohol molecules to aldehyde in the consecutive steps.

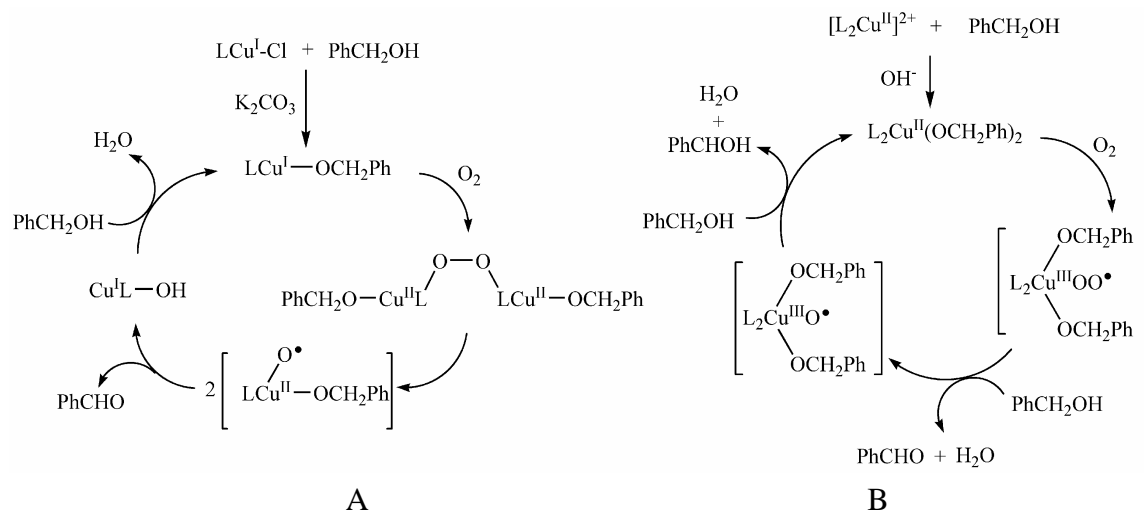


Figure 3. Essential steps in the oxidation of alcohol with Cu-bipy and dioxygen in acetonitrile according to Capdevielle *et al.* (A)<sup>45</sup> and Sawyer *et al.* (B)<sup>43</sup>.

### 3.5.2 Galactose oxidase mimics

Galactose oxidase (GO) is a fungal enzyme containing the mononuclear copper(II) ion, which catalyses the oxidation of primary alcohols to aldehydes by the reduction of  $O_2$  to  $H_2O_2$ . In the catalytically active form of GO, copper(II) ion is located in a distorted square-based pyramidal environment with a tyrosine-495 in the apical position, the amino acids Try-272, His-496 and His-581 and a solvent molecule forming the  $N_2O_2$  square planar geometry around the copper.<sup>50</sup> The enzyme combines two one-electron acceptors, a Cu(II)

metal centre and a stable protein radical, into a complex that functions as a two-electron redox unit during the catalytic cycle. The mechanism of the galactose oxidase has been widely studied<sup>51</sup> and the steps of the reaction are fairly well known (Figure 4). The oxidation is initiated by the coordination of alcohol to copper and deprotonation by the phenolic Tyr-495. The rate-determining step is the hydrogen atom abstraction from the  $\alpha$ -carbon of the alcohol by the phenoxyl radical. The ketyl radical anion formed undergoes rapid intramolecular electron transfer to the Cu(II) centre and aldehyde is formed. Copper(I) is then re-oxidised by dioxygen, hydrogen peroxide is formed and finally a new alcohol molecule can coordinate to the copper centre.

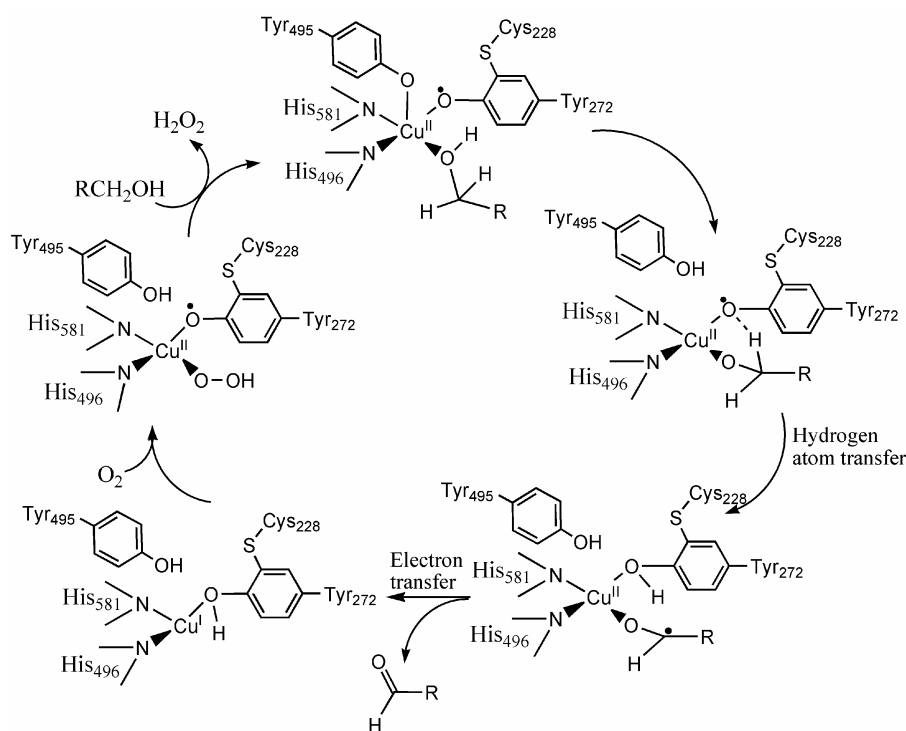


Figure 4. Mechanism of galactose oxidase catalysed oxidation of alcohol to aldehyde.<sup>51</sup>

Various ligands forming active phenoxyl radical complexes with copper, and thus mimicking the galactose oxidase, for the oxidation of alcohols have been reported. One indication of a reaction mechanism similar to GO has been the selective oxidation to aldehyde and the formation of an equimolar amount of hydrogen peroxide as a side product. Oxidation with phenoxyl radical catalysts can usually be conducted under very mild reaction conditions (room temperature and 1 atm air or dioxygen). The first example of complexes bearing a stable phenoxyl radical moiety, Cu(II)BSP (Figure 5, 1), was developed by Stack and co-workers.<sup>52</sup> From different salen-type copper complexes Cu(II)BSP with a binaphthyl backbone was the most active one oxidising primary alcohols with several turnovers. Even higher initial rates for aerobic alcohol oxidation were measured for the copper-phenanthroline-phenolate<sup>53</sup> complex (Figure 5, 2). However, with both catalysts only ~25% total conversion was achieved.

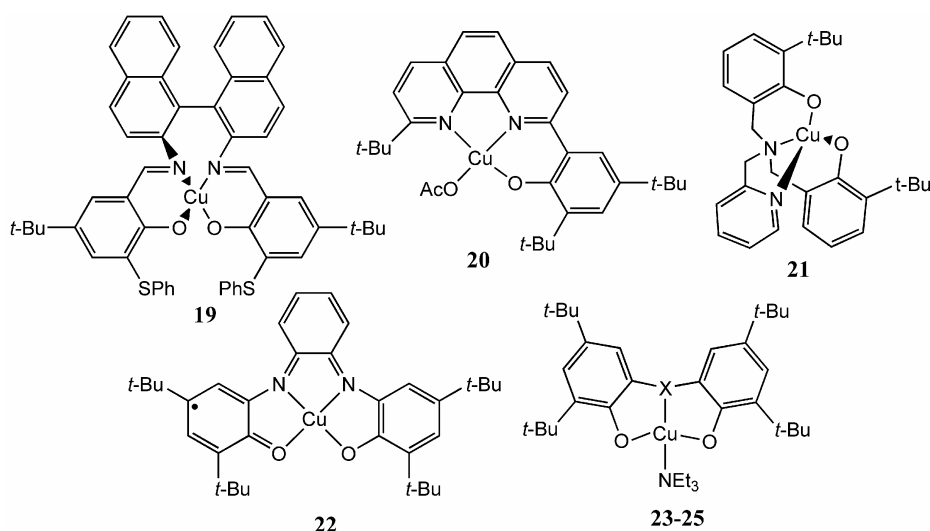


Figure 5. Structures of phenoxyl radical complexes, 19<sup>52</sup>, 20<sup>53</sup>, 21<sup>54</sup>, 22<sup>55</sup>, 23: X = S<sup>56</sup>, 24: X = NH<sup>57</sup>, 25: X = Se<sup>58</sup>.

The most extensive studies of copper-phenoxyl radical complexes have been reported by Wieghardt *et al.* The aniline bridged phenoxyl complex (Figure 5, complex 22) catalyses the aerobic oxidation of a variety of primary alcohol substrates, including methanol, to aldehydes in THF solution at room temperature.<sup>55</sup> The authors showed using an electrochemical study that the preceding complex can be oxidised and reduced to five different oxidation states and all these states are ligand based. In the presence of oxygen, a catalytic cycle using the ligand oxidation and producing aldehyde and hydrogen peroxide was reported.

In the catalytically active form copper with a thiobisphenol ligand (Figure 5, complex 23) forms a bridged binuclear complex which is capable of also oxidising secondary alcohols.<sup>56</sup> The reaction produces hydrogen peroxide as a side product, but the mechanism is described as being non-galactose oxidase based. The mechanism proceeds by the redox reactions of the two phenoxyl radical ligands and the oxidation states of copper ions are not changed during the catalytic cycle (Figure 6 A). With secondary alcohols the minor formation of 1,2-glycols was reported. This was explained by the binuclear active complex; simultaneous coordination of two alcohol molecules to copper centres leads to two reactive  $\alpha$ -carbon radical being close to each other.

Nitrogen<sup>57</sup> and selenium<sup>58</sup> analogues of similar phenoxyl radical complex (24, 25) forms mononuclear active species and the mechanism presented in Figure 6 B is very similar to GO. The reaction is initiated by the deprotonation of (benzyl)alcohol with the base followed by coordination to the copper(II) centre. Hydrogen atom transfer from the  $\alpha$ -methylene of the coordinated alcohol to phenoxyl radical species yields the bound ketyl radical anion, which reduces the Cu(II) to Cu(I) and releases an aldehyde. Reoxidation of the catalyst with O<sub>2</sub> forms spectroscopically characterised Cu(II)-superoxide species,

which regenerates the active catalyst by concomitant formation of hydrogen peroxide. The kinetic isotope measurements reported for these catalysts indicate that the rate determining step is the hydrogen atom abstraction from the  $\alpha$ -carbon atom.

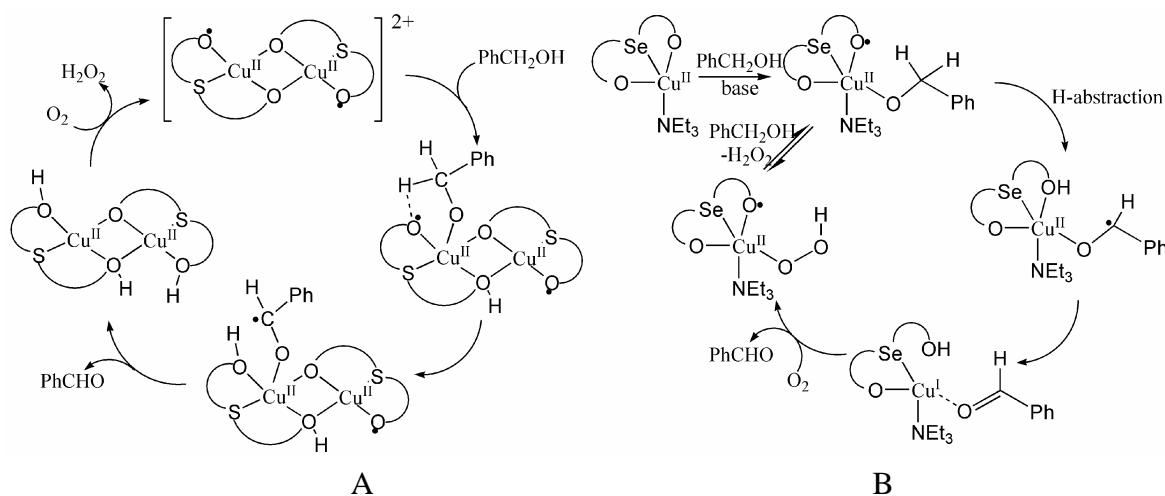


Figure 6. Two different mechanisms for Cu-phenoxy radical catalysts by Wieghardt *et al.*<sup>56, 57</sup>

### 3.5.3 Copper-diimines with co-catalyst

The oxidation of primary and secondary alcohols using nitroxyl radicals was first described in 1965<sup>59</sup> and has been widely studied ever since.<sup>60</sup> As early as 1966 Brackman and Gaasbeek reported the activity of Cu-phen-nitroxyl radical (di-*tert*-butylnitroxyl) catalyst in the oxidation of methanol to formaldehyde.<sup>61</sup> Almost twenty years later Semmelhack *et al.* studied a similar system again and introduced the combination of copper chloride and 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) for alcohol oxidation.<sup>62</sup> They reported that the role of the copper(II) chloride was only to oxidise TEMPO to nitrosonium ion, which then oxidises the alcohol in the actual catalytic cycle (Figure 7 A). However, the mechanism was re-examined by Sheldon and co-workers recently.<sup>63</sup> They reported that the active catalyst is formed by the coordination of nitroxyl radical to copper(I) complex (Figure 7 B). The first steps of the catalytic cycle are similar to galactose oxidase as alcohol is coordinated to the copper centre, a hydrogen atom is abstracted within the alkoxycopper(II)-TEMPO complex and Cu(II) is reduced to Cu(I). However, no hydrogen peroxide as a side product was observed, and therefore reduction of O<sub>2</sub> to water was proposed. To improve the recyclability of the Cu-TEMPO catalyst, a catalyst system using polymer impregnated TEMPO (PIPO) has also been developed.<sup>64</sup> For Cu-PIPO, a catalytic activity comparable to Cu-TEMPO in the oxidation of alcohols was reported.

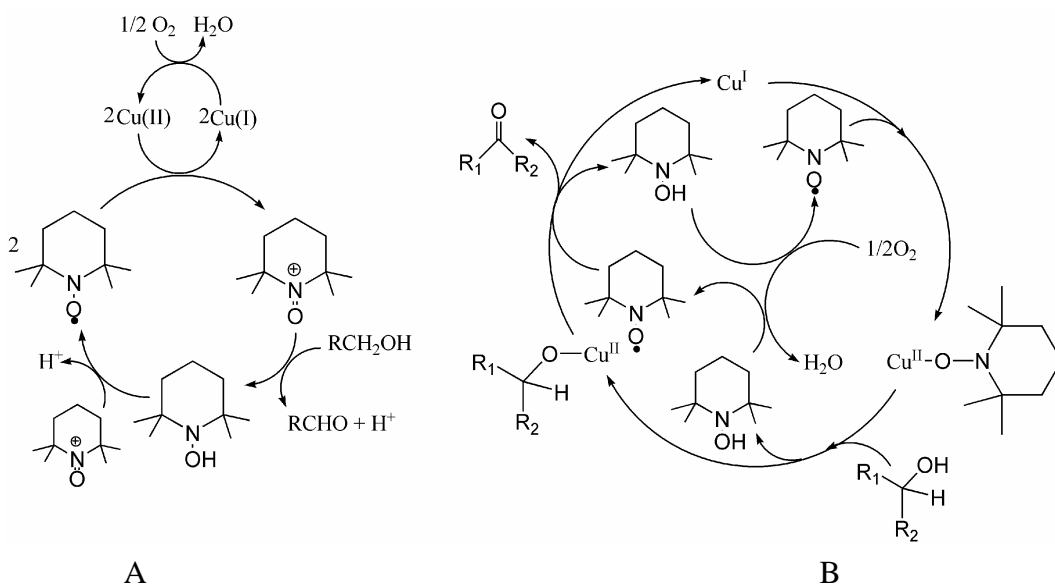


Figure 7. CuCl-TEMPO catalysed oxidation of alcohol according to Semmelhack *et al.*<sup>62</sup> and Sheldon *et al.*<sup>63</sup>

The first example of combining Cu-diimine catalyst with TEMPO for alcohol oxidation was reported by Knochel *et al.* The catalyst system combining CuBr and bipyridine ligand bearing perfluorinated substituents (4,4'-di[C<sub>8</sub>F<sub>17</sub>(CH<sub>2</sub>)<sub>4</sub>]bipy) catalysed the oxidation of primary, secondary, benzylic and allylic alcohols under biphasic solution of perfluorooctyl bromide and chlorobenzene.<sup>65</sup> The two-phase reaction solution was used to ease the separation of the reaction products and recycling of the catalyst. The combination comprising of CuBr<sub>2</sub>, 2,2'-bipyridine and TEMPO has been under active investigation by Sheldon and co-workers.<sup>66</sup> Optimising the catalytic oxidation of benzyl alcohol showed that the highest conversions are achieved in acetonitrile-water (2:1) solution, *t*-BuOK as a base, CuBr<sub>2</sub> as a copper precursor and electron donating *para*-substituents (-Me, -OMe) in the bipyridine rings. The mechanism presented in Figure 8 shows similarities with galactose oxidase in the half concerned with hydrogen atom abstraction, but the co-product of the reaction is water instead of hydrogen peroxide.<sup>67</sup> In addition, reduced copper(I) species is oxidised by TEMPO, which is then regenerated with dioxygen.

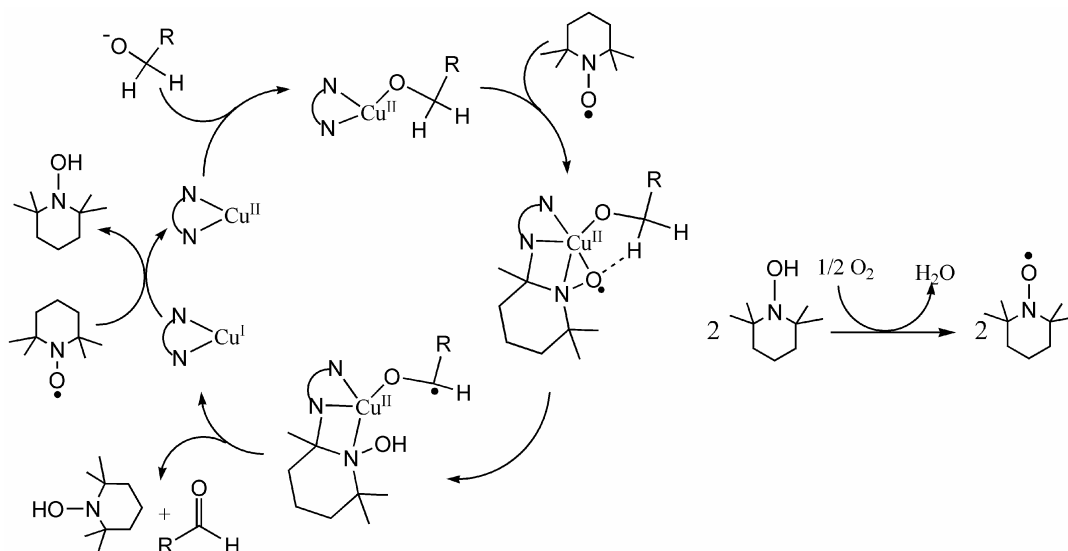


Figure 8. Oxidation of alcohol by Cu-bipy-TEMPO system.<sup>67</sup>

Another catalyst system using Cu-diimine and a co-catalyst for alcohol oxidation has been described by Markó *et al.*<sup>68</sup> CuCl-phen with a co-catalyst was reported to oxidise various primary and secondary alcohols selectively to aldehydes and ketones with simultaneous reduction of oxygen to water. Different co-catalysts such as DEAD (=diethyl azodicarboxylate) and DBAD (=di-*tert*-butyl azodicarboxylate) have been introduced. The function of these co-catalysts is similar to those used in the Cu-bipy-TEMPO system above; they act as hydrogen atom acceptors in the oxidation and stabilise the reaction intermediates. When DEAD was used as a co-catalyst, some undesired by-product of mixed carbonate from hydrazine and alcohol was formed (PhCH<sub>2</sub>-O-COOEt) and the catalyst was deactivated. By replacing DEAD with DBAD, only traces of by-product were reported to form.<sup>69</sup> The highest alcohol conversions were achieved in fluorobenzene solution with *t*-BuOK as a base.<sup>70, 71</sup>

By introducing a new additive, NMI (N-methylimidazole), in the Cu-phen-DBAD system, also the oxidation of primary aliphatic alcohols (for example C<sub>10</sub>H<sub>21</sub>OH) was shown to be possible.<sup>72</sup> The role of NMI was to rapidly coordinate to the copper complex (C) (Figure 9), generating intermediate (F) in which the oxygen coordination can substitute NMI. If the alcohol molecule coordinates to copper in the complex (C), hydrazine can be removed from the coordination sphere and the catalyst is deactivated. In the actual catalytic cycle, the hydrogen transfer from the  $\alpha$ -methylene to the azo ligand generates copper(I)-hydrazide (B). Release of the aldehyde produces Cu(I) complex (C), which is rapidly oxidised to Cu(II) by dioxygen as a peroxo-bridged species (D) is formed. This complex is transferred to the hydroxycopper(I) species (E), which completes the catalytic cycle by the elimination of water.

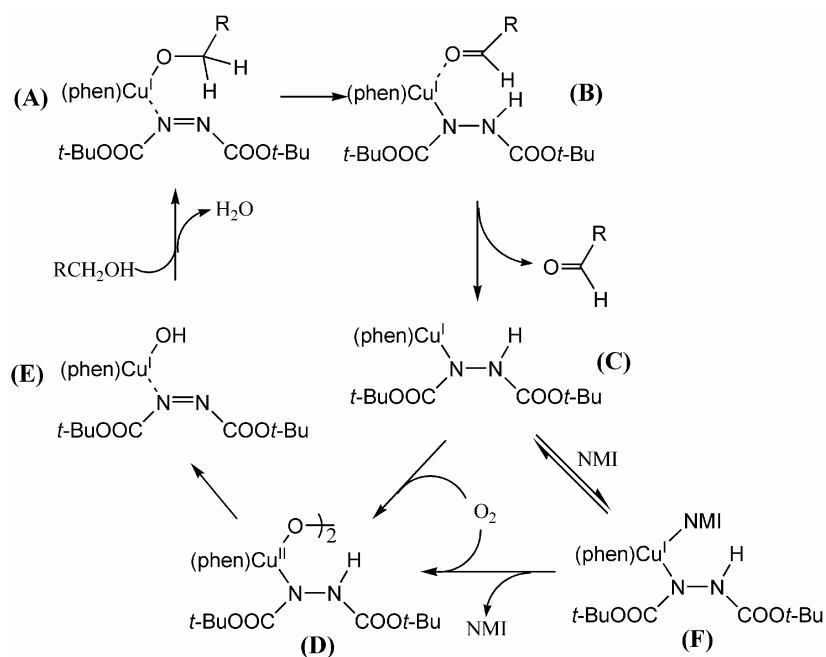


Figure 9. Oxidation of alcohol with Cu-phen-DBAD-catalyst.<sup>72</sup>

### 3.5.4 Laccase-mediator system

A special example of copper catalysed alcohol oxidations discussed here is the Laccase-mediator system. Laccases are enzymes that have an important role in the delignification of wood in nature by white rot fungi. This interesting feature makes laccase studies of importance also for industrial applications in pulp delignification (which is discussed in more detail in chapter 3.6.3). Laccase contains four copper centres and three different coordination types which all have a distinct role in the oxidation of organic substrates.<sup>73</sup> The type 1 copper centre binds the substrate molecule, while the type 2 and type 3 centres are involved in the binding and reduction of  $\text{O}_2$  as well as the storage of electrons from the substrates. Laccases oxidise phenolic substrates as such, but for the oxidation of non-phenolic compounds additional assistance is required.<sup>74</sup> The large size of laccase decreases the interaction between substrates and active metal centres, so mediators, small organic molecules capable of redox reactions, have been introduced. The principle of the laccase-mediator system is shown in Figure 10. Mediator acts as an electron carrier between laccase and substrate. After oxidising the substrate, reduced mediator returns to laccase for regeneration. The “cycle” is completed by the oxidation of laccase by dioxygen.

A variety of compounds having the ability to form nitroxyl radicals (Figure 10) have been studied as mediators for the laccase catalysed oxidation of benzylic alcohols.<sup>75</sup> The highest conversion of alcohol to aldehyde was achieved with TEMPO as a mediator. Laccases as

enzymes are stable only under close to neutral conditions and low reaction temperatures. However, decent turnovers are achieved in these mild reaction conditions. Two drawbacks of the laccase-mediator systems are that a high excess of mediator has to be used and only benzylic alcohols can be used as alcoholic substrates.

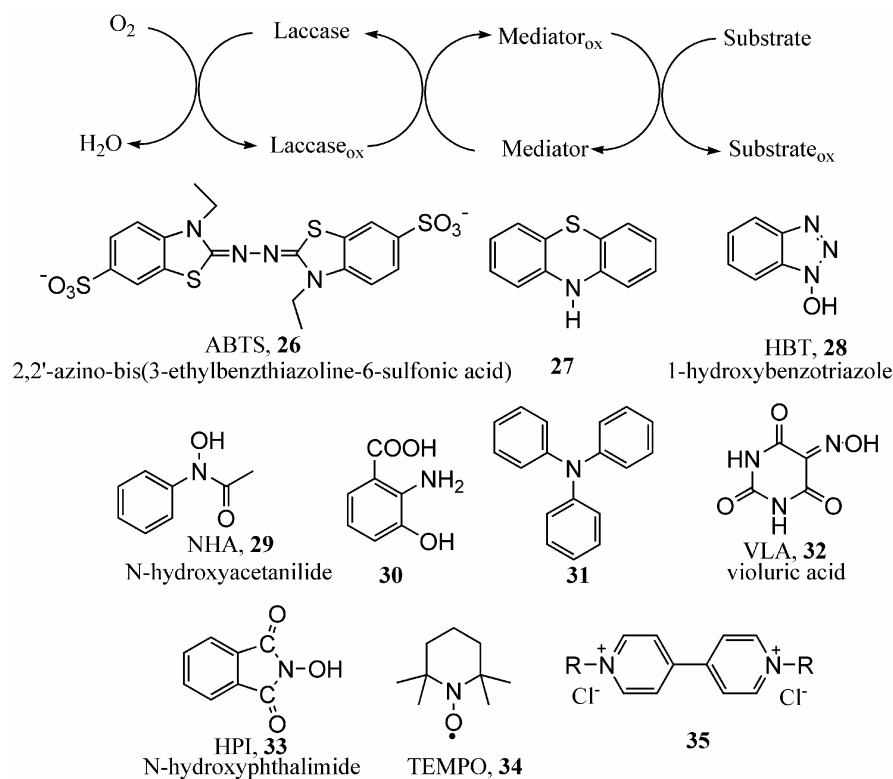


Figure 10. Principle of oxidation with laccase mediator system and some possible mediators.<sup>76</sup>

### 3.6 Transition metal catalysed oxygen delignification

Wood comprises of three major components, cellulose, hemicelluloses and lignin. These polymeric structures are constituents of the cell wall with different ratios depending on the wood-type and regions in the wood.<sup>77</sup> While cellulose is a long chain carbohydrate polymer, lignin is a highly cross-linked amorphous biopolymer acting as natural glue to give wood its physical properties. The amount of lignin remaining in the pulp affects both the physical properties, such as strength and flexibility, and the chemical stability of the finished paper. Even though lignin properties and composition have been under active investigation for decades, a complete description of its structure is still unknown.<sup>78</sup> The structure of lignin has been studied for example by analysing milled wood lignin or the reaction products of lignin degradation or by biosynthesis of lignin. Figure 11 illustrates one example of softwood lignin structure.<sup>79</sup> Various functional groups can be found in its structure such as; alcohols, phenols, ethers, aldehydes and ketones.

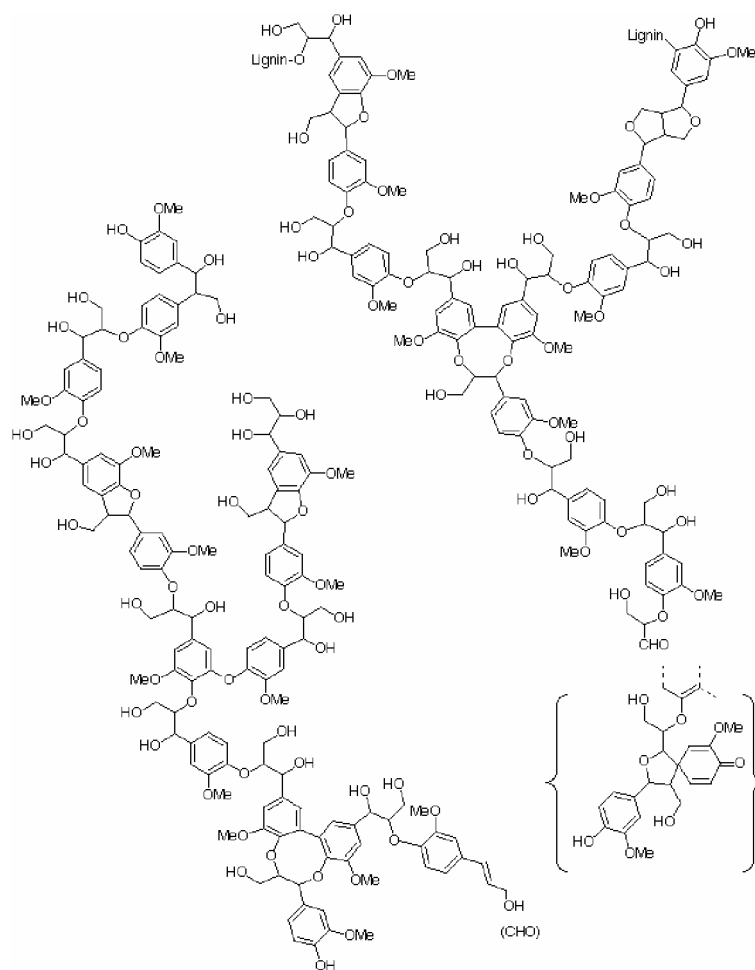


Figure 11. Schematic representation of softwood lignin structure.<sup>79</sup>

In the pulping of wood the cellulose fibres are separated from each other chemically or mechanically. In chemical pulping, separation is achieved by dissolution of lignin under acidic or alkaline hydrolytic conditions. Because of the poor selectivity and the slow delignification in the final stage of pulping, cooking is interrupted and residual lignin (2-4% of pulp) is removed in the bleaching stages. In alkaline oxygen delignification, 50-60% elimination of the residual lignin has been achieved, but at higher levels severe losses in pulp strength and quality takes place. In pulp bleaching, lignin is depolymerised with the help of oxidising agents such as oxygen, hydrogen peroxide, chlorine dioxide and ozone.<sup>80</sup>

Growing environmental awareness and more stringent pollution legislation have induced higher demands also for the oxidising agents used in pulp bleaching. The aim of catalytic delignification is to develop environmentally friendly and economically feasible processes by decreasing the consumption of the chemicals used. In the search for “greener” industrial processes, the catalytic activation of dioxygen for such large scale production would be highly preferable. The catalyst systems developed for this purpose can be categorised into three groups; homogeneous transition metal complexes, polyoxometalates and laccase-mediator systems.

### 3.6.1 Transition metal complexes

In the pulping process, traces of metal ions from wood material and process equipment are present. Transition metal ions, particularly manganese, copper and iron, react with hydrogen peroxide to produce dioxygen and water via hydroxyl- ( $\cdot\text{OH}$ ) and superoxodianion ( $\text{O}_2^{\cdot-}$ ) radicals. The radicals give rise to carbohydrate depolymerisation and thereby lower pulp quality (lowering the tear and burst strengths).<sup>81</sup> In order to prevent viscosity losses, metal ions are removed by chelating compounds. The metal ions can also have a negative effect on the brightness and optical properties of pulp by attaching to fibre surfaces.

The first example of transition metal catalysed oxygen delignification is from 1978, when Fullerton and Ahern<sup>82</sup> studied Co(salen) catalyst in pulp bleaching. Later on, also catalytic oxidation of different phenolic<sup>83</sup> and non-phenolic<sup>9, 84</sup> lignin model compounds by Co(salen)-type complexes have been reported. The delignification studies of Fullerton and Ahern as well as those of Meguro *et al.*<sup>85</sup> showed that Co(salen) complexes were active catalysts, but under highly alkaline reaction conditions also carbohydrate depolymerisation was observed. Higher selectivity was obtained in decreased pH (8-10), but for sufficient delignification long reaction times were required. Various cobalt Schiff-bases (Figure 12, 37-40) have been studied in oxygen delignification with a similar conclusion as reported for Co(salen); catalysts increased the brightness and decreased the kappa levels of pulp, but simultaneously viscosity was decreased.<sup>86</sup> Highest activities were measured with complexes 37 and 38, but they also caused the highest viscosity losses.

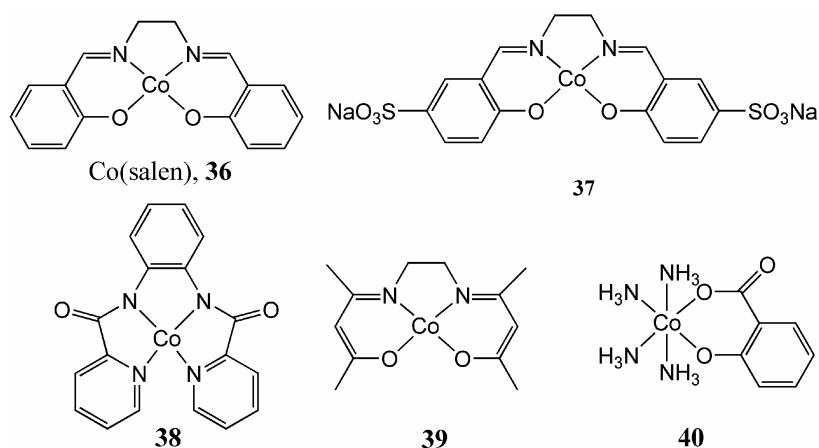


Figure 12. Cobalt Schiff-bases studied in oxygen delignification.<sup>86</sup>

Metal porphyrins such as cytochrome c oxidase, myoglobin and hemoglobin are known to act as dioxygen carriers, storages and catalysts for reduction reactions in human metabolism.<sup>87</sup> Perng *et al.*<sup>88</sup> have studied cobalt, iron and manganese porphyrins in oxygen delignification. They observed that only manganese complexes decreased the kappa and suppressed cellulose degradation, while the corresponding cobalt complex only promoted

carbohydrate decomposition with no effect on the delignification efficiency. The manganese complexes (Figure 13, complexes 41 and 42) possessed highest catalytic activity and selectivity in high pH (1.0 M KOH), oxygen pressure (8 bar) and at elevated temperature (100 °C). A disadvantage of porphyrins is that they require multi-step synthesis, which makes them considerably expensive and their structures are often prone to oxidative degradation during bleaching.

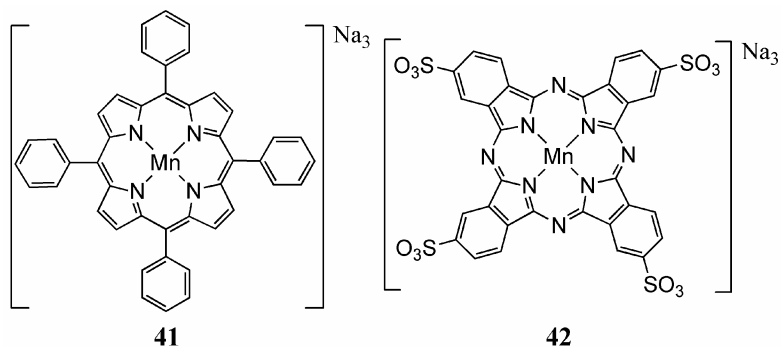


Figure 13. Manganese porphyrin complexes for catalytic delignification.<sup>88</sup>

Hall and co-workers have studied different metal (Ni, Fe, Co, Mn Ru) complexes and salts in oxygen delignification with low consistency pulp.<sup>89</sup> The modified Co(salen) compound (Figure 14, complex 43) was the most active, but also the most unselective delignification catalyst. Actually, a similar viscosity drop was reported for both complex 43 and Co(NO<sub>3</sub>)<sub>2</sub> salt, indicating that the complex either decomposes in the reaction, or the ligand has no effect on the selectivity of the catalyst. The nickel complex 44 (Figure 14) and nickel sulphate together with tartrate possessed the highest selectivities of the studied compounds. However, the positive effect was seen only in low consistency pulp while in medium consistency conditions no increase in delignification was observed.<sup>90</sup>

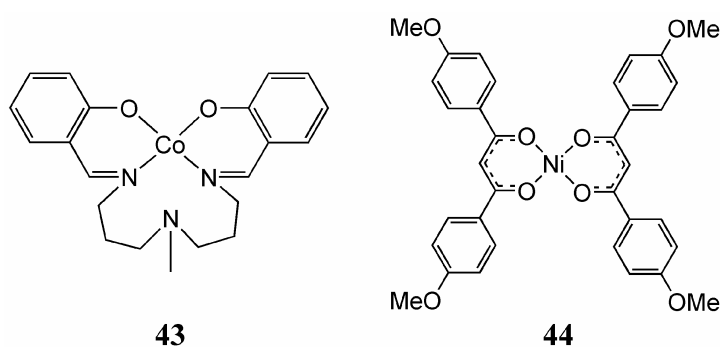


Figure 14. Nickel and cobalt complexes studied by Hall *et al.*<sup>89, 90</sup>

Ahuja *et al.* reported the activity of cerium(IV)sulphate in delignification under acidic conditions.<sup>91</sup> However, they conclude the article with the following: “the effect of the chosen catalysts in the oxygen delignification stage is quite small” and “the catalyst is not regenerated at the end of the reaction”. These conclusions indicate that at best the catalyst

works as a stoichiometric oxidant. In these experiments molybdenum acetylacetonate showed no activity, while Agnemo<sup>92</sup> has reported that under acidic conditions molybdate anion increases the delignification rate.

The activity of copper-phenanthroline as a catalyst for oxygen delignification has been studied by Germer.<sup>93</sup> Copper salts together with 1,10-phenanthroline or 2,2'-bipyridine was reported to accelerate the rate of oxygen delignification considerably. In the delignification reaction,  $[\text{Cu}(\text{phen})_2]^{2+}$  complex was presented to be responsible for the catalytic activity.<sup>94</sup> Copper sulphate and phen were added simultaneously to reaction mixture, but also the addition of phenanthroline alone was observed to decrease kappa by activating “natural” copper from wood.<sup>95</sup> With the use of the Cu-phen catalyst, a considerable improvement in delignification was observed. For example in the Cu-phen catalysed reaction, the kappa number of pulp was decreased from 97 to 27-29 while similar experiment without catalyst gave a kappa of 62. However, as has been reported for many transition metal catalysts the viscosity of the pulp was decreased.

An interesting article related to the activity Cu-phen catalyst was recently presented by Argyropoulos *et al.*<sup>96</sup> They reported that addition of only a diimine compound, particularly 1,10-phenanthroline, to peroxide-reinforced oxygen delignification enhanced the lignin removal and preserved the selectivity. To eliminate the possibility of complex formation between transition metals in solution and diimine, chelated pulp was used. Addition of 1%  $\text{H}_2\text{O}_2$  (of dry pulp) and 0.6% phen, kappa was decreased from 29.9 to 11.4, while without these additives kappa of 14.8 was measured. Only a minor decrease in viscosity was reported, while in a similar experiment the addition of  $\text{Cu}^{2+}$  results in significant viscosity losses (24.8 vs. 9.5 mPa·s).

### 3.6.2 Polyoxometalates

Polyoxometalates (POMs) are metal oxygen anion clusters constituting of  $d^0$  early transition metal cations (in particular  $\text{W}^{\text{VI}}$ ,  $\text{Mo}^{\text{VI}}$ , and  $\text{V}^{\text{V}}$ ) and oxide anions. POMs are composed primarily of  $\text{MO}_6$  octahedra linked together by oxygen atoms. Polyoxometalates can be divided into two classes, the isopolyanions, which contain only the  $d^0$  metal cation and oxide anions ( $\text{M}_x\text{O}_y^{n-}$ ) and the heteropolyanions, which contain one or more d or p block elements in addition to the  $d^0$  metal cation, for example Si or P. The most investigated of these are Keggin heteropolyanions having the formula  $[\text{X}^{\text{n+}}\text{M}_{12}\text{O}_{40}]^{(8-n)-}$ , where  $\text{M} = \text{W}^{\text{VI}}$  or  $\text{Mo}^{\text{VI}}$ . In addition, under appropriate conditions, some of the  $d^0$  metal atoms can be substituted with transition metal “addenda ions”, such as Co, Cu, Ni, Zn, Mn, and Fe. POMs can be easily prepared, their properties can be tuned by choice of precursors and conditions, and they are simultaneously resistant to oxidation but can still be reversibly reduced. The structures<sup>97</sup> as well as chemical<sup>98</sup> and catalytic<sup>99</sup> properties of POMs have

been widely studied and reviewed, and therefore only a short view to the activity of POMs in oxygen delignification reactions is given.

In delignification, the polyoxometalates should have reduction potential sufficient for oxidising lignin substructures and to be oxidised by dioxygen. The first applications of POM catalysed delignification under anaerobic conditions were developed by Weinstock *et al.*<sup>100</sup> In their system the reaction was conducted in two stages. In the first step (Figure 15) POM oxidises lignin stoichiometrically under anaerobic conditions. In the second step lignin remnants are oxidised to CO<sub>2</sub> and H<sub>2</sub>O by another POM catalyst in a separate reactor under aerobic conditions and high temperature. The reduced POM from the first step is regenerated by O<sub>2</sub>. In an ideal process the same POM would catalyse both reactions. The purpose of the separated reactors was to diminish the viscosity decrease caused by the radical reactions. Since the reaction between the catalyst and lignin is stoichiometric, a high concentration of polyoxometalates (0.05-0.1 mol/l) was used. The most promising results were obtained with [SiVW<sub>11</sub>O<sub>40</sub>]<sup>5-</sup> and [PV<sub>2</sub>Mo<sub>10</sub>O<sub>40</sub>]<sup>5-</sup>.<sup>101</sup> More recently, a high activity with catalyst composition Na<sub>6,9</sub>[SiV<sub>0,9</sub>MoW<sub>10,1</sub>O<sub>40</sub>] in the oxidation of lignin model compounds has been reported.<sup>102</sup> Under optimum pH 5-6, the active species were reported to be Na<sub>5</sub>[SiVMoW<sub>10</sub>O<sub>40</sub>] and Na<sub>5</sub>[SiVW<sub>11</sub>O<sub>40</sub>].

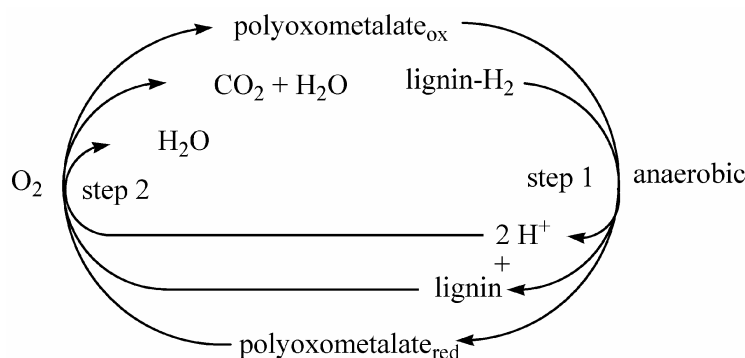


Figure 15. Schematic representation of POM catalysed delignification by Weinstock *et al.*<sup>101</sup> Step 1 is conducted under anaerobic conditions and step 2 for oxidising lignin fragments in a separate reactor.

In contrast to the anaerobic reaction conditions required by the system of Weinstock and co-workers, Evtuguin and Pascoal Neto have actively developed POM catalysts for delignification under aerobic conditions. Most of their studies are focused on heptamolybdopentavanadophosphate anions (HPA-*n*), where *n* is the number of vanadium atoms, for example PMo<sub>12-*n*</sub>V<sub>*n*</sub>O<sub>40</sub><sup>(3+*n*)-</sup> (usually *n* = 4-6).<sup>103</sup> The oxidation of organic substrates is mainly caused by vanadium(V) ions of POM but some oxidation also occurs by VO<sub>2</sub><sup>+</sup> ions, which are released from polyoxometalate by partial dissociation in acidic media. VO<sub>2</sub><sup>+</sup> ions are very active delignification catalysts, however, they are also mainly responsible for the decreased selectivity. Optimum conditions for the most active

heteropolyanion HPA-5 ( $[\text{PMo}_7\text{V}_5\text{O}_{40}]^{8-}$ ), were: POM concentration of 2-4 mmol/l, temperature of 90-100 °C and pH 2-3.<sup>104</sup> Reactions were carried out at low pH because of the decomposition of HPA-5 at pH higher than 4, and decreasing of the delignification rate already at pHs over 3. On the other hand, the highly acidic conditions (pH 2) resulted in carbohydrate depolymerisation and viscosity decrease. This could be partly avoided by carrying out the experiments in water-ethanol solutions which decreased the acidity of  $\text{H}_2\text{SO}_4$  and increased the oxygen solubility.<sup>105</sup> Furthermore, an increase in ethanol decreases the liberation of  $\text{VO}_2^+$  from HPA.

New polyoxometalates which are stable at higher pH have been developed to avoid the viscosity losses observed at low pH. For example, POMs  $[\text{SiW}_{11}\text{Mn}^{\text{III}}(\text{H}_2\text{O})\text{O}_{39}]^{n-}$ <sup>106</sup> and HPA-5- $\text{Mn}^{\text{II}}$ <sup>107</sup> with manganese as addenda atoms were stable at close to neutral conditions. In delignification,  $[\text{SiW}_{11}\text{Mn}^{\text{III}}(\text{H}_2\text{O})\text{O}_{39}]^{n-}$  increased the selectivity of catalytic oxidation under slightly acidic conditions (catalyst concentration 5.9 mmol/l, 2 h, pH 4, 100 °C,  $\text{O}_2$  pressure 5 bar). However, compared to oxygen-alkaline delignification there is only minor improvement (kappa number 7.9 vs. 8.1, viscosity 1230 vs. 1170  $\text{cm}^3/\text{g}$ ). This was explained by the insufficient re-oxidation of the catalyst with dioxygen during the delignification.

The development of the HPA-5- $\text{Mn}^{\text{II}}$  catalyst recently reached first pilot scale experiments.<sup>108</sup> The higher selectivity and slightly lower delignification efficiency of HPA-5- $\text{Mn}^{\text{II}}$  compared to HPA-5 was explained by the improved control against the formation of  $\text{VO}_2^+$  ions. The pilot scale runs were conducted with eucalyptus kraft pulp under the following conditions: catalyst concentration 1.5 mmol/l, pH 3.8, temperature 95 °C and  $\text{O}_2$  pressure 5.5 bar. Even though the catalyst concentration in these experiments has decreased to a reasonable level, a few questions in the reported results were left open. For example, in the loading of the reactor a 10-15% viscosity decrease was observed. The decrease was reported to be due to acid hydrolysis and oxidation of carbohydrates by the  $\text{VO}_2^+$  ions, and it was avoidable by using proper treatment. The main advantage of POM catalysed delignification was that the selectivity of the reactions was maintained even at degrees of delignification over 50%. However, no significant savings in chlorine dioxide consumption in the following treatments was observed.

### 3.6.3 Laccase-mediator systems

Use of enzymes in pulp bleaching has been widely studied and commercial applications<sup>109</sup> have also been developed to enhance the delignification and decrease the chemical consumption.<sup>110</sup> Laccases are the most actively studied enzymes in delignification because of their excellent oxidative properties. Various reports and review articles<sup>109, 110, 111</sup> on the oxidation of lignin and its model compounds with laccases have been published. The

benefit and limitation of enzymatic reactions is that they can/have to be carried out in mild conditions (close to neutral pH and ambient temperature) because of the low stability of the enzymes. In addition, for delignification applications a mediator is needed for at least two reasons. First, laccases are able to oxidise only the phenolic groups of lignin. Secondly, the small size of the mediator makes it able to diffuse into the fibre wall and gain better access to the oxidisable groups of lignin than laccase itself.

The basic idea of the laccase-mediator system (LMS) was presented in Figure 10 (chapter 3.5.4), but the true role of the mediator in delignification is still a mystery. It has been shown that for effective delignification, the mediator should have suitable oxidation potential to be oxidised by laccase and on the other hand able to oxidise lignin fragments. In addition, the mediator should be stable in both of its oxidation states and the redox reactions should also be fast to prevent unwanted side-reactions i.e. the mediator should selectively oxidise lignin and leave the cellulose fibres undamaged. For commercial applications, the mediator should be cheap and non-hazardous for the environment.<sup>111</sup> As the compounds in Figure 10 show, most of the mediators are nitrogen containing compounds able to form radical species. Some phenolic mediators have also been introduced, but due to the instability (irreversible oxidation) of these compounds they had to be used at impractically excessive concentrations.<sup>112</sup>

The first laccase-mediator system was introduced by Bourbonnais *et al.* in 1990.<sup>113</sup> They reported that laccase together with ABTS (2,2'-azino-bis(3-ethylbenzthiazoline-6-sulfonic acid) enhanced delignification considerably, but also minor colouring of the pulp was observed. HBT (1-hydroxybenzotriazole) has been reported to be one of the most reactive mediators, but it also caused some deactivation of laccase.<sup>109</sup> Deactivation was due to mediator attacking amino acids on the enzyme's surface. In addition, HBT itself could be partly deactivated by the formation of benzotriazole. In experiments combined with alkaline extraction a laccase-HBT catalysed reaction yielded over 50% delignification. The reaction conditions for a common laccase-mediator reaction were: pulp consistency 10-15%, time 1-2 h, temperature 40-60 °C, pH 4-5, O<sub>2</sub> pressure 3 bar, mediator 1-2% of pulp and laccase 5-20 U/g pulp.<sup>114</sup>

More recently, mediators such as NHA (N-hydroxyacetanilide) and VLA (violuric acid)<sup>115</sup> have been reported as even more active mediators than HBT. In the oxidation of the lignin model compound adlerol (secondary benzylic alcohol) to adlerone, laccase-VLA gave the highest conversion.<sup>116</sup> It should be observed that in these experiments considerably high molar ratios of mediator to model compound were used (1:1-1:3). The reactivity order for different mediators was determined to be: VLA > NHA > HBT > HPI > TEMPO > ABTS. However, because of the highest reactivity, violuric acid also resulted in degradation of laccase. The low activity of the laccase-TEMPO system was explained by the reactivity of TEMPO for only primary alcohols. Relevant to this, d'Acunzo *et al.*<sup>117</sup> have shown that

laccase-HPI (N-hydroxyphthalimide) system oxidised only the phenolic groups of their lignin model compound, while the laccase-TEMPO catalyst preferred the oxidation of benzylic OH-groups.

Recently, a method for the bleaching of non-wood (flax) pulp using laccase together with ABTS and HBT has been introduced.<sup>118</sup> After a 24 h experiment, a higher decrease in kappa levels than with laccase-mediator delignified wood-pulp was reported. It was proposed that with flax pulp, the higher price of the high quality product would compensate the costs of the enzymatic process. However, only moderate delignification was observed after a 4 h reaction time. Again, the use HBT gave higher delignification rate and selectivity compared to ABTS.

Also, transition metal compounds have been studied for use as mediators. The molybdenum complex  $K_4Mo(CN)_8$  as a mediator was reported to increase the delignification, but high molybdenum dosage decreased the viscosity.<sup>119</sup> Lately, a few applications using polyoxometalates as mediators have been introduced. As was described before, one of the drawbacks of POM technology is that highly acidic conditions are required. Polyoxometalate  $[SiW_{11}V_1O_{40}]^{5-}$  has been reported to be stable under neutral conditions, but rather inactive towards reoxidation by dioxygen.<sup>100</sup> However, Evtuguin *et al.* showed that  $[SiW_{11}VO_{40}]^{5-}$  could be reactivated with laccase and act as a moderately active mediator for delignification.<sup>120</sup> As like laccase-mediator systems in general, also with laccase-POM system high selectivity was achieved. Recently, a new technique for highly selective delignification with  $[SiW_{11}Mn^{III}(H_2O)O_{39}]^{5-}$  as a mediator was reported.<sup>121</sup> The delignification rate was not significantly enhanced if the laccase and POM were used simultaneously, but by dividing the reactions into POM catalysed oxidation of lignin at 110 °C and re-oxidation of POM by laccase at 45 °C, about 50% delignification was reported. However, alternating these sequences required 14 h, and even with the reduced reaction times a 3-5 h process would be needed.

### 3.7 Conclusions

Various copper-catalysts for the oxidation of different alcohols by dioxygen have been presented. Many of these are highly active in considerably mild reaction conditions. In an attempt to obtain a better understanding of the oxygen reactions in catalytic systems and in enzymes activating oxygen in nature, the reaction mechanisms have received increasingly interest. The difficulty in studying the mechanism of homogeneous metal catalysed oxidation is that most of the reaction intermediates are short-living and it is difficult to provide experimental evidence for their existence. For copper catalysed alcohol oxidations, the proposed mechanisms indicate that the hydrogen atom abstraction of  $\alpha$ -methylene is the rate determining step and different ways such as phenoxyl radical ligands and co-catalysts have been introduced to enhance this step. The main differences between the mechanisms are the oxidation states of copper, the coordination mode of oxygen and the reduced form of dioxygen; is it converted to water or hydrogen peroxide.

The development of new delignification catalysts is based on the noble ideal of an economically and environmentally sustainable process. However, these aspects are also the main reasons for discarding many new catalyst systems. For several catalysts, their suitability for large scale process, price, and recyclability are the major challenges to their development. Various transition metal compounds are active in oxidising phenolic and non-phenolic lignin substructures, but unfortunately they are also active towards depolymerisation of carbohydrates leading to lower pulp quality. With polyoxometalates the viscosity problems have been partly overcome, they are easily synthesised, stable over a wide temperature range, and reusable. Even though the quality of POM delignified pulp is comparable to alkaline oxygen delignification, the process is not yet economically suitable.

Enzymatic delignification with mediators is conducted in mild reaction conditions, the reactions are highly selective and even higher pulp strength and yields are obtained compared to oxygen delignification. The challenges of laccase-mediator systems are lowering the chemical costs, increasing the stability of laccases and the selectivity of mediators, and the effective regeneration of mediators. In some experiments almost half of the mediator has been consumed during the delignification, which means the process has significant wastes and economic losses. Until now, a large scale production of a commercial mediator has not been possible.

## 4 Results and Discussion

### 4.1 Introduction

To efficiently evaluate the performance of catalysts in pulp delignification, a simple model system is needed for laboratory scale experiments. Because of the complexity of lignin (Figure 11), the oxidation of veratryl alcohol (3,4-dimethoxy benzylalcohol) was chosen as a model reaction (Figure 16). Veratryl alcohol is known as a lignin substructure, it is oxidised almost selectively to veratraldehyde (sometimes traces of veratric acid are formed) and the oxidation reaction can be easily analysed by chromatographic methods. Under reaction conditions applied, no oxidation of veratryl alcohol was observed without a catalyst. With this method, the activity of the catalysts could be measured as the conversion of veratryl alcohol to aldehyde, or as turnover number (TON, moles of aldehyde produced per mole of catalyst). In the beginning of this work, the oxidation experiments were performed in glass vessels, the oxygen atmosphere was obtained with balloons and after extraction and evaporation the oxidation products were analysed with NMR-spectroscopy. To bring the reaction conditions closer to the ones in the industrial delignification, a steel autoclave fitted with glass vessel was applied and the reaction conditions of 80 °C and 10 bar of oxygen were selected as standard conditions.<sup>9b</sup>

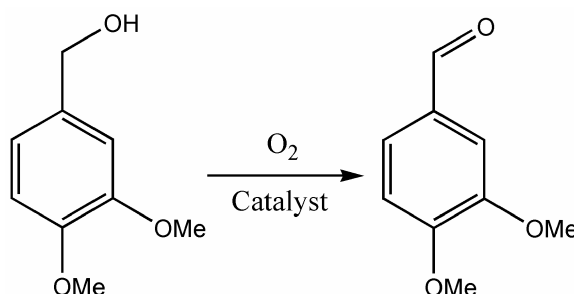


Figure 16. The oxidation of veratryl alcohol to veratraldehyde.

Due to combinatorial approach used in this thesis, the majority of studied compounds were commercially available and used without further purification. For oxidation reactions, deionised water, oxygen (AGA 99.5) and veratryl alcohol (96%, from Acros) were used. Reaction products were analysed with gas chromatography (GC/MS Varian Saturn 2100 and GC/Fid Agilent 5890N) using an HP-5 30 m\*320  $\mu$ m\*0,25  $\mu$ m capillary column. UV-Vis measurements were carried out with an HP 8453 spectrophotometer with 1 cm cells and the data was analysed with UV-Visible ChemStation software. The pH of the reaction solution was monitored with a Schott pH-meter. Online ATR-IR spectra were recorded using a Mettler Toledo ReactIR<sup>TM</sup>1000 spectrometer with a DiComp<sup>TM</sup> probe, which was

fitted in a two-neck roundbottom flask (for reactions under atmospheric oxygen pressure) or to a high pressure steel autoclave (for reaction under 10 bar oxygen pressure) containing the reaction solution.

## 4.2 Development of parallel screening method

To enhance catalyst investigation, a reactor set-up of one litre steel autoclave fitted with 14 small glass reactors including magnetic stir-bars was developed (Figure 17, described in publications **I** and **II**). This parallel system made it possible to study large amounts of metal-ligand combinations as well as different reaction conditions. After loading the solvent, metal and ligand compounds and veratryl alcohol, the autoclave was pressurised with oxygen and heated to the reaction temperature in an oil bath. Over 50 three hour experiments could be conducted in one day with two of these reactors. As a response to the high amount of samples, also the product analysis was optimised. Instead of multi-phase sample preparation, a gas chromatographic method was developed. A small amount of reaction solution (0.5 mL) and ethyl acetate (1.5 mL) were combined in a sample vial. The sample vial was then shaken in order to extract the oxidation products to the organic phase and it was placed on the plate of a GC autosampler, which was programmed to take a sample from the organic phase. With the method described above, a fast and quantitative evaluation of the oxidation reactions was obtained.



Figure 17. Reactor for parallel screening of catalysts (**II**).

### 4.3 Catalyst screening

Catalytic properties of organometallic and inorganic complexes are highly dependent on the ligand framework around the metal centre. The number of d-electrons in the metal ion and their spin state as well as the steric surrounding provided by the ligands are the major factors determining which complexes are inactive and which are catalytically active. Ligands suitable for our studies needed to be to some extent soluble in an alkaline water solution and able to form metal complexes *in situ*. Nitrogen-containing compounds were chosen as leading ligand structures for investigation, because they have high complex formation constants in aqueous solutions and nitrogen heterocycles such as bipy and phen were known to form active oxidation catalysts with copper<sup>43</sup>, cobalt<sup>122</sup> and iron<sup>123</sup> compounds.

The aim of the primary screening was to identify metal-ligand combinations having catalytic activity under the selected reaction conditions. In the first stage the oxidation activity of nine metal compounds in combination with 20 different ligands was studied (Figure 18). Water-soluble transition metal sulphates, namely MnSO<sub>4</sub>, FeSO<sub>4</sub>, CoSO<sub>4</sub>, CuSO<sub>4</sub> and ZnSO<sub>4</sub>, were chosen as the metal sources. This series was supplemented with Cu<sub>2</sub>O, with alkaline earth metal compounds MgSO<sub>4</sub> and CaAc<sub>2</sub>, and with Al<sub>2</sub>(SO<sub>4</sub>)<sub>3</sub> as examples of main group metals. A schematic representation of the oxidation activity of the 189 metal–ligand combinations is presented in Figure 19 (I).

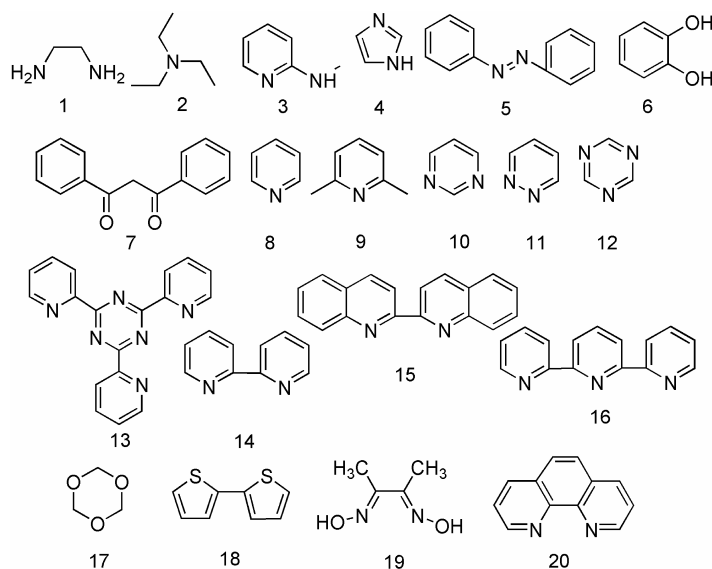


Figure 18. Ligands applied for *in situ* complexation in the primary screening (I).

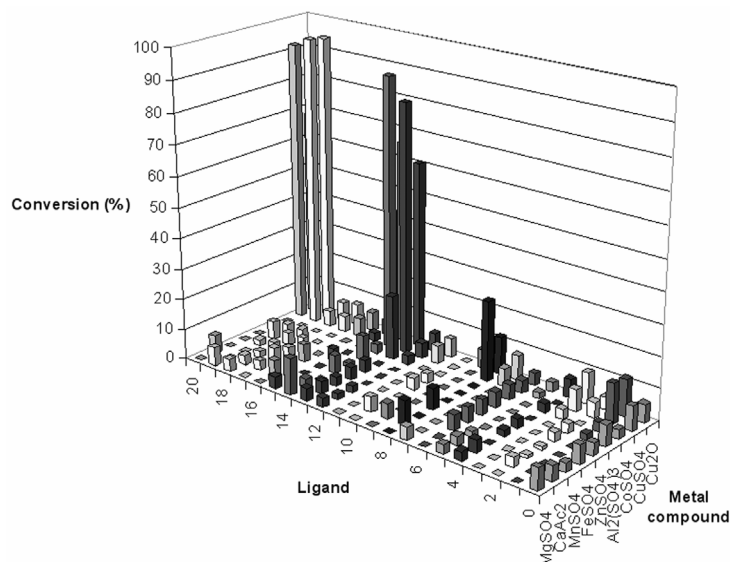


Figure 19. Conversions of veratryl alcohol to aldehyde with different metal-ligand combinations (**I**). The ligands are shown in Figure 18. Without a catalyst, no oxidation was observed. Ligand:metal molar ratio 2:1, veratryl alcohol:catalyst molar ratio 10:1, temperature 80 °C, O<sub>2</sub> pressure 10 bar, reaction time 3 h, 0.2 ml veratryl alcohol, 10 ml 0.05 M NaOH (pH~12.6).

Previously known Cu-bipy (Figure 18, compound 14) and Cu-phen (Figure 18, compound 20) turned out to be highly efficient catalysts in the oxidation of veratryl alcohol. The high activity obtained with 2,4,6-tri(2-pyridyl)-1,3,5-triazine (Figure 18, compound 13), which has three distinct coordination sites, most probably arises from a coordination site resembling bipyridine and it was not included in the further studies. Dimethylglyoxime (DMG, Figure 18, compound 19), which has structural similarity to bipy and phen, demonstrated considerable activity under the applied conditions. In general, ligands coordinating from oxygen or sulphur showed no significant activity with any of the metals, and no metal except copper could be activated with the studied ligands.

After copper complexes with nitrogen coordinating ligands had shown their potential in the oxidation of veratryl alcohol, a further investigation with various diamine-type ligands at different pHs was performed (**II**). From these ligands, three new catalysts Cu-TMEDA (*N,N,N',N'*-tetramethyl ethylenediamine), Cu-DACH (1,2-diaminocyclohexane) and Cu-DAPHEN (9,10-diaminophenanthrene) showed catalytic activity in the oxidation of veratryl and benzyl alcohol (Figures 20 and 21).

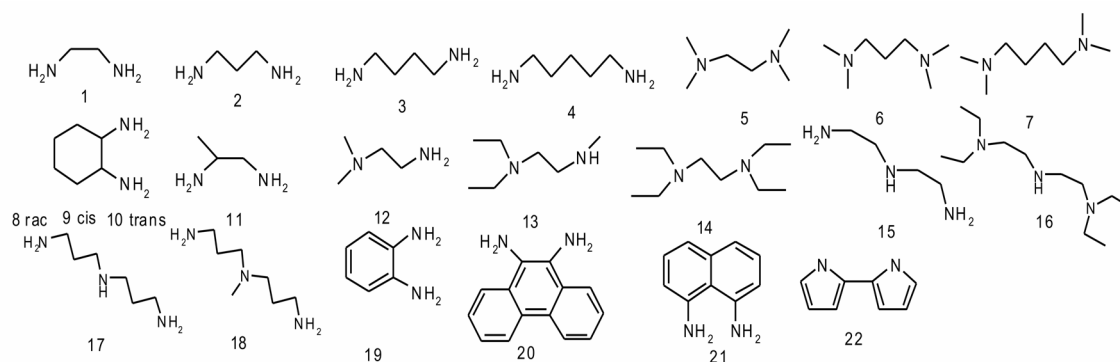


Figure 20. Ligands complexed with copper sulphate for the oxidation of veratryl and benzyl alcohol (**II**).

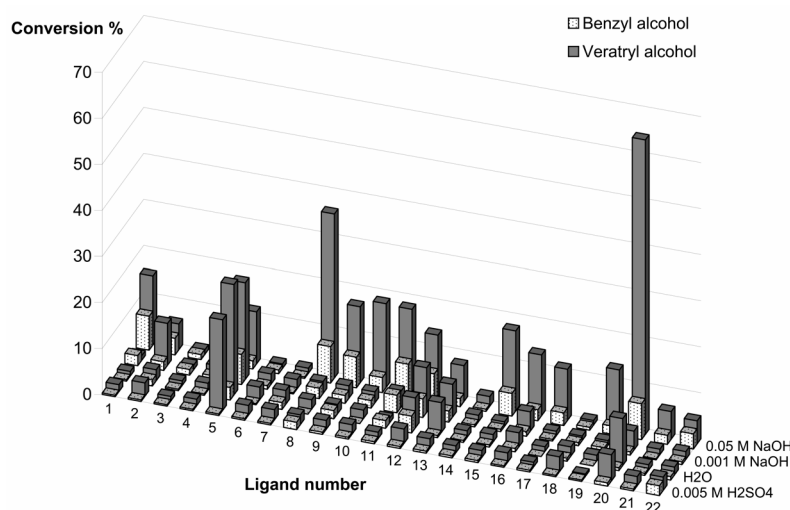


Figure 21. Conversions of veratryl and benzyl alcohols to aldehydes with different copper-ligand combinations. The ligands are shown in Figure 20. Without a catalyst, no oxidation was observed. Ligand:copper molar ratio 2:1, alcohol:catalyst molar ratio 20:1, temperature 80 °C, O<sub>2</sub> pressure 10 bar, reaction time 3 h, 0.2 ml veratryl alcohol, 10 ml water (**II**).

On the basis of these primary screening experiments and some supplementary experiments seven new copper-based oxidation catalysts were found (Figure 22). In secondary screening the effect of different reaction variables on the oxidation activity was studied. It was observed that reaction conditions have a considerable effect on the activity of the catalyst and high activities are obtained with all catalysts under conditions suitable for oxygen delignification; alkaline solution, temperature 80 °C and O<sub>2</sub> pressure 10 bar. The most important parameters, pH of the solution and ligand to metal molar ratio were observed to be interlinked. Under highly alkaline conditions a high excess of ligand was also needed for high activity. For all catalysts, a specific optimum for ratio between these two was found (Table 1). Last four of these catalysts Cu-phen, Cu-bipy, Cu-dmg and Cu-PAO were chosen for further investigation.

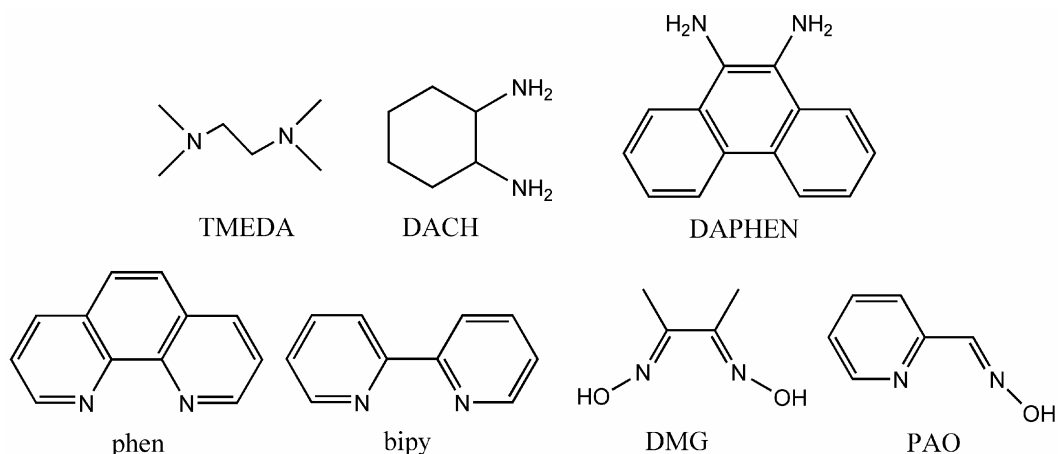


Figure 22. Ligands forming active oxidation catalysts with copper.

Table 1. Optimised initial pHs and ligand:metal molar ratios for active catalysts presented in Figure 22. Temperature 80 °C, O<sub>2</sub> pressure 10 bar, reaction time 3 h, 0.2 ml veratryl alcohol, 10 ml solvent.

ligand	TMEDA	DACH	DAPHEN	phen	bipy	DMG	PAO
initial pH <sup>a</sup>	11	14	13.2	12.6	12.2	13.3	12.6
L:Cu molar ratio	10	2-3	<2 <sup>b</sup>	5	20	10	2
alcohol:Cu ratio	95:1	115:1	73:1	1000:1	1000:1	1000:1	80:1
TON	18	11	26	760	830	420	36

<sup>a</sup> at room temperature

<sup>b</sup> very low solubility

#### 4.4 Complexes in solution and structures of catalytically active species

Identification of the active catalyst in parallel experiments was made difficult by the fact that the metal salts and ligands were added to reaction solution separately and the complex structures formed were determined by the prevailing reaction conditions. For different ligands specific conditions for the maximum activity were found. It was observed that the choice of ligand is the major factor determining the nature of the copper species present in the solution. For complexes with high stability<sup>124</sup> the optimum pH was high and the ligand excess needed for maximum activity was lower than for weakly coordinating ligands. For example, strongly coordinating phen and DMG have high optimum pHs, and smaller excess of the ligand is required for maximum activity than for the more weakly coordinating bipy.

To measure the changes in the catalyst structure in actual reaction solution, UV-Vis spectroscopy was found to be highly useful. UV-Vis spectroscopy has been widely used to investigate changes in the coordination sphere of Cu(II) species in aqueous media. In fact, the first Vis spectra of copper diimine complexes have been measured already in the 1950's<sup>125</sup> followed by numerous studies concerning the structures of these complexes and their spectroscopic properties.<sup>41</sup> Because of available reference data and similarities in the coordination geometry of these two catalysts, Cu-phen and Cu-bipy were used in the catalyst structure studies. With Cu-DMG the measuring of the Vis spectra was not successful since the main absorbance was observed at about 450 nm, in the region were the edge of the stronger absorbance UV-region considerably interfered with the interpretation of the spectra. Solutions suitable for Vis-measurements were rather concentrated; a copper concentration of 0.01 M was needed to clearly see the differences in the absorbance maxima.

When the reaction conditions are varied, the formation of different Cu-diimine complexes in aqueous solutions is fast and reversible. The structures of Cu-phen complexes formed under different reaction conditions and corresponding Vis-spectra are shown in Figures 23 and 24 (III). Similar spectra were measured also for Cu-bipy, the only difference being that coordinated bipy is more easily (i.e. at lower pH) replaced by the hydroxo ligands (V). In pure aqueous solution, copper sulphate forms a light blue copper hexa-aqua complex<sup>126</sup>,  $[\text{Cu}(\text{H}_2\text{O})_6]^{2+}$ , which has a wide absorbance maximum in the 800 nm region (Figures 23 and 24, species A). The addition of two equivalents of phenanthroline to this solution forms the  $[\text{Cu}(\text{phen})_2\text{X}]^{n+}$  complex in which a counter ion or water molecule complete the coordination sphere of the copper. Depending on the atom occupying the fifth coordination place, the 2:1 molar ratio of phenanthroline with different copper salts ( $\text{CuSO}_4$ ,  $\text{CuAc}_2$ ,  $\text{CuCl}_2$  and  $\text{Cu}(\text{NO}_3)_2$ ) has an absorbance maxima in the 700–730 nm region and another wide band in the 950 nm region (B).

If more than two equivalents of phenanthroline are added to an aqueous copper solution, a tris-chelated  $[\text{Cu}(\text{phen})_3]^{2+}$  complex is formed (C), the absorbance maximum is shifted to 680 nm and the shoulder at 920 nm assigned as a five-coordinate complex disappears. The addition of NaOH to aqueous solution with phen:Cu molar ratio higher than 2:1 readily forms a five-coordinate  $[\text{Cu}(\text{phen})_2\text{OH}]^+$  complex as the main absorbance is shifted to a wavelength of 690 nm (formation of complex D from species B and C). When  $\text{OH}^-$  concentration is further increased, the absorbance maximum is shifted to the 620-630 nm region indicating the replacement of a phenanthroline by a hydroxo ligand and the formation of  $[\text{Cu}(\text{phen})(\text{OH})_2]$  complex (E). Between the conditions preferable for the species D and E, a hydroxide bridged binuclear  $[(\text{phen})\text{Cu}(\text{OH})_2\text{Cu}(\text{phen})]^{2+}$  complex is also observed. Based on these results, it is obvious that by varying hydroxide ion and ligand concentrations, the amount of coordinated phenanthroline and hydroxo ligands can be controlled.

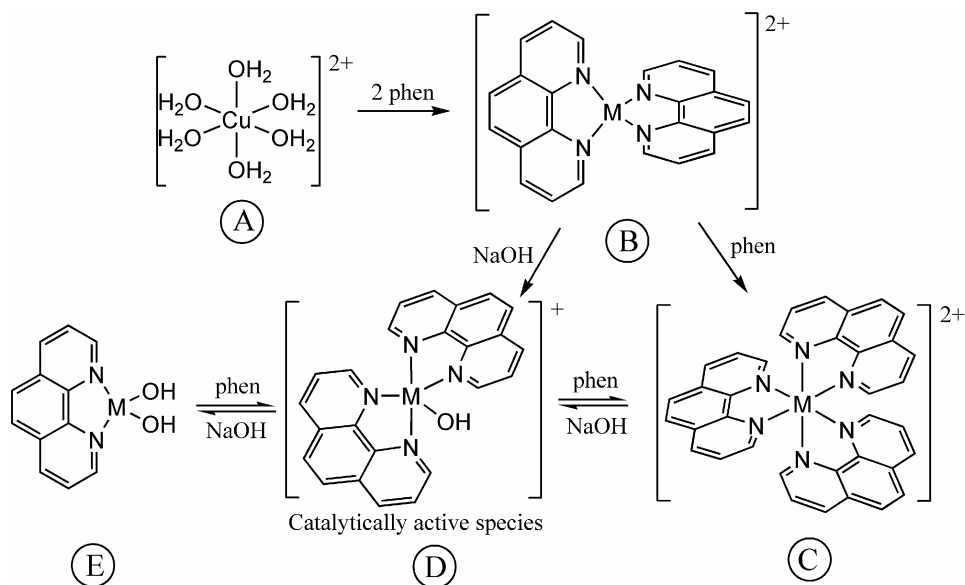


Figure 23. Cu-phen complexes formed under different reaction conditions (III). Corresponding VIS-spectra are presented in Figure 24. The labels phen and NaOH in C-E express the addition of the compounds, but not the exact molar ratio.

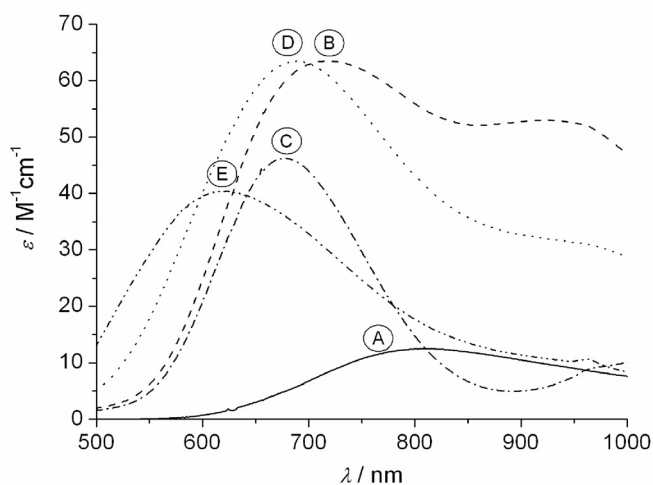


Figure 24. VIS-spectra of different Cu-phen species. Corresponding structures are presented in Figure 23. Measurements were carried out at ambient temperature and pressure with 0.01 M copper concentration.

The Vis-spectra and presented species above explain the changes observed in the alcohol conversions when pH and L:Cu molar ratio were varied in the oxidation reactions. For Cu-phen catalyst the optimum  $\text{OH}^-$  concentration was 0.05 M and L:Cu ratio 5:1. Under these conditions the absorbance maximum of the solution was at 690 nm, indicating that  $[\text{Cu}(\text{phen})_2\text{OH}]^+$  is the catalytically activity species. It is obvious that other species (Figure 23, C-E) can also be present in the solution, but the relation between the Vis measurements

and the oxidation results show the main species in the solution. Increasing the  $\text{OH}^-$  concentration shifts the absorbance maximum towards shorter wavelengths and also the oxidation activity is decreased as the main species in the solution has changed to  $[\text{Cu}(\text{phen})(\text{OH})_2]$ . On the other hand, higher ligand excess in high pH increases the oxidation activity as the conditions are more favourable for species D and C. It can be concluded that, while the high pH is prerequisite for the efficient oxidation, the role of the excess ligand is to protect the catalytically active Cu-complex from the destructive hydroxide ion coordination.

The UV-Vis measurements of Cu-bipy catalyst gave similar results as the measurements of Cu-phen. The main absorbance of active species  $[\text{Cu}(\text{bipy})_2\text{OH}]^+$  was observed at 680 nm ( $\epsilon = 60 \text{ M}^{-1}\text{cm}^{-1}$ ). To further investigate the relation between the species in solution and the catalytic activity, the reported stability constants<sup>41, 127</sup> were used to calculate the percentages of presented complexes under different conditions. When the species distributions were calculated with copper, bipy and  $\text{OH}^-$  concentrations in the oxidation experiments, a clear dependence between the concentration of  $[\text{Cu}(\text{bipy})_2\text{OH}]^+$  and the conversion of veratryl alcohol was found (Figure 25). The difference in pH-values can be partly explained by the decrease of pH during the reaction. This dependence indicates clearly that the  $[\text{Cu}(\text{bipy})_2\text{OH}]^+$  complex is the active catalyst in the oxidation of veratryl alcohol.

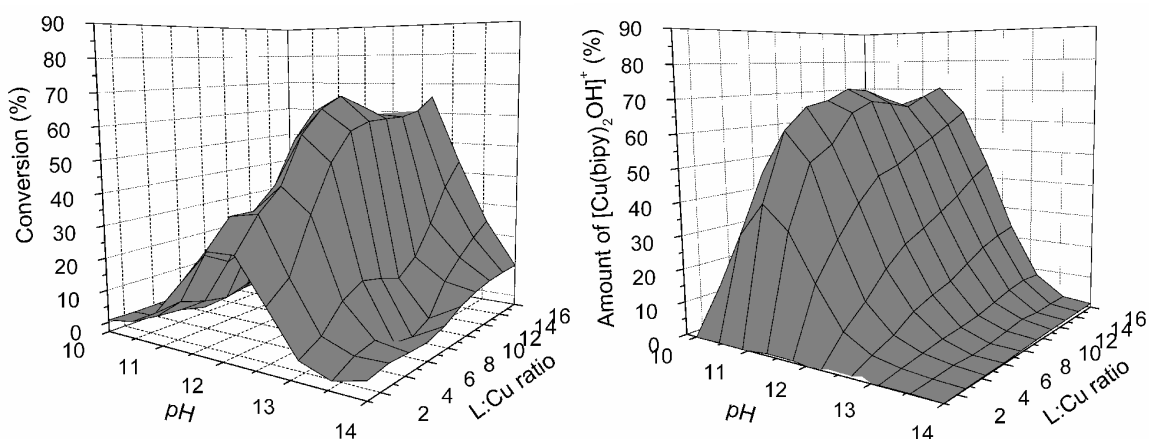


Figure 25. Optimisation of the veratryl alcohol conversion and the percentage of copper as  $[\text{Cu}(\text{bipy})_2\text{OH}]^+$  under different pH and bipy:Cu molar ratios (**V**). Reaction conditions for optimisation experiment were: temperature  $80^\circ\text{C}$ ,  $\text{O}_2$  pressure 10 bar, reaction time 3 h, 0.2 ml veratryl alcohol, 10 ml solvent, veratryl alcohol:copper molar ratio 500:1.

Pyridine-2-carboxaldehyde oxime (PAO) was studied as a ligand which combines the structures of bipyridine and dimethyl glyoxime (**IV**). Unfortunately, the activity of the Cu-PAO catalyst was lower than the activities of both Cu-bipy and Cu-DMG. The structure and Vis spectra of Cu-PAO complexes are slightly different from Cu-phen and Cu-bipy because the oxime groups in the ligand are also deprotonated under highly alkaline

conditions. Copper sulphate together with PAO forms a dark green solution with an absorbance maximum at 600 nm (Table 2). Already in the neutral solution one of the ligands is deprotonated forming the intramolecular hydrogen bridge (=N–O–H··O–N=) between two oxime oxygen atoms of the *cis*-oriented ligands. As the OH<sup>-</sup> concentration is increased the absorbance maximum of the main band is shifted from the 600 to 630 nm region and its intensity is increased significantly. This shift is due to deprotonation of the remaining OH-group of the oxime ligands. At optimum OH<sup>-</sup> concentration (0.05 M) for oxidation reaction, absorbance maximum is at 625 nm. Under considerably alkaline conditions the absorbance maximum is shifted to the 600 nm region and molar absorptivities are considerably lowered, because of the replacement of pyridine-2-carboxaldehyde oxime by hydroxo ligands as was observed with Cu-bipy and Cu-phen complexes. When comparing these results to optimum conditions (0.05 M NaOH, L:M ratio 5:1-2:1) of veratryl alcohol oxidation and species formed with Cu-bipy and Cu-phen, it is suggested that the structure of the active catalyst is [Cu(PAO)<sub>2</sub>OH]<sup>-</sup> with both ligands deprotonated.

Table 2. UV-Vis spectra of Cu-PAO under different pH and L:M ratios. Measurements were carried out at ambient temperature and pressure with a 5 mM copper concentration.

PAO:Cu molar ratio	[NaOH] (M)	$\lambda_{max}$ (nm)	$\epsilon_{max}$ (M <sup>-1</sup> cm <sup>-1</sup> )
2:1	-	600	80
2:1	0.01	635	240
2:1	0.05	625	150
2:1	> 0.5	595	66

## 4.5 Solid state structures

It was shown in chapter 4.4 that under alkaline conditions copper(II) ions together with diimines readily form five-coordinated structures with hydroxide ions occupying the fifth coordination site. To obtain detailed information about the bonding and coordination geometry needed for the catalytic activity, crystals suitable for structure determination by x-ray diffraction were grown from alkaline catalyst solutions by slow evaporation of water. In solutions containing phen and PAO ligands bis(diimine)copper(II) complexes Cu(phen)<sub>2</sub>CO<sub>3</sub> · 7 H<sub>2</sub>O and Cu(PAO)<sub>2</sub>SO<sub>4</sub> · 3 H<sub>2</sub>O were crystallised (Figure 26). The phenanthroline complex crystallised with carbonate as a counter ion as a consequence of carbon dioxide dissolution from air. The coordination polyhedron of the copper atom in both complexes is a distorted square pyramid where the three nitrogen and one oxygen atoms form the base of the polyhedron. One of the ligand nitrogen atoms (N4 in phen and

N2 in PAO) occupies the axial position and its Cu-N bond is significantly elongated. It is interesting that even though the Cu-PAO complex was crystallised under highly basic conditions, the ligands remain unprotonated and the charge of the complex is balanced by the sulphate anion while in solution the OH-groups of the ligands are protonated.

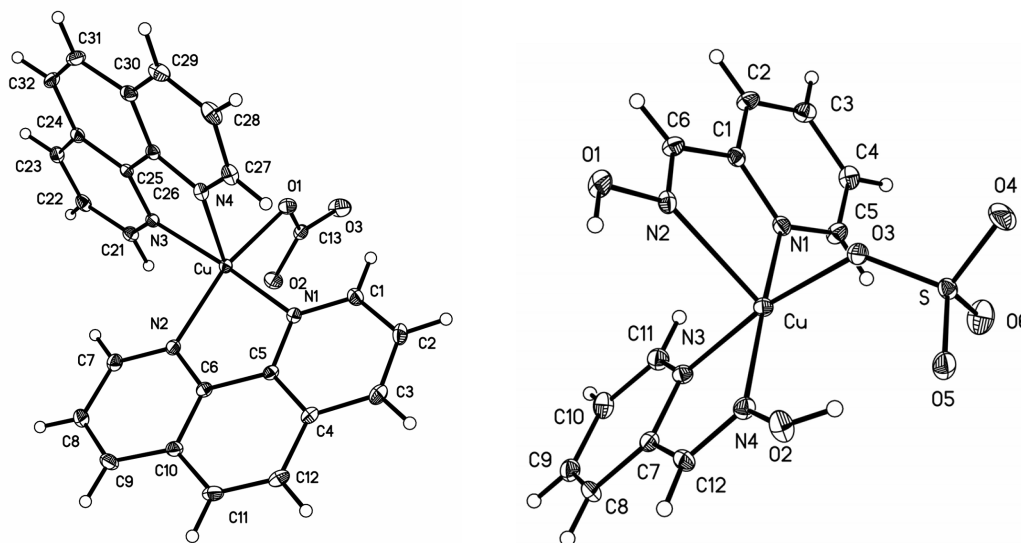


Figure 26. Molecular structures of  $\text{Cu}(\text{phen})_2\text{CO}_3 \cdot 7 \text{H}_2\text{O}$  (**III**, determined also by Eldik and coworkers<sup>128</sup>) and  $\text{Cu}(\text{PAO})_2\text{SO}_4 \cdot 3 \text{H}_2\text{O}$  (**IV**). The solvent molecules are omitted for clarity.

Cu-DMG crystallises as a dinuclear complex where the fifth coordination place of copper is occupied by an oxygen atom of the neighbouring complex (Figure 27).<sup>129</sup> One reason for the maximum activity of Cu-DMG at pH over 13 might be the destabilisation of the dimeric structure as more space for oxygen and alcohol coordination is available in the mononuclear complex.

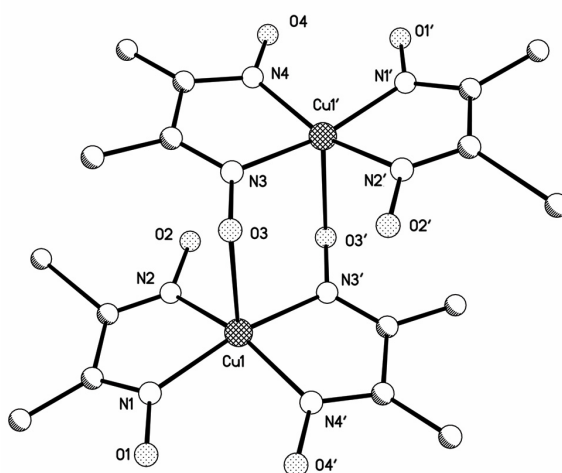


Figure 27. Structure of  $\text{Cu}(\text{DMG})_2$ . The hydrogen atoms are omitted for clarity.

Crystallisation of Cu-bipy catalyst was not so successful as only brittle blocks were formed and experiments also using  $\text{Cu}(\text{NO}_3)_2$  as copper precursor were carried out. Even though

the data set from first measured crystals was not sufficient enough for high quality structure determination, Figure 28 is presented to describe the different coordination spheres of the Cu(II) ions. A picture describing only the coordination spheres is also presented. Interestingly, this structure includes both of the most common coordination modes for copper diimines, the bisligated  $[\text{Cu}(\text{bipy})_2\text{X}]$  and hydroxide bridged  $[(\text{bipy})\text{Cu}(\text{OH})_2\text{Cu}(\text{bipy})]$ . These structures are further bridged with  $\text{NO}_3^-$  anion. Coordination geometries of copper atoms seem to be square pyramidal where N2 and N7 atoms of the  $[\text{Cu}(\text{bipy})_2\text{O}]$  core, and O2 and O5 of the  $(\text{bipy})\text{Cu}(\text{OH})_2\text{Cu}(\text{bipy})$  core occupy the axial position.

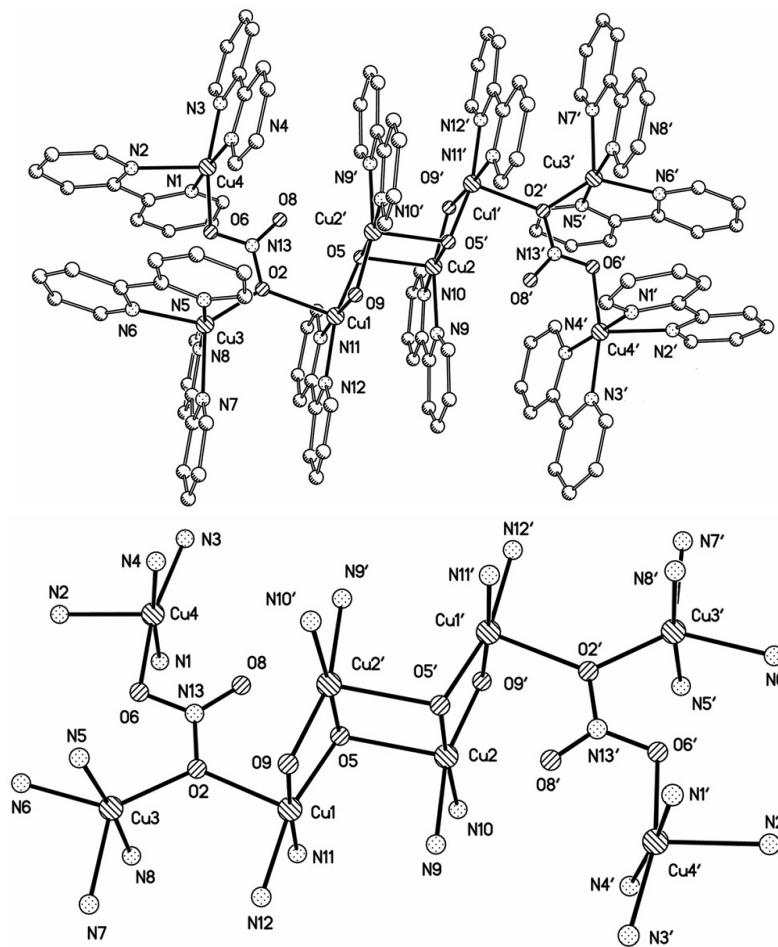


Figure 28. Structure of a Cu-bipyridine complex and copper coordination spheres. In the lower figure the carbon atoms are also omitted for clarity.

In further crystallisation experiments, higher quality crystals were obtained from both copper sulphate and nitrate solutions. However, these complexes included only the  $\text{OH}^-$  bridged structures (Figure 29). The same structures for the binuclear sulphate<sup>130</sup> and nitrate<sup>131</sup> complexes have been measured earlier.

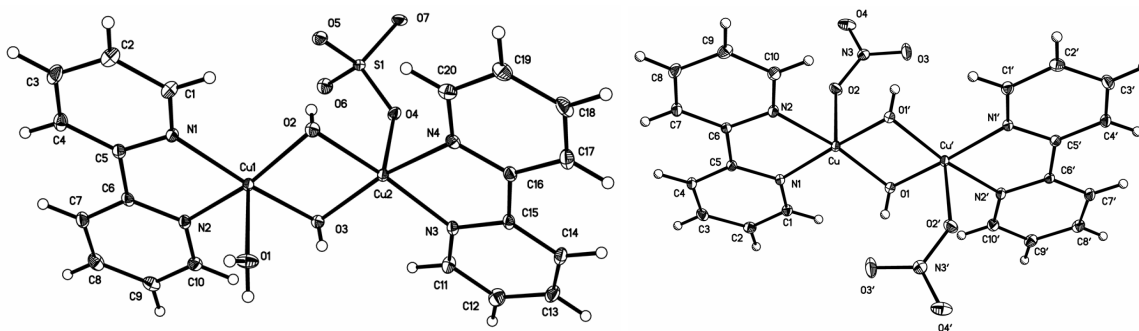


Figure 29. Molecular structures of  $(bipy)Cu(H_2O)(OH)_2Cu(SO_4)(bipy) \cdot 3 H_2O$  and  $(bipy)Cu(NO_3)(OH)$  (the asymmetric unit is formed by half of the molecule). Uncoordinated solvent molecules are omitted for clarity.

In general, all the determined structures have bond lengths and angles typical for copper diimine complexes.<sup>132</sup> In square pyramidal coordination the axial Cu-N distance was about 2.2 Å while the lengths of other Cu-N distances were 1.9-2.0 Å. The coordinating ligands and copper atoms formed N-Cu-N bite angles of 78-82°.

#### 4.6 Effect of the ligand structure on catalytic activity

After solving the solution and solid state structures of the catalysts, an investigation of the effects of ligand substituents was carried out (V). To clarify both steric and electronic effects, a set of substituted Cu-bipy complexes was studied in the oxidation of veratryl alcohol. The oxidation results of 3-, 4-, 5- and 6-substituted bipyridines were compared to determine the steric effects and methyl, methoxy and carboxylic acid substituents in 4,4'-position were used for comparing the electronic effects (Figure 30).

Substituents of the ligand had a considerable effect on the oxidation activity. It was observed that chelation similar to that with the unsubstituted bipyridine is a prerequisite for high catalytic activity. The oxidation activities of ligands that altered the coordination sphere of copper relative to unsubstituted 2,2'-bipyridine were considerably lower. Only the ligands substituted from the 4- or 5-positions of pyridine rings (no steric hindrance) formed copper complexes with high oxidation activity. For example, in ligand 5 (Figure 30) the steric interaction of bulky carboxylic acid groups twists the planar structure of the ligand and practically no activity in the oxidation was observed. Further studies with different 4,4'-substituted ligands (2-4) showed that electron donating methyl and methoxy groups increased the oxidation activity of their Cu-complexes. For these catalysts, the reaction conditions were optimised (Table 3) and the highest conversions were obtained in 0.05 M NaOH solution with high ligand excess (L:Cu molar ratio 16:1).

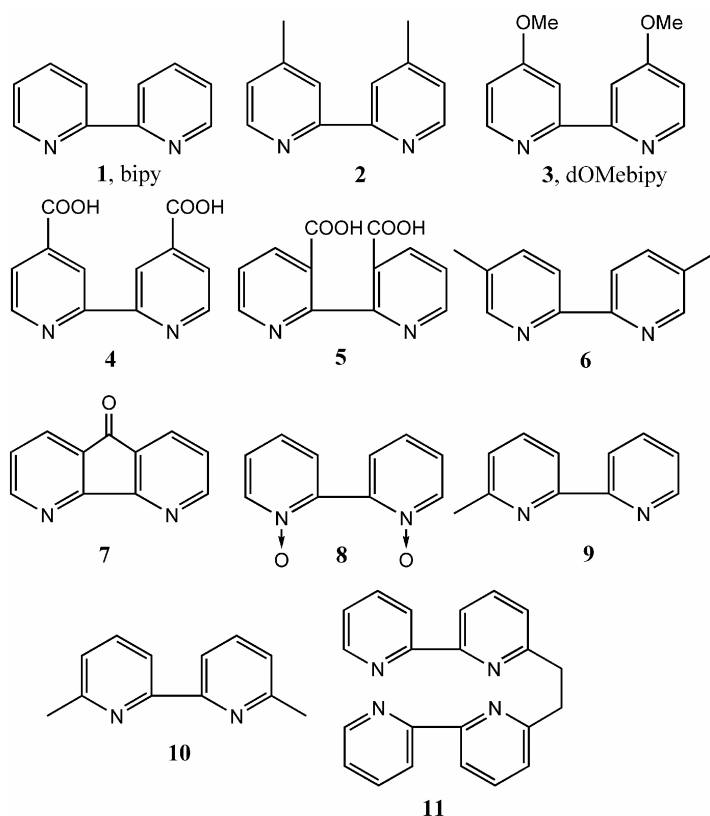


Figure 30. Bipyridine ligands with different substituents (**V**).

Table 3. Optimised pH and L:Cu molar ratios and oxidation results with copper and ligands 1-4 and 6 (**V**). Temperature 80 °C, O<sub>2</sub> pressure 10 bar reaction time 3 h, 0.2 ml veratryl alcohol, 10 ml solvent, veratryl alcohol:copper molar ratio 500:1.

Ligand	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>6</b>
Optimised pH	12	12.7	12.7	12.7	12.7
Optimised L:Cu molar ratio	8:1	16:1	16:1	16:1	16:1
Conversion (%) <sup>a</sup>	67	86	87	68	82
TON <sup>a</sup>	335	430	435	340	410

## 4.7 Monitoring of the oxidation reaction

To obtain information on the mechanism and conditions affecting the veratryl alcohol oxidation, a series of reaction monitoring techniques were applied. For these studies Cu-phen catalyst was used. With parallel pH and gas chromatographic analysis information of hydroxide consumption during the oxidation is obtained. To follow the bulk trends of the reaction, *in situ* ATR-IR spectroscopy was applied, while UV-Vis spectroscopy was a key method to determine the structure and oxidation states of the catalyst.

#### 4.7.1 Reaction monitoring by pH and GC-analysis

The oxidation of veratryl alcohol with Cu-phen catalyst was monitored by parallel pH and GC-analysis in order to find out possible correlations between aldehyde formation and the consumption of hydroxide ions (III). These experiments were carried out in 400 ml glass vessel fitted inside the same steel reactor used for the screening experiments. Samples were withdrawn from the reaction solution via a lead-through installed on the cover of the reactor. During the reaction, the pH decreased and the oxidation decelerated at pHs below 10. The reaction could be restarted by the addition of NaOH, which is marked in Figure 31. It seems that the veratryl alcohol oxidation and  $\text{OH}^-$  consumption proceed in parallel (Figure 31), but the actual molar ratio between these two variables is around 10. The high aldehyde: $\text{OH}^-$  ratio indicates that the catalytic cycle itself does not consume  $\text{OH}^-$  ions, at least not stoichiometrically to aldehyde formation. However, the alkaline conditions are needed to preserve the structure of active catalyst and for the initiation of the reaction. A possible reason for the minor  $\text{OH}^-$  consumption during the reaction could be the formation of hydroperoxy radical, which consumes base to form superoxide radical anion. Another reason for pH decrease can be the formation of small amounts of veratric acid.

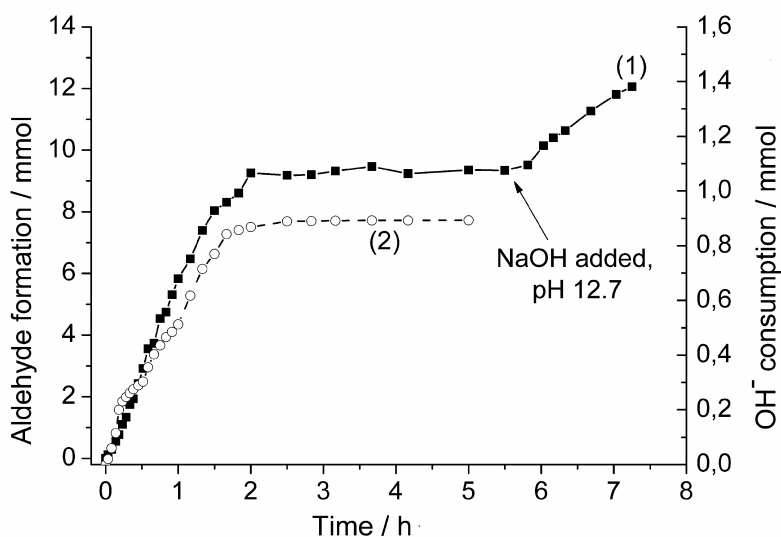


Figure 31. Rate of oxidation and total  $\text{OH}^-$  consumption in the Cu-phen catalysed reaction: (1) formation of veratraldehyde and (2) consumption of  $\text{OH}^-$  ions. Reaction conditions were: temperature 80 °C,  $\text{O}_2$  pressure 10 bar, initial pH at room temperature 11.6, 200 ml solution, 4.0 ml veratryl alcohol, veratryl alcohol:Cu molar ratio 500:1 (III).

## 4.7.2 Reaction monitoring by ATR-IR

In our previous studies, *in situ* ATR-IR spectroscopy was found to be highly useful for monitoring Co(salen) catalysed oxidation of veratryl alcohol.<sup>9c</sup> An aqueous solution is a challenging media for IR measurement as the strong absorption of water might interfere with the absorption from the sample. However, in ATR (Attenuated Total Reflection) the path length of the evanescent wave is in the order of microns, and the interference from highly absorbing solvents is overcome. ATR-IR can be used to observe bulk trends like the rate of the product formation or the formation possible side products and long-living, accumulating intermediates.<sup>133</sup>

The spectra of the Cu-phen catalysed reaction under 10 bar of oxygen show a rise of vibration peaks belonging to the veratraldehyde (Figure 32).<sup>134</sup> The oxidation of veratryl alcohol is clearly observed as the appearance of a peak at  $1675\text{ cm}^{-1}$  (C=O stretching of the aldehyde carbonyl group) and the shift of the absorption of the methoxy-substituents from  $1264$  to  $1273\text{ cm}^{-1}$ . Various measurements under different reaction conditions were carried out, and the following observations were made: No oxidation occurs without both an oxygen atmosphere and alkaline conditions the oxidation rate is faster at the beginning of the reaction but slows down as alcohol concentration decreases, and aldehyde is the main oxidation product (**III**).

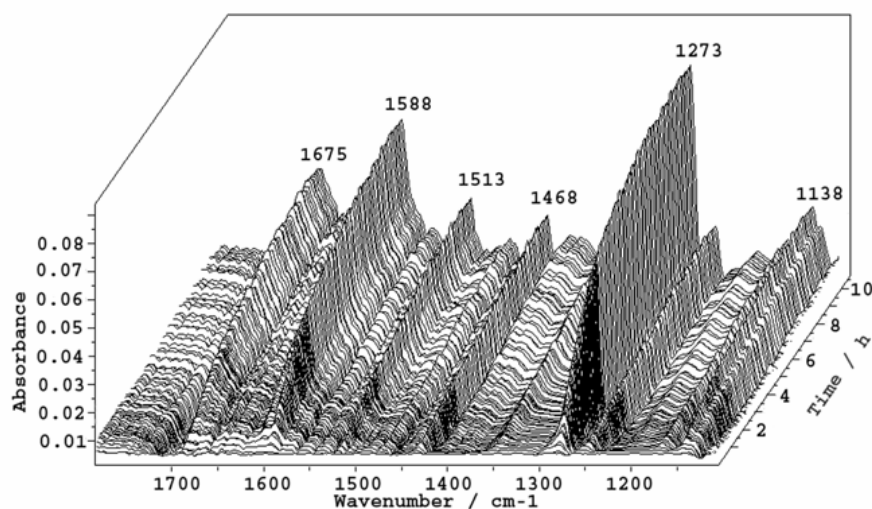


Figure 32. *In situ* ATR-IR spectra of the oxidation of veratryl alcohol. The main absorbances of aldehyde formation are:  $\nu(\text{C}=\text{O})$   $1675$ ,  $\nu(\text{aromatic C-C})$   $1588$  and  $1513$ ,  $\nu(\text{methoxy C-O})$   $1273$  and  $1138\text{ cm}^{-1}$ . Reaction conditions were: temperature  $80\text{ }^{\circ}\text{C}$ ,  $\text{O}_2$  pressure 10 bar, 100 ml water-dioxan solution, 4.0 ml veratryl alcohol, pH 12.6, veratryl alcohol:Cu molar ratio 100:1 (**III**).

### 4.7.3 Reaction monitoring by UV-Vis spectroscopy

UV-Vis spectroscopy can be used also for monitoring the oxidation reaction. The veratryl aldehyde formation is seen in the UV region as growth of a peak at 308 nm. This absorption is assigned to  $n \rightarrow \pi^*$  transitions in the aldehyde C=O group. The growth of the peak is presented in Figure 33. The same figure also expresses how the edge of the UV region is shifted from the 350 to 400 nm region as aldehyde concentration is increased. In measurements in the UV region, the samples had to be diluted to a thousandth of the concentration for Vis measurement to obtain appropriate absorbances.

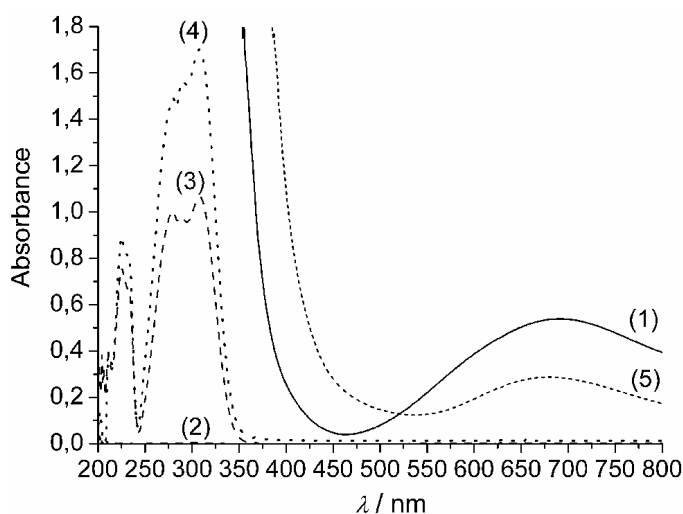


Figure 33. UV-Vis spectra of veratryl aldehyde formation and shifting of the edge of UV-absorption: (1) Catalyst as 0.01 M solution, (2) veratryl alcohol added, (3) after a 5 h reaction, 58% of aldehyde formed (by GC-analysis), (4) 20 h, 93% aldehyde, (5) after 20 h (0.01 M solution. Spectra 1 and 5 have been measured with H<sub>2</sub>O as the blank spectrum, while the blank for spectra 2-4 was measured after the addition of veratryl alcohol. These samples were diluted to 0.01 mM (of Cu). Reaction conditions were: temperature 80 °C, O<sub>2</sub> pressure 1 bar, pH 12.6, veratryl alcohol 2.9 ml, 100 ml solvent, veratryl alcohol:Cu molar ratio 20:1.

The changes in the catalyst structure as well as the oxidation state of copper during the reaction can be seen in the visible region of the UV-Vis spectra. When veratryl alcohol is added to an aqueous solution of  $[\text{Cu}(\text{phen})_2]^{2+}$ , the absorbance maximum is shifted from the 700 nm region to 730–740 nm, indicating coordination of veratryl alcohol to the copper complex. Without a base the alcohol cannot be deprotonated and the reaction does not proceed. Addition of NaOH to this solution turns the colour from blue to green and small bands at 410 and 525 nm regions in the spectrum are observed as an indication of the formed Cu(I) species. A pure Cu(I)-phen complex has a dark red colour and strong absorbances at 405 and 535 nm. The reduction is seen more clearly when the reaction is done under an argon atmosphere (Figure 34, spectra 1–3); when veratryl alcohol is added,

the Cu(II) complex is slowly reduced to Cu(I) as absorbance at 690 nm decreases, and those at 410 nm and 525 nm increase. After the addition of oxygen, the absorbance of Cu(II) species increases again (spectra 4-5) and aldehyde production starts. If the reaction solution is degassed and placed under an argon atmosphere again, the colour changes to dark brown and only the absorbances of Cu(I) are observed. As a conclusion, the cycle between Cu(I) and Cu(II) species alters as long as there is enough alcohol and hydroxide for the reduction of the Cu(II) species and oxygen to re-oxidise the Cu(I) species.

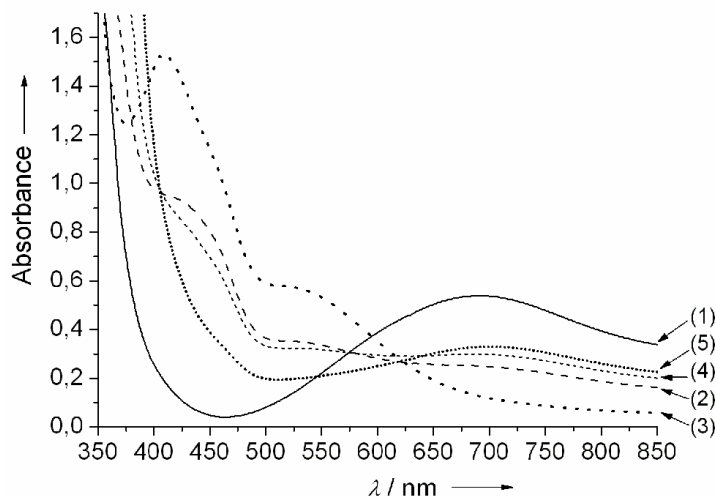


Figure 34. A UV-Vis spectrum of Cu(II) reduction to Cu(I) by alcohol under argon, and reoxidation after oxygen addition. (1) Cu(II)-phen complex under argon, (2) veratryl alcohol added, (3) 60 h under argon, no aldehyde formation, (4) 1 h after O<sub>2</sub> addition, 18% aldehyde (5) 23 h, 93% aldehyde. Cu(I) samples were diluted for the measurement. Reaction conditions as in Figure 33 (III).

## 4.8 Oxidation mechanism

Previous chapters have described the use of complementary techniques to gain information about the Cu-phen catalysed oxidation of veratryl alcohol by dioxygen. Based on these results, a suggestion for the reaction mechanism is expressed in Figure 35. The structure of catalytically active species was shown by Vis spectroscopy and the correlation between the high catalytic activity and existence of active [Cu(phen)<sub>2</sub>OH]<sup>+</sup> complex in solution. The presented mechanism finds some similarities with the mechanism of galactose oxidase; in the catalytic cycle, alcohol is oxidised to aldehyde and oxygen converted to hydrogen peroxide. In addition, the results indicate a mechanism very similar to one proposed by Tretyakov *et al.* for the oxidation of propanol.<sup>46</sup>

It seems that the coordination of hydroxo ligand to [Cu(phen)<sub>2</sub>]<sup>2+</sup> is essential for the reduction of the catalyst to Cu(I) species by alcohol (B), as in neutral or acidic media no reaction occurs. As the reduction is observed under an argon atmosphere, the catalyst should simultaneously oxidise a half equivalent of alcohol to aldehyde. By decreasing the

alcohol:copper ratio to 10:1-20:1, a low percentage of aldehyde was detected but no accurate molar ratio between the catalyst concentration and aldehyde formation could be determined. The coordination of  $\text{OH}^-$  to  $[(\text{phen})_2\text{Cu}^{\text{I}}]^+$  and deprotonation of coordinating alcohol molecule yields Cu(I)-alkoxo complex (C). When oxygen is added, a Cu(II)-peroxo species (D) is formed. This species is able to remove hydrogen atoms from the  $\alpha$ -methylene of alcohol forming a Cu(II)-hydroperoxo complex with coordinated ketyl-radical (E). The ketyl radical of alcohol reduces Cu(II) to Cu(I) in intramolecular one-electron transfer from carbon to copper and aldehyde is formed (F). In the last step the new veratryl alcohol is coordinated to copper and hydrogen peroxide is released. The formation of hydrogen peroxide has been shown earlier with phenylglyoxylic acid, a reagent which reacts with hydrogen peroxide to form benzoic acid.<sup>135</sup>

For the short living intermediates in the catalytic cycle, no direct spectroscopic evidence is available. However, for observations like the reduction of Cu(II) by alcohol, only minor  $\text{OH}^-$  consumption during the reaction, oxidation of Cu(I) by oxygen, and formation of hydrogen peroxide can be reasonably explained by the presented mechanism. In addition, the catalytic cycle is in good agreement with the mechanisms of galactose oxidase<sup>51</sup> and the phenoxy radical complexes mimicking it<sup>52-58</sup>.

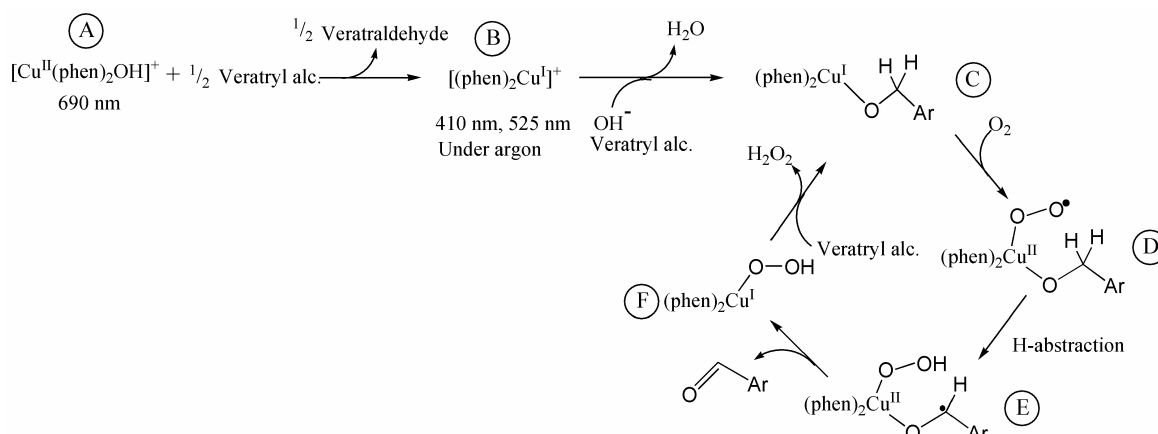


Figure 35. Proposed reaction mechanism for  $[\text{Cu}(\text{phen})\text{OH}]^+$  catalysed oxidation of veratryl alcohol by dioxygen. The catalytic cycle -C-D-E-F- proceeds without consumption of NaOH (III).

## 4.9 Delignification studies

To finally evaluate the catalytic performance of the developed catalysts in softwood oxygen delignification, two series of experiments were done at KCL. The first experiments for Cu-phen and Cu-bipy catalysts were carried out using a Mark 2 autoclave. Reaction conditions for these experiments were: water 3.2 l, pulp 250 g, NaOH 5.75 g,  $\text{MgSO}_4 \cdot 8 \text{H}_2\text{O}$  (= Epsom salt) 1.25 g, 0.07-0.08 wt-% copper (of dry pulp), ligand in molar ratio 2:1,

O<sub>2</sub> pressure 8 bar, temperature 90 °C and reaction time 60 minutes. The results in Table 4 (experiments 1-4) show that Cu-phen and Cu-bipy are highly active in delignification, but also cause significant viscosity losses in the concentration used. In the presence of the catalysts, kappa levels were lowered from 31.8 to 15-16 and viscosity from 1230 to 620-630 dm<sup>3</sup>/kg, while the corresponding values for uncatalysed pulp were 20.1 and 1070 dm<sup>3</sup>/kg.

The second series of delignification experiments were carried out after the oxidation experiments with the substituted Cu-bipyridines. Because of its high activity in model compound studies, copper sulphate together with 4,4'-dimethoxy-bipyridine (dOMebipy) was also studied in pulp delignification. It was also hoped that the high oxidation activity would yield higher selectivity, i.e. decreased fibre damage. The reaction setup for these experiments was quite different from the previous one: The experiments were done in zirconium-lined one-litre autoclaves with 25 g of softwood pulp, 0.02% copper (of dry pulp) and L:Cu molar ratios 2:1 and 5:1. The reaction time was set as at 30 min heating period (by hot air bath) and 30 min at reaction temperature (90 °C). These experiments were carried out using a very low catalyst concentration (0.02 wt-% Cu of dry pulp). As in the model compound studies, the Cu-dOMebipy catalyst was more active than Cu-bipy, but also resulted in the highest loss in the viscosity of pulp (Table 4, lines 5-10). Increasing the L:Cu ratio from 2:1 to 5:1 also gave increased delignification for both Cu-bipy and Cu-dOMebipy catalyst.

Table 4. Results of the delignification experiments with high (experiments 2-4) and low (experiments 6-10) catalyst concentrations. Temperature 90 °C, reaction time 60 min, initial O<sub>2</sub> pressure 8 bar, kappa of pulp 31.8 (31.3 in exp. 5-10), brightness 26.8 and viscosity 1230 dm<sup>3</sup>/kg (1200 dm<sup>3</sup>/kg in exp. 5-10).

Exp.	Catalyst	ligand:Cu molar ratio	Final pH	Kappa number	ISO brightness (%)	viscosity (ml/g)
1	no catalyst		10.6	20.1	30.5	1070
2	CuSO <sub>4</sub>		10.5	20.1	29.6	1050
3	Cu-phen	2:1	10.0	16.1	31.6	630
4	Cu-bipy	2:1	9.8	15.0	32.4	620
5	no catalyst		12.21	18.1	32.4	1040
6	CuSO <sub>4</sub>		12.12	18.0	30.9	870
7	Cu-bipy	2:1	12.16	17.9	31.9	830
8	Cu-bipy	5:1	12.11	17.1	32.2	810
9	Cu-dOMebipy	2:1	12.14	17.6	31.8	870
10	Cu-dOMebipy	5:1	12.05	16.1	33.0	800

When the results of our delignification studies are compared with reported experiments with transition metal complexes<sup>85-95</sup>, a similar trend can be observed in all the cases: lignin removal is increased to some extent, but the catalysts cause also depolymerisation of carbohydrates. In the studies of Germer<sup>93-95</sup>, the conclusions of the catalytic properties of Cu-phen were more optimistic than what our studies indicated. The reason could be that in Germer's experiments a high kappa number pulp was used, giving higher decrease of the kappa values during the reaction. In addition, the decrease of the viscosity has not been clearly reported.

## 5 Conclusions

The parallel screening method presented in this thesis is a simple, cheap and easily available system for studying different catalyst combinations as well as for optimisation of reaction parameters. The method enables reliable testing and analysis of tens of samples per day and as has been shown here, is a highly useful tool for catalyst research. By changing the solvent and oxygen atmosphere inside the reactor, it can be easily used for different applications, for example in a search for new polymerisation catalysts.

New catalysts active in the oxidation of veratryl alcohol were found by the screening of over 200 metal-ligand combinations. These copper-diimine and copper-diamine complexes oxidised veratryl alcohol from moderate to high activity under conditions suitable for oxygen delignification; alkaline aqueous solution, temperature 80 °C and O<sub>2</sub> pressure 10 bar. The most active catalysts were also tested in the final application, oxygen delignification of softwood pulp. As was predicted by the model compound studies, copper-diimine complexes were active delignification catalysts but caused simultaneous depolymerisation of carbohydrate fibres. It can be concluded that the main aim of the thesis to find active delignification catalysts was partly reached, but it seems that enhancing catalyst selectivity is one of the main challenges for transition metal based delignification catalysts.

The secondary aim of understanding of the active catalyst structures and catalytic reactions can be considered to be reached. Even though the actual catalyst structures are ignored during the screening experiments, the catalytically active species could be determined on the basis of reaction optimisation experiments, UV-Vis spectroscopy, species distribution calculations and XRD measurements of complexes crystallised from catalyst solutions. The development of substituted bipyridines with increased activity showed that after finding the active complexes, the fine-tuning of the structure provided enhanced catalytic properties. The oxidation reaction of veratryl alcohol was monitored with GC-analysis, pH measurements, ATR-IR spectroscopy and UV-Vis spectroscopy. These complementary techniques gave valuable information about the oxidation of veratryl alcohol and a suggestion for the catalytic cycle based on these observations was made. In mechanism investigation the reaction intermediates are often short-living in nature and therefore difficult to verify experimentally. Even though direct evidence for all steps in the mechanism could not be presented, different mechanistic studies on catalytic oxygen activation are of general importance; if not giving a complete solution, they can provide new insights for other researchers investigating similar systems.

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