Studies on Veratryl Alcohol Oxidation Catalyzed by Co(salen) Type Complexes and Molecular Oxygen in Aqueous Solution

Kaisa Kervinen

Laboratory of Inorganic Chemistry
Department of Chemistry
University of Helsinki
Finland

Academic Dissertation

To be presented, with the permission of the Faculty of Science of the University of Helsinki, for public criticism in the Auditorium A110 of Chemicum, A.I.Virtasen Aukio 1, on 4th of February, 2005 at 12 noon.

Supervisor

Professor Markku Leskelä
Laboratory of Inorganic Chemistry
Department of Chemistry
University of Helsinki
Finland

Reviewers

Dr. Tom Visser
Department of Inorganic Chemistry and Catalysis
Debye Institute
University of Utrecht
The Netherlands

Professor Riitta Keiski
Department of Process and Environmental Engineering
Mass and Heat Transfer Process Laboratory
University of Oulu
Finland

Opponent

Dr. Isabel Arends
Laboratory of Biocatalysis and Organic Chemistry
Department of Biotechnology
Delft University of Technology
The Netherlands

Abstract

The catalytic activation of dioxygen to perform selective oxidations of organic substrates would provide greener chemical processes, as the side products of these reactions are mostly water or hydrogen peroxide. It is also preferred to perform such reactions in aqueous media, as water is a cheap and harmless solvent. Several transition metal complexes have been studied for oxygen activation, but mainly in organic solvents. Also, the mechanisms of these reactions are not fully understood. However, for a more rational catalyst design it is imperative to understand the catalytic process in detail.

In this thesis Co(salen) [salen = N,N'-bis(salicylidene)ethylenediamine] type complexes were studied as oxygen activators for the selective oxidation of a lignin model compound using water as the solvent and molecular oxygen as the oxidant. In the first part of this work, several Co(salen) type complexes were tested for catalytic oxidation of veratryl alcohol and the effect of reaction conditions on activity was carefully monitored by varying temperature, pH, concentration, oxygen pressure, solvent and the type of the axial base.

In the second part of this work, the reaction mechanism of Co(salen) catalyzed oxidation of veratryl alcohol was studied with *in situ* ATR-IR, UV-Vis and Raman spectroscopic techniques. The combination of three complementary spectroscopic techniques was shown to be a powerful method to observe different intermediates during an on-going reaction and consequently help to elucidate the reaction mechanism. In addition, the *in situ* ATR-IR spectroscopy was used to study the similar Cu(phenantroline) catalyzed oxidation reaction.

Preface

The experimental part of this thesis was carried out at the Laboratory of Inorganic Chemistry, University of Helsinki, Finland, the Department of Materials and Catalysis, University of Ulm, Germany and the Department of Inorganic Chemistry and Catalysis, University of Utrecht, The Netherlands during the years 2000-2004. I want to thank all the staff in these laboratories for their help during this work.

I owe my deepest gratitude to my supervisor Professor Markku Leskelä for providing me guidance, criticism and support during my studies, for giving me the freedom to explore new opportunities and for always welcoming me back to my homelab. I am greatly indebted to Docent Timo Repo for all the help and advice during this work. This book would not exist without the support I received at the times when it got tough.

I am thankful for my reviewers Dr. Tom Visser and Professor Riitta Keiski for valuable comments and criticism on this work. My sincere thanks go to Dr. Isabel Arends. I am deeply honoured to have such an expert on alcohol oxidation as my opponent.

I am grateful to Professor Bernhard Rieger and Dr. Markus Allmendinger for welcoming me to Ulm and for introducing me to ATR-IR spectroscopy. Also thanks to the whole group in Ulm for many memorable times in- and outside work. I am sincerely thankful to Professor Bert Weckhuysen for giving me the opportunity to learn *in situ* spectroscopy in Utrecht, and for being so understanding during my struggle to finish this study. My warmest thanks go to Gerbrand Mesu, I really appreciate all the help I got and all the work we did together. I wish you a lot of success in the future. And Fouad, it was a lot of fun to measure Raman with you.

I want to thank my co-oxidation-team members in Finland, Petro Lahtinen and Heikki Korpi. It has been inspiring, rewarding and fun working with you guys! I hope to keep in touch with you, wherever you end up in. Many thanks go to the whole Catlab for such a great working atmosphere and also to the "B-wing" for coffeeroom company. Additional thanks to Eki-setä for all the analytical coffeebreak discussions.

I want to thank my mother Silja and my father Aarre, my sister Sanna and my brother Esa for always supporting and helping me over the years. Thank you Mari, Riikka, Nina, Mirka, Ellu, Kati, Tuulia, Ari, Anca, Kerstin, Martin and others for being wonderful friends and helping me to forget work in my freetime. And my dear Kees; thank you for being there for me during the tough writing part and for making Utrecht my new home.

Utrecht, January 2005

Kaisa Kervinen

Contents

List of Original Publications

This thesis is based on the following original publications, which are referred to in the text by Roman numerals I-V.

I. K. Kervinen, P. Lahtinen, T. Repo, M. Svahn and M. Leskelä: 'The effect of reaction conditions on the oxidation of veratryl alcohol catalyzed by cobalt salen-complexes' *Catalysis Today 75* (2002) 183-188.

II. K. Kervinen, H. Korpi, M. Leskelä and T. Repo: 'Oxidation of veratryl alcohol by molecular oxygen in aqueous solution catalyzed by cobalt salen-type complexes: the effect of reaction conditions' *J. Mol. Catal. A: Chemical 203* (2003) 9-19.

III. K. Kervinen, M. Allmendinger, M. Leskelä, T. Repo and B. Rieger: 'In situ ATR-IR spectroscopy: a powerful tool to elucidate the catalytic oxidation of veratryl alcohol in aqueous media' *Phys. Chem. Chem. Phys. 5* (2003) 4450-4454.

IV. K. Kervinen, H. Korpi, J.G. Mesu, F. Soulimani, T. Repo, B. Rieger, M. Leskelä and B.M. Weckhuysen: 'Mechanistic insights into the catalytic oxidation of veratryl alcohol with Co(salen) and oxygen in aqueous media: an in situ spectroscopic study' submitted to *Eur. J. Inorg. Chem.*

V. H. Korpi, K. Kervinen, M. Leskelä and T. Repo: 'Oxidation of veratryl alcohol by Cu-phenantroline activated molecular oxygen in aqueous alkaline solutions: catalytic active species and mechanism' submitted to *J. Chem. Soc., Dalton Trans.*

Abbreviations

acacen	N,N'-bis(acetylacetone)ethylenediamine)
ATR	Attenuated Total Reflection
bipy	bipyridine
DMF	dimethylformamide
d	duplet (related to a vibration peak in IR-spectrum)
e_g	axial d-orbitals after energy "splitting" in octahedral ligand field
en	ethylenediamine
EPR	Electron Paramagnetic Resonance
GC	Gas Chromatography
Im	Imidazole
IR	Infrared
LiP	lignin peroxidase
LMCT	ligand to metal charge-transfer
m	medium (related to a vibration peak in IR-spectrum)
MeO	methoxy
MLCT	metal to ligand charge-transfer
m-s	medium-strong (related to a vibration peak in IR-spectrum)
MS	Mass Spectrometry
N-Me-salpr	bis(salicylideniminato-3-propyl)methylamine
NMR	Nuclear Magnetic Resonance
Phen	phenantroline
PhenS	bathophenantroline disulfonate
Py	pyridine
s	strong (related to a vibration peak in IR-spectrum)
S	spin
salen	N,N'-bis(salicylidene)ethylenediamine
sh	shoulder
sulfosalen	N,N'-bis(5-sulfonatosalicylidene)ethylenediamine
t_{2g}	non-axial d-orbitals (see e_g)
TEMPO	2,2,6,6-tetramethylpiperidinyl-1-oxy
TOF	turnover frequency
TON	turnover number
UV	Ultraviolet
Vis	Visible
w	weak (related to a vibration peak in IR-spectrum)
αCH_3salen	N,N'-bis(αmethylsalicylidene)ethylenediamine
ν	vibration
4OHsalen	N,N'-bis(4-hydroxosalicylidene)ethylenediamine

1 INTRODUCTION

Oxidation of organic substances is one of the most important methods for producing diverse chemicals from oil derivatives and vegetable raw materials.[1-2] In the production of fine chemicals it is imperative that the reactions are selective. The traditional methods often involve the use of stoichiometric amounts of inorganic oxidants, such as chromates, which clearly cause serious wasteproblems.[3-4] In addition, these reactions usually require high temperatures and pressures, which consume a lot of energy and cause lower selectivities.[1] It would be of great economical and ecological importance to develop processes, which take place at milder conditions and produce less waste.

In nature enzymes can perform selective oxidation reactions at mild conditions.[5-6] Their active centers consist of metal complexes, which are able to activate molecular oxygen. Many synthetic transition metal complexes are able to mimic these enzymes and reversibly bind and activate molecular oxygen.[7-9] Thus, for the past few decades there has been a growing interest in transition metal catalyzed activation of O_2 or H_2O_2 for organic oxidations.[1,3,5,7,10-14] An especially fascinating attempt is to develop a catalytic system which can perform specific oxidations in water.[15] Unfortunately this approach is often hampered by the instability and insolubility of transition metal catalysts in this medium.[15]

Oxidation of alcohols is one of the most intriguing topics in the area of catalytic oxidation, as the selective transformation of primary and secondary alcohols to corresponding carbonyl compounds plays a central role in organic synthesis.[3,16] However, the activities of alcohol oxidations catalyzed by transition metal complex have remained low, normally in the order of TOF = 10 h^{-1} or less (TOF = turnover frequency, number of moles of oxidized substrate per one mole of catalyst per hour).[3] To further improve the activity and selectivity of these catalytic systems, it is vital to know how the reactions proceed.

The oxidation mechanisms of transition metal complexes are not completely understood. There are many well accepted models,[3,14,16-21] but direct proof for suggested steps is often lacking. The development of analytical and experimental techniques over the past decades has tremendously improved the possibilities to study reaction mechanisms. For example, in-situ spectroscopy is a powerful technique to elucidate reaction kinetics and mechanisms, as the spectra are taken under experimental conditions with no need of sample separation.[22] This can improve the direct observation of reaction intermediates, sideproducts or, in the best case, the catalytically active species.

2 THE SCOPE OF THE PRESENT STUDY

The pulp and paper industry has searched for alternatives for chlorine-based bleaching since the beginning of 1980's. In the totally chlorine free bleaching the main drawback is the damaging of the cellulose fibres during the multistage delignification.[23-24] A very attractive attempt is to catalytically enhance the oxygen stage in the bleaching

cycle. This approach involves development of a transition metal catalyst, which can selectively oxidize lignin functionalities without harming the cellulose fibres.

This thesis started as a part of the project on Catalytic Bleaching of Pulp, in which transition metal complexes were studied as catalysts for the oxygen stage in the bleaching sequence. Water as the preferred reaction medium for pulp and paper industry limits the number of catalyst alternatives, as most of the other studies published about aerobic oxidation of alcohols have been performed in organic solvents.[18,19,25-32]

In this study, Co(salen) [salen = N,N'-bis(salicylidene)ethylenediamine] type complexes were studied as oxygen activators for the selective oxidation of lignin model compounds using water as the solvent and molecular oxygen as the oxidant (Figure 1). The aim was to oxidize the hydroxyl-functionalities in lignin (-OH to =O) to aldehydes and ketones, which will decrease the amount of hydrogen bonding. This helps to break the lignin structure into smaller units, which are then easier to remove in the washing steps of pulp bleaching.

The chosen substrate is veratryl alcohol (Figure 1). It models the substructures of lignin and is often used in studies of lignin degradation by enzymes.[33] Radicals are also not expected to be formed in the reactions of benzylic alcohols as easily as in the oxidation of phenolic substrates. The effect of reaction conditions on the oxidation activity were studied thoroughly using commercial Co(salen) as the catalyst and veratryl alcohol as the substrate.
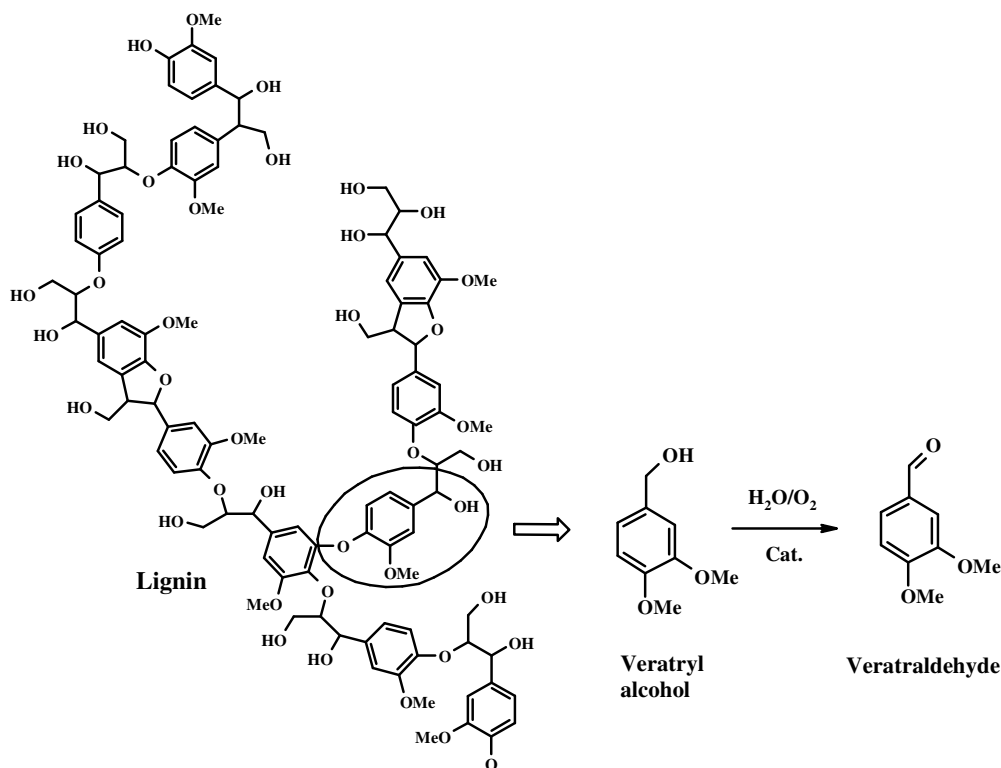

Figure 1. Veratryl alcohol, the substrate of this study, is a model for substructures of lignin (left). The alcohol is catalytically oxidized to aldehyde (right) with molecular oxygen in aqueous solutions.

Furthermore, the mechanism of Co(salen) catalyzed oxidation of veratryl alcohol was examined in detail. Several in situ spectroscopic techniques were used to study this oxidation reaction under experimental conditions. Veratryl alcohol oxidation by Cu(phen) complexes (phen = phenantroline) was also examined by in situ ATR-IR (Attenuated Total Reflectance-Infrared) spectroscopy and compared with the Co(salen) system.

3 BACKGROUND

3.1 Molecular Oxygen

The complete oxidation of organic compounds with molecular oxygen to produce carbon dioxide and water is thermodynamically possible, but fortunately for the life on earth it has a high kinetic barrier.[10] This is due to molecular oxygen favouring a triplet state $^3O_2$ (Figure 2),[5] which cannot react with singlet organic molecules to form singlet products.[7,34] This kind of process is spin-forbidden and has a very slow reaction rate. Such a barrier can be overcome by free radicals, as in that case a singlet molecule is reacting with triplet oxygen to form two duplet molecules (free radicals). This reaction is spin-allowed, but for most substrates endothermic.[7,10] In addition, the reactions involving free radicals are not very selective and lead therefore to the formation of several sideproducts.
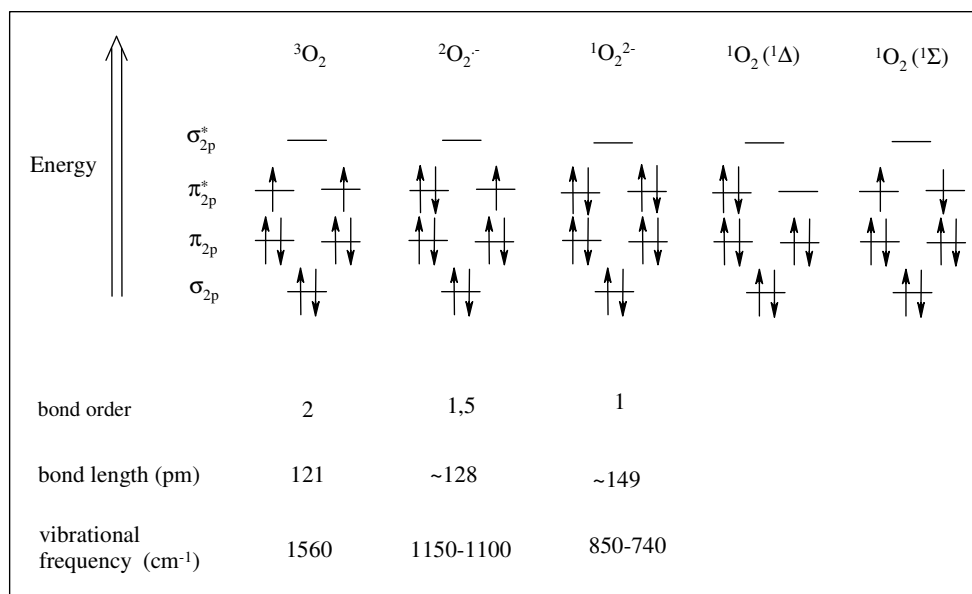

Figure 2. The possible electron configurations for an oxygen molecule. The ground state of the oxygen molecule: a triplet $^3O_2$.[5] Reduction by one electron: a radical type duplet $^2O_2^{\cdot-}$ and reduction by two electrons: a singlet $^1O_2^{2-}$.

A complete four-electron reduction of molecular oxygen to produce two water molecules has a very high free energy change, but is restricted by mechanistic limitations. Usually the reduction of dioxygen occurs via successive steps of one- or two-electron transfer.[35] Thus, the compounds, which can react with the oxygen molecule $^3O_2$ must be able to perform electron transfer reactions or they need to initially have unpaired electrons.

In most reactions of dioxygen with metal complexes, oxygen is reduced by two electrons and oxides, hydroxides or water are being produced. These reactions are irreversible and the O-O bond is broken. During the first two electron reductions to a superoxo radical ($O_2^{\cdot-}$, S = ½) or to a peroxide dianion (O_2^{2-}, S = 0) the O-O bond is not broken, but its bond order decreases gradually from a double bond to a single bond. During this process the excess electrons are located to the degenerate antibonding π^* (2p) orbital until it is filled. In the four electron reduction the further electrons are located to σ^* (2p) anti-bonding orbital and eventually the O-O bond is broken. The redox potential for oxygen reduction diminishes in the presence of electrophiles, such as metal ions or H^+.[5]

3.2 Transition metal complexes as oxygen activators

Many industrial processes already exist in which oxidative transformations are driven by molecular oxygen and catalyzed by transition metal complexes.[1] Such reactions include the copper- and palladium-catalyzed Wacker process or the cobalt-catalyzed Mid-Century process. In these reactions, however, the transition metal is involved in catalyzing an auto-oxidation reaction between the hydrocarbon and oxygen and metal-oxygen complexes are not involved in the oxidation pathways.[10,36] Activation of oxygen, however, involves the formation of a metal-dioxygen complex which can react selectively with organic molecules at moderate temperatures.

Activation of molecular oxygen is a very difficult task, especially to do selective oxidations of only a certain functionality. Consequently, other oxidants are still more commonly used, such as hydrogen peroxide or tert-butyl alkyl peroxide. The problem with dioxygen activation is the same in synthetic chemistry as in biological systems, that is, how to selectively oxidize a substrate without destroying the reagents in free radical reactions with oxygen. Thus, such a catalyst must be found, that can reversibly bind dioxygen and activate it in such a way, that an organic substrate is selectively oxidized.[7,10]

Only a few metals are found in the active centers of oxygen activating enzymes. These are copper, iron and manganese.[6] Cobalt is also indirectly involved in enzyme catalyzed oxidation reactions via cobalamin vitamine B_{12}, which acts as a cofactor.[5,6,37] These four metals are the most commonly used in synthetic attempts to produce oxygen activating transition metal complexes.[14] For all of these metals, only certain oxidation and spin states can react with dioxygen to form active sites.

Paramagnetic transition metal ions have the ability to donate unpaired electrons and at the same time receive and donate electron density (π-backbonding), which enables the paramagnetic ($^3O_2$) oxygen molecule to bind reversibly.[5,34] The number of d-electrons on the metal ion affects the stability of the formed oxygen complex. The electron density on the metal and its spin state can be tuned by choosing appropriate ligands. The field effect of the ligands is determined by the spectrochemical series, that is, the ligand field is increasing according to the experimentally determined series: $I^- < Br^- < S^{2-} < Cl^- < NO_3^- <$ $OH^- \sim RCOO^- < H_2O \sim RS^- < NH_3 \sim Im$ (imidazole) $<$ en (ethylenediamine) $<$ bipy (bipyridine) $< CN^- < CO$.[38] The strength of the ligand field determines how the d-orbitals are split, that is, how big energy difference exists between the e_g and t_{2g} orbitals.[5,38] The triplet state $^3O_2$ can only bind to the metal ion if the metal has unpaired electrons which it can donate to the oxygen molecule. Due to this reason there are distinct differences in oxygen activation ability between the 'low-spin' and 'high-spin'-states of a certain metal. For example, only the 'low-spin' Co(II) ion can bind dioxygen reversibly.

The oxygen molecule can coordinate to the transition metal complex in several different ways (Figure 3).[5,7,14] The different coordination modes arise mainly from the differences in the electron configurations of the metals and from their ability to donate electron density to the oxygen molecule. The superoxo mode is observed in metal centers, which can donate only one electron to the antibonding orbital of the oxygen molecule. In dinuclear complexes, in which both metals donate one electron to the oxygen, a peroxo-bridge is formed. In some cases part of the electron density is received by a ligand and a superoxo-bridge can be formed, in which the oxygen molecule has been reduced by only one electron. In every other coordination mode the metal must be oxidized by more than one electron. To break the oxygen-oxygen bond, four electrons must be donated to the oxygen molecule. This can usually be done only by metals, which have several oxidation states. For example, oxo-complexes (M=O) are not usually observed with cobalt as the central metal but are commonly the active species in reactions involving iron or manganese.[9,39-42]

Nevertheless, all the oxidation-reduction reactions taking place during the oxygen binding are arbitrary and the actual oxidation state of the metal is something between two formal oxidation states.[35] By making appropriate choices of the metal, ligand and the reaction conditions, active oxygen binding systems can be designed.

Not all the oxygen complexes are active towards the oxidation of substrates. The nature of the bound oxygen determines whether electrophilic or nucleophilic substrates can be oxidized or whether the oxygen complex is too stable to be reactive. The field of oxidation catalysis is so vast and the literature on characterized oxygen complexes so numerous that the whole field cannot be analyzed in this thesis. The following sections of this literature review deal with cobalt as the central metal and the stability and reactivity of its oxygen complexes.
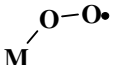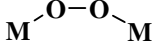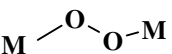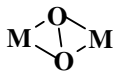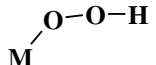
structure	symbol	name
M—O—O• (M—O$-$O•)	η^1	**superoxo**
M with side-on O–O	η^2	**'side-on' superoxo**
M—O—O—M	cis-μ–η^1:η^1	*cis* 1,2 μ-peroxo
M—O / O—M	trans-μ–η^1:η^1	*trans* 1,2 μ-peroxo
M–O–O–M (bridged)	μ–η^2:η^2	*μ–η^2:η^2*-peroxo
M—O—O—H		**hydroperoxo**
M(O)(O)M		**bis-μ-oxo**
M—O—M		*μ-oxo*
M=O		**oxo**

Figure 3. Different ways in which the oxygen molecule can bind to a transition metal ion.[5,7,38]

3.3 Oxygen activation by cobalt complexes

Cobalt is one of the most studied oxygen activating metals. Many of its chelate compounds are known to reversibly bind oxygen to form superoxo- or peroxo-type complexes.[5,14,18] There are no enzymes in nature which have cobalt as the central metal, but there are several enzymes which are dependent on a coenzyme B_{12}, which has cobalt as the active metal.[6,35]

Cobalt is an electron rich metal, which is known to bind molecular oxygen well. Alfred Werner was the first one to observe more than hundred years ago that cobalt reacted with oxygen in air, which caused its complexes to change colour.[43] The formed complex was a dinuclear, peroxo-bridged cobalt-oxygen species, which is the first

characterized compound in which molecular oxygen is bound to a metal ion.[44] Since then cobalt and its reactions with oxygen have been under intense study, especially the mononuclear cobalt complexes with Schiff base- or porphyrin type ligands.[7-8,18,35,44]

The five-coordinated cobalt(II) has one unpaired electron, which can pair up with the unpaired electron of dioxygen. This involves a one electron transfer from the cobalt to the oxygen. This gives rise to a superoxo species in the case of a mononuclear complex or a μ-peroxo species in the case of a dinuclear complex.[18,35,45] Figure 4 shows the molecular orbital diagram for the superoxo complex of cobalt.[46] Planar cobalt complexes, such as Co(salen), need an axially bound base ligand, which pulls the cobalt ion away from the plane and donates extra electron density to the metal so that the coordination of the oxygen molecule is facilitated.[18]
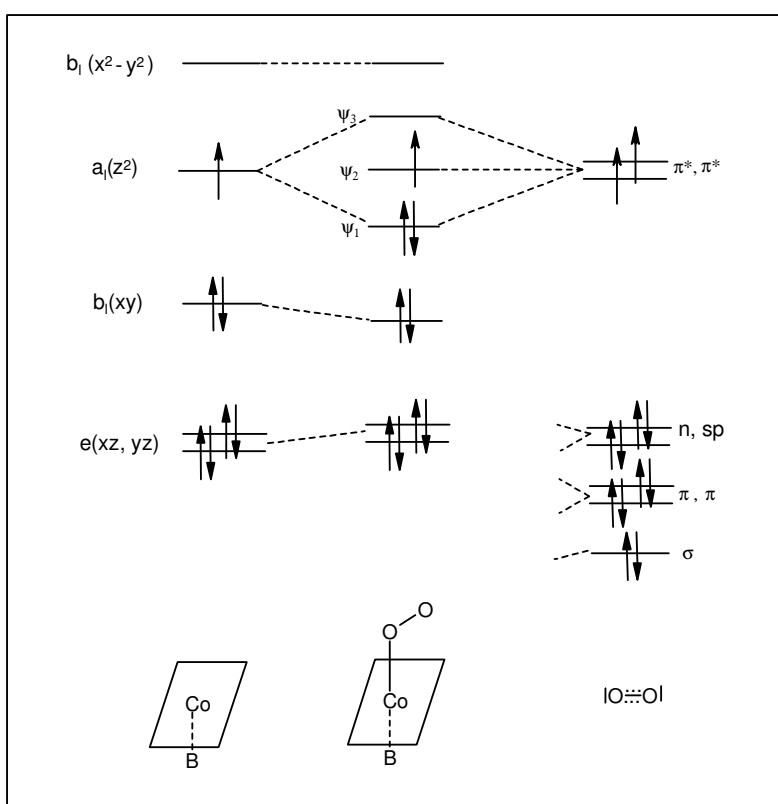
Figure 4. Molecular orbital diagram for the cobalt superoxo complex. B represents an axially bound base ligand, such as pyridine.[46]

Many cobalt complexes react with dioxygen to form a μ-peroxo-bridged species. In the solutions of mononuclear cobalt complexes an equilibrium is usually reached between the dinuclear μ-peroxo-bridged species and the mononuclear superoxo-species (Figure 5).[8,14,18,35,47-48] There is a delicate energy and/or kinetic balance between the formation of the mononuclear and binuclear complexes, which is affected by solvents, ligands, temperature, pH and several other factors.[8,35] In aqueous solutions and at room temperature binuclear peroxo-complexes are thermodynamically favoured. In general,

low temperature, high oxygen partial pressure and high polarity of the solvent should favour the formation of a mononuclear superoxo-complex, whereas at high temperature, low oxygen partial pressure and in a non-polar solvent a binuclear peroxo-bridged species should be dominating.[35]
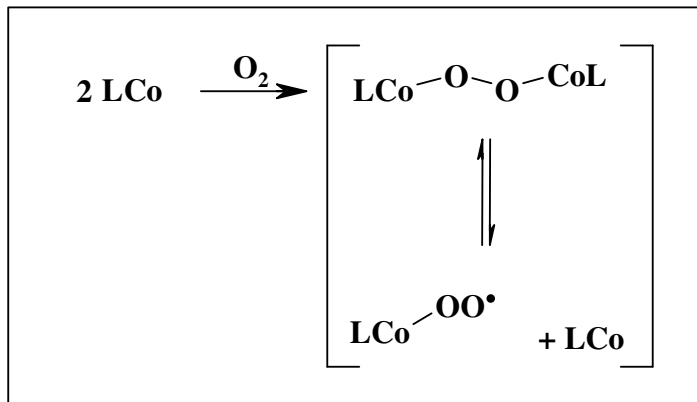
Figure 5. In solution, mononuclear cobalt complexes usually form an equilibrium between the dinuclear peroxo-bridged species and the mononuclear superoxo-species.[18,47-48]

Cobalt complexes can also form dibridged species, such as μ-peroxo-μ-hydroxo-bridged,[8,48] μ-peroxo-μ-acetato-bridged or μ-peroxo-μ-amino-bridged oxygen complexes (Figure 6).[18,45,49] Formation of a μ-peroxo-μ-hydroxo-bridged species is common in aqueous solution and it seems to be always observed if a singly-bridged μ-peroxo complex has a labile ligand cis to dioxygen.[48] The doubly bridged species is thermodynamically favoured in aqueous solutions and it is thus more stable than a singly bridged species.[48] The effect of dibridging is said to "lock in" more tightly the dioxygen bridge.[8] In some doubly bridged cases the dioxygen bridge is exhibiting similar characteristics as the oxygen molecule of a mononuclear superoxo complex, and this species is therefore called a μ-hydroxo-μ-superoxo-species.[45,50-51] The reactivity and the spectroscopic characteristics of μ-hydroxo-μ-superoxo-bridged and μ-hydroxo-μ-peroxo-bridged species differ.[50-52]

Figure 6. μ-Hydroxo-μ-peroxo-bridged species (right) formed from cobalt complexes in alkaline aqueous solution.[8]

15

Compounds, in which dioxygen would be coordinated in other ways are less common with cobalt.[53] There are some examples of mononuclear side-on peroxo-complexes, but these are not often observed. The formation of the $\mu:\eta^2:\eta^2$-peroxo- or bis-μ-oxo bridge has been observed with some cobalt complexes of hy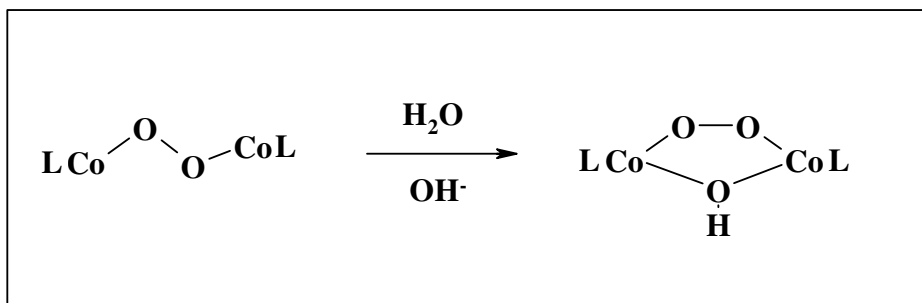drotris(pyrazolyl)borate-type ligands[53-55] and the formation of Co^{IV}=O species has also been reported.[56] In the case of mononuclear cobalt complexes, the formation of a peroxo-bridge is strongly depended on the number and Lewis basicity of the other coordinated groups around the central cobalt ion.[48] It is difficult to establish a precise relationship between the coordinated groups and the stability and structure of the formed bridge, but as a rule of thumb three relatively strong, electron donating groups must be coordinated to cobalt for the bridge to form. As the Lewis basicity of the ligands increases, the formed peroxo-bridge also stabilizes. One good example of this phenomenon is the notable decrease in the stability of a bridged cobalt complex when the aliphatic amines of the ligand are replaced by less basic aromatic amines.[48]

3.4   Oxygen activation by Co(salen) type complexes

Co(salen) [salen = N,N'-bis(salicylidene)ethylenediamine] is a tetradentate, planar Schiff's base complex. Tsumaki discovered already in 1930s that solid samples of Co(II)(salen) can bind dioxygen reversibly.[57] This caused a widespread and continuing interest in the oxygen-carrying properties of cobalt chelates, especially the complexes of Schiff's base ligands.[45] In the 1940's, Co(II) complexes with salen type ligands were extensively studied for oxygen storage for military purposes.[35,58-63] They are also considered to be models for many active centers of enzymes, even though in nature the central metal is different.[8,64]

The ligand array around the cobalt ion in a salen complex is essentially square planar. When O_2 coordinates, it occupies an axial position in the octahedral structure.[35] The other axial position is usually occupied by a base, which enhances the oxygen binding capabilities of Co(salen) type complexes.[14,65-69] The coordination of dioxygen to Co(II)salen usually involves transfer of some electron density from the metal to the oxygen molecule. In other words, the cobalt ion is partially oxidized. This partial oxidation is facilitated by N-donor ligands, which compensate for electron withdrawal by the oxygen molecule.[36]

Co(salen) complexes usually form either mononuclear superoxo- or dinuclear μ-peroxo type complexes with dioxygen (Figure 7). At room temperature the dibridged species normally dominates.[35,70] It is possible that other cobalt-oxygen complexes are formed in solution. For example pH affects strongly the stability of cobalt-oxygen species.[70] By choosing the reaction conditions carefully, the equilibrium can be shifted towards the catalytically more active species.[35] The reactivity of the bound oxygen depends on its charge, i.e. the superoxo-complex reacts very much like a radical and is usually assumed to be responsible for catalytic activity. However, the chosen substrate can also affect the reaction mechanism.
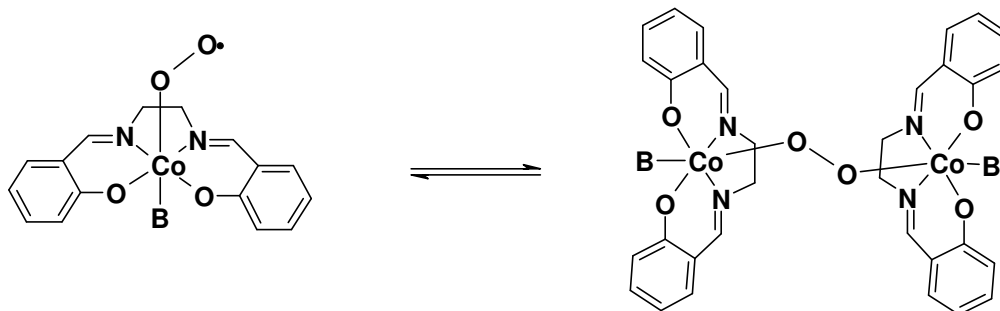
Figure 7. Mononuclear superoxo-type species (left) and dinuclear peroxo-type species (right) formed from Co(salen) type complexes and dioxygen (B = base).[14,65]

Co(salen) type complexes catalyze the oxidation of certain p-substituted phenolics to p-benzoquinones with dioxygen as the oxidant (Figure 8).[20,65-66,71-77] Various mechanisms have been suggested for this reaction. The most accepted one involves a cobalt-superoxo complex, which abstracts a hydrogen atom from the phenolic group producing a radical. This radical is attacked by a second superoxo complex or a molecule of oxygen producing the quinone.[65-66] Experimental results have indicated that the structure of the model compounds has a profound impact on the oxidation activity.[14,71] Syringyl model compounds are readily oxidized while guaiacyl and p-hydroxyl analogs often exhibit no reaction. Therefore it has been suggested, that the dehydrogenation step is controlling the reaction, which explains the effect of substituents on the reactivity of different substrates.[20,65]
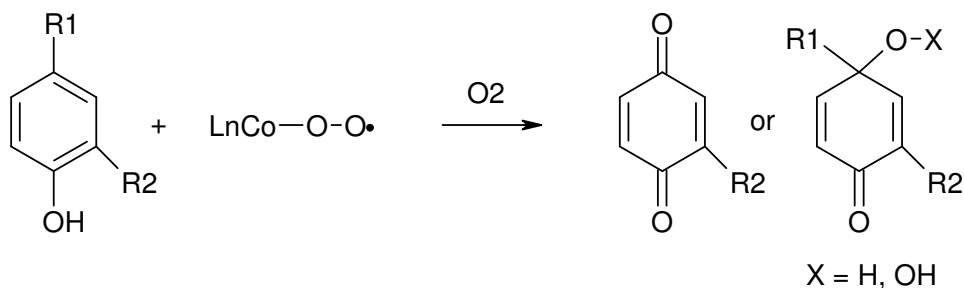
Figure 8. The reaction equation for the oxidation of *p*-phenolics to benzoquinones by Co(salen) type complexes.[65]

3.5 Oxidation of benzylic alcohols by transition metal complexes

Catalytic alcohol oxidations have more often been conducted in other solvents than water.[16,19,25-31,78] Most examples of aerobic oxidation of alcohols involve the use of group 8 metals as catalysts. The most commonly used metals are ruthenium and palladium.[3,19,25,31-32] These metal ions often react with alcohols via hydridometal pathways (Figure 9).[3,16]
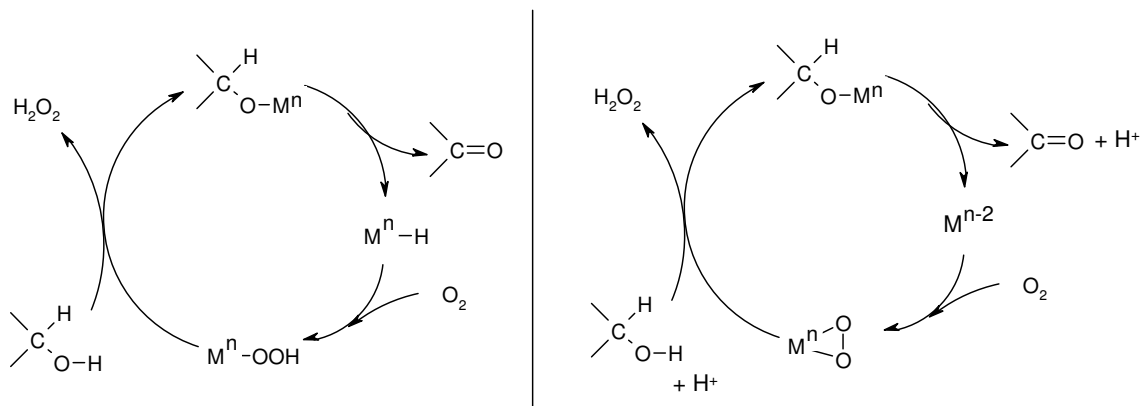
Figure 9. Hydridometal pathway for catalytic alcohol oxidation by group 8 metals.[3]

Recently a palladium-catalyzed system was reported, in which a PhenS/Pd complex (PhenS = bathophenantroline disulfonate) catalyzes the oxidation of alcohols in biphasic aqueous media at 100°C and under 30 bar of air.[79] This reaction proceeds via a dihydroxyl-bridged palladium dimer, to which the substrate coordinates. Oxygen is used for reoxidizing Pd^0 to Pd(II) (Figure 10).[19]
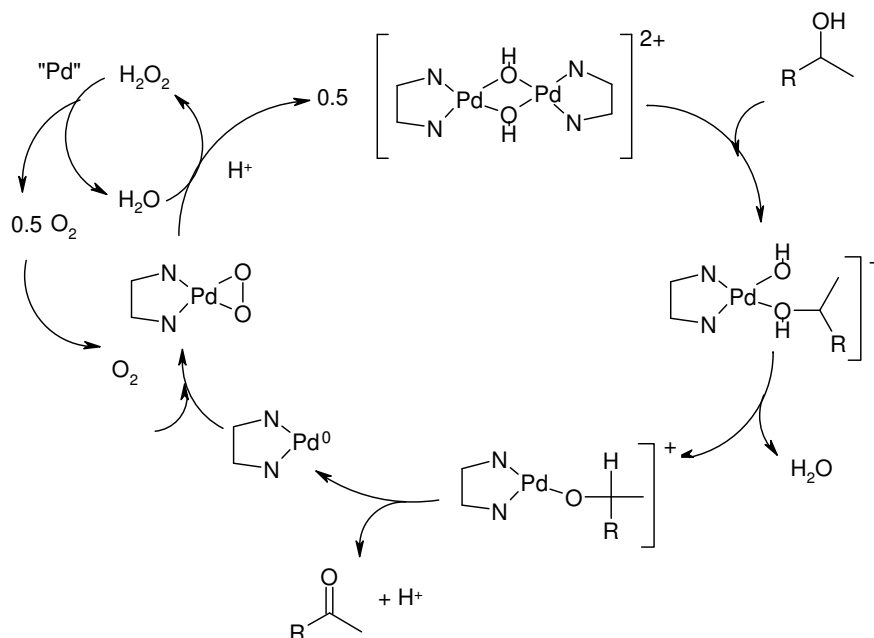
Figure 10. Suggested mechanism for the PhenS/Pd catalyzed oxidation of alcohols.[19]

Co(bipy)$_2$ type complexes catalyze the dehydrogenation of some primary alcohols and aldehydes in acetonitrile. In these reactions the substrate coordination is a key step followed by the formation of the μ-peroxo-bridge between two cobalt-substrate units.[47]

In nature copper is often found in the active centers of enzymes which are involved in alcohol oxidation, for example tyrosinase or galactose oxidase.[5,6,11] Several synthetic model systems have been designed to mimic galactose oxidase.[80-81] Galactose oxidase is a copper enzyme which catalyzes the oxidation of a wide variety of primary alcohols,

including substituted benzylic alcohols.[82] Here, the reaction is suggested to initiate by proton abstraction from a coordinated substrate, after which electron transfer occurs between the alcohol and the metal center resulting in Cu(I) and an alkoxy radical. The tyrosine-cysteine phenoxyl free radical ligand abstracts a hydrogen atom from the alkoxy group forming the aldehyde as the reaction product. Cu(I) is re-oxidized to Cu(II) by dioxygen, which is reduced to hydrogen peroxide.[21,82]

TEMPO (2,2,6,6-tetramethylpiperidinyl-1-oxy) has been extensively used as a mediator in oxidation of alcohols to carbonyl compounds with sodium hypochlorite in the presence of NaBr and dichloromethane. These reactions, however, are not wastefree and therefore modifications to this system have been widely studied. There are examples of recyclable oligomeric TEMPO catalysts, but these reactions still use sodium hypoclorite as the oxidant.[25]

CuCl can promote the TEMPO mediated aerobic oxidation of benzyl alcohol to benzaldehyde. This method, however, cannot catalyze aliphatic and allylic alcohols. If $RuCl_2(PPh_3)_3$ is used instead of CuCl, a broad range of alcohols can be oxidized.[16,19,25] Supported, high-valent ruthenium complexes are also known to catalyze the aerobic oxidation of nonactivated alcohols.[78] Recently, copper complexes with bipyridine type ligands were used as catalysts for TEMPO mediated aerobic oxidation of alcohols in CH_3CN:water.[83] In copper catalyzed oxidation reaction, copper(I) is at first oxidized by TEMPO to a piperidinyloxyl copper(II) complex. Further reaction with alcohol affords a alkoxycopper(II)complex, and a second molecule of TEMPO gives the product carbonyl, copper(I) and reduced TEMPOH. Oxygen reoxidizes TEMPOH to TEMPO. This mechanism resembles the one suggested for a copper enzyme galactose oxidase (Figure 11).
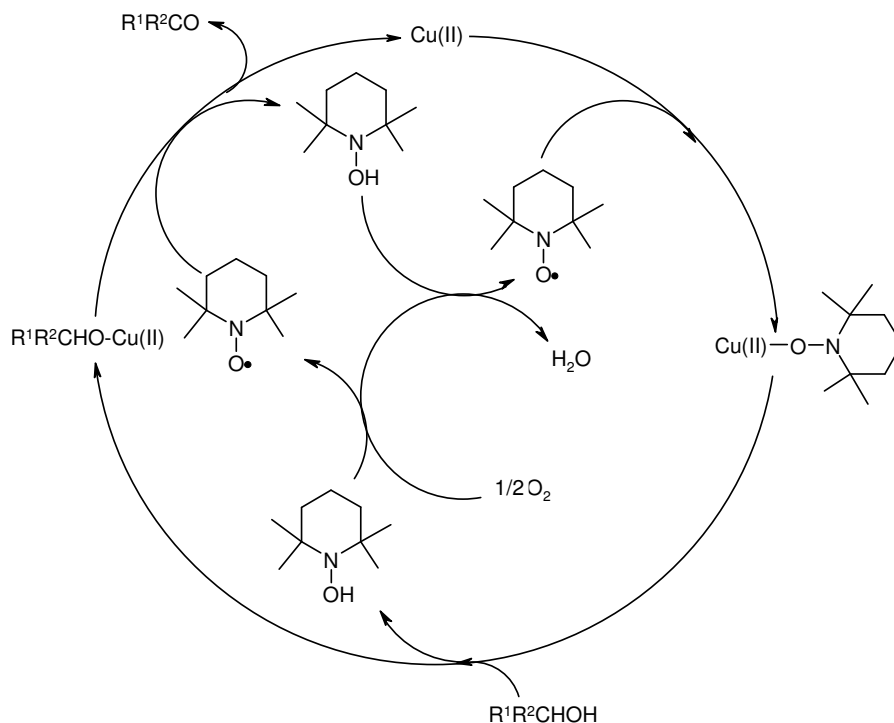

Figure 11. Postulated mechanism for the CuCl/TEMPO catalyzed oxidation of alcohols.[19]

There are also examples of laccase catalyzed aerobic oxidation of alcohols with the mediation by TEMPO or ABTS.[84-85] In nature laccase enzymes are involved in the oxidation of phenolic substrates, but with the mediation of TEMPO they can also catalyze the oxidation of benzylic substrates. These reactions take place in water and a wide range of benzylic alcohols is oxidized to aldehydes, including veratryl alcohol.[84-85]

Veratryl alcohol is a methoxy-substituted benzylic alcohol. It has been extensively studied as a substrate for laccase/mediator oxidation systems[85-86] or as a mediator in lignin peroxidase (LiP) catalyzed degradation of lignin.[87-90] In the oxidations promoted by LiP, veratryl alcohol has been suggested to act as a freely diffusing one-electron redox mediator transferring oxidizing equivalents from the enzyme to the lignin polymer,[90] or as a reducing agent, which helps to regenerate the active enzyme thus completing its catalytic cycle.[89] In these reactions veratryl alcohol is suggested to form a radical cation, which can react further in aqueous solutions to produce veratraldehyde.[90] Cobalt(II) phtalocyanines also catalyze the oxidation of veratryl alcohol to veratraldehyde with dioxygen in water at 85°C and pH 11.[66] However, no mechanistic details have been proposed for this reaction.

4   PART I: OXIDATION ACTIVITY OF CO(SALEN) TYPE COMPLEXES

4.1   Experimental

Co(salen) (**1**) and Co(N-Me-salpr) (**6**) were purchased from Aldrich and used as such without further purification. Complexes **2-5** were prepared according to the published procedures.[58,91-97]

Veratryl alcohol (3,4-dimethoxybenzyl alcohol), 1,4-dioxane, pyridine, veratraldehyde (3,4-dimethoxybenzaldehyde), veratrylic acid (3,4-dimethoxybenzylic acid) and benzyl alcohol were purchased from Aldrich and ACROS and used as received.

The standard procedure for oxidation experiments is described in detail in articles I and II and the modifications made due to the spectroscopic measurements are explained in article III and below in Part II of this thesis. In short, the experimental procedure is a modification of the one described by Bozell et al.[65] In the first experiments, in which the activity of the complexes **1-6** was monitored (article I), the standard procedure was to dissolve the substrate and pyridine (when used) in water and adjust the pH with 2 M NaOH. After that the complex was added, the reaction flask was evacuated and oxygen atmosphere was introduced by balloon technique.[II] The temperature was then set to the desired value and the reaction was allowed to run for 24 h. The reaction was stopped by cooling the solution to ambient temperature, after which the final pH was measured. The pH of the reaction mixture was adjusted to 6-7 with 2M HCl and soluble organic products were extracted with ethyl acetate. The organic phase was separated, dried with sodium sulphate, filtered and finally the solvent was removed. The products were characterized by ^{1}H-NMR (Varian Gemini 2000) - spectroscopy. Afterwards, when it was noted that

the reaction was quite slow and the complexes needed time to dissolve, the procedure was changed in such a way that the cobalt complex was stirred with pyridine (when needed) before addition of other reagents. The reaction products were also analyzed by chromatographic methods (GC/MS, HP 5890/HP 5972 MSD).

4.2 General remarks on the oxidation activity of complexes 1-6 in oxidation of veratryl alcohol

A series of salen type cobalt complexes Co(salen)(**1**) [salen = N,N'-bis(salicylidene)ethylenediamine], Co(αCH$_3$salen)(**2**) [αCH$_3$salen = N,N'-bis(αmethylsalicylidene)ethylenediamine], Co(4OHsalen)(**3**) [4OHsalen = N,N'-bis(4-hydroxosalicylidene)ethylenediamine], Co(sulfosalen)(**4**) [sulfosalen = N,N'-bis(5-sulfonatosalicylidene)ethylenediamine], Co(acacen)(**5**) [acacen = N,N'-bis(acetylacetone)ethylenediamine) and Co(N-Me-salpr)(**6**) [N-Me-salpr = bis(salicylideniminato-3-propyl)methylamine] were chosen as catalysts for the oxygen activation in the oxidation of veratryl alcohol in basic aqueous conditions (Figure 12). These different complexes were selected to study the influence of ligand structure on catalytic activity.

1 : R = R' = R" = H
2 : R = R" = H, R' = SO3Na
3 : R = Me, R' = R" = H
5 : R = R' = H, R" = OH
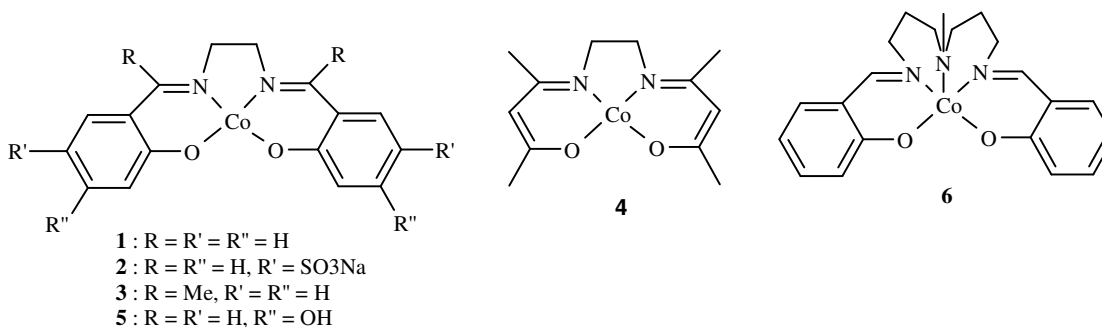
Figure 12. Schematic structures of cobalt complexes **1-6**.

The unsubstituted salen complex **1** is considered as a standard when compared to the catalytic performance of the substituted ones. Complex **2** has sulfonyl groups at 3,3´-positions, which make the complex highly water soluble and therefore an attractive candidate for pulp bleaching processes. In complex **3** the labile imine protons have been replaced by methyl groups, which should stabilize the complex against nucleophilic attacks. Complex **4** is otherwise similar to complex **3** but the aromaticity of the ligand is removed while the conjugation in the ligand framework remains. Complex **5** was selected to study the influence of the OH-groups at 4,4´-position, which should improve water solubility of the complex. Complex **6** resembles complex **1**, but it has an additional amine functionality on the bridge between the imido groups and it is one of the most active cobalt salen type complex in the oxidation of phenolic substrates. The substituents in the ligand also influence the way oxygen coordinates to the complex, i.e. whether 1:1 or 1:2 O$_2$:Co species is favored.[67,98-99]

Major differences were observed among the tested complexes (Table 1). The unsubstituted complex **1** turned out to be the most active complex, although complex **2** was nearly as active. Considerable decrease in activity was observed for the other tested complexes.

An unexpected result was the inactivity of complex **6**, with the axial nitrogen embedded in the ligand structure. This complex is known to be able to reversibly bind oxygen and oxidize phenolic substrates.[8,20,66,97] The inactivity of complex **6** compared to the other complexes is so striking that it can only be explained by its biggest difference; the third amine included in the bridge. This amine acts as an axial base and it promotes the formation of a mononuclear superoxo-type oxygen species.[99] However, it is an immobile axial base, which means it cannot be replaced by the substrate. Thus, the inactivity of complex **6** was the first clue to substrate coordination being the key step in the studied reaction.

Table 1. Oxidation activity of complexes **1-6** at pH 11 and 12.5 at 80°C expressed in TON (TON = turnover number, moles of product per one mole of catalyst). (0.15 mmol complex and 6 mmol veratryl alcohol in 10 ml of water)

Complex	TON pH = 11	TON pH = 12.5
1	9	29
2	3	17
3	5	12
4	3	11
5	2	8
6	<1	<1

The preference of complex **6** to form superoxo-type complexes can also be an explanation for its low activity in the present system. This might as well explain the relative inactivity of Co(αCH$_3$salen) (**3**) compared to complex **1**, as complex **3** is noted to prefer the 1:1 oxygen complex, whereas complex **1** exists usually in the 2:1 (Co:O$_2$) form.[67] Complex **3** is more active than complex **6**, which could be accounted for by the empty coordination site available in the axial position of complex **3** which is occupied by the amine from the bridge in complex **6**.

In summary, complexes **1-5** can catalyze the oxidation of veratryl alcohol in water, whereas complex **6** is virtually inactive. Substituents in the ligand-frame do not improve the catalytic activity, but complex **1** is the best candidate for further studies.

4.3   The effect of reaction conditions on oxidation activity

The screening for the optimum reaction conditions and the study of the effects of different reaction parameters on the oxidation activity are described in detail in articles I and II. It is, however, important to summarize these results here in order to emphasize their importance in elucidating the reaction mechanism.

4.3.1 The effect of solvent

Much of the research on synthetic oxygen carriers has been done in aprotic solvents as the use of protonic solvents often results in irreversible oxidation of the metal complex.[8] However, certain cobalt(II) complexes can react reversibly with dioxygen in aqueous solutions. In fact the first cobalt-oxygen complex, $[(NH_3)_5Co-O-O-Co- NH_3)_5]^{4+}$ was isolated from aqueous solution and formulated as the μ-peroxo low-spin cobalt(II) complex.[43]

One of the aims of this study is that the catalyst must be active in water. It was indeed observed for Co(salen) type complexes **1-5** that they can catalyze the oxidation of veratryl alcohol in water at pH values higher than 10. The activity of the catalysts was lower in methanol or ethanol and it turned out that with these solvents the presence of water is necessary for the reaction to occur. A mixture of methanol and water is a fairly good solvent, but its use is limited by the low boiling point of methanol. The highest temperature that can be used for such a solvent is 60°C, at which the turnover number of less than 15 can be reached (water:methanol mixture 2:1). If a reaction mixture in methanol was refluxed, there was practically no oxidation activity, as the complex seemed to have decomposed (blue colour of cobalt salts in the evaporated reaction mixture). Therefore water is a better solvent, as higher temperatures can be applied. No formation of aldehyde was observed in acetonitrile, toluene, acetone or dichloromethane.

The fact that water increases the activity can mean that aqueous media is needed as a proton reservoir and storage. At different steps of the cycle, water can either receive or donate a proton from/to the reaction intermediates and that way promote the catalytic reaction. Another point is that the formation of a mononuclear superoxo complex is enhanced in polar, non-aqueous solvents,[69] but the μ-peroxo species should dominate in aqueous solutions.[35] Thus, the increased activity in water suggests that the active species in this reaction is the dimeric μ-peroxo species.

4.3.2 The effect of temperature

The activity of the studied catalytic reaction is very low at room temperature and practically no product can be extracted after a 24 hour experiment. The activity of the studied complexes increases dramatically at temperatures higher than 60°C, except for complex **6**, which remains inactive, and complex **5**, for which there is a steady increase in activity with increased temperature (Figure 13). For other complexes than complex **5** the activity decreases at temperatures higher than 90°C, which could be due to the decomposition of the complex.

The need of temperatures higher than 60°C could be caused by several factors. First of all, the solubility of the studied complexes is quite low at room temperature and the higher temperature might be needed to dissolve the catalyst. Nevertheless the activity of complex **2** is also negligible at temperatures lower than 60°C and this complex is highly soluble at room temperature.

Another reason could be the need of higher temperatures for deprotonation of the substrate, which is considered to be the initial step in the oxidation of benzylic alcohols.[47,82] This is, however, difficult to prove. Also, higher temperatures support the formation of the dimeric μ-peroxo species, but this species should already be dominating

23

at room temperatures. Therefore no such improvement should be expected by raising the reaction temperature to 80°C. The effect of temperature thus needs further investigation. This will be discussed below in Part II.
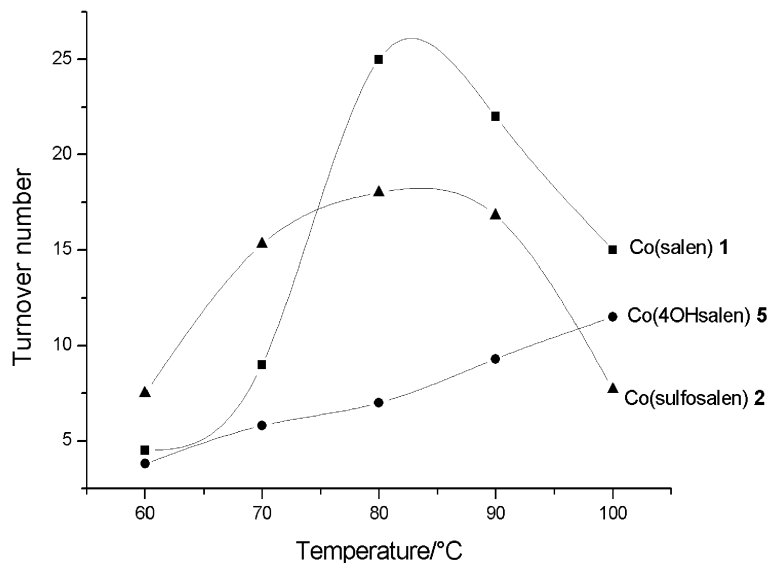

Figure 13. The activity of complexes **1**, **2** and **5** in the oxidation of veratryl alcohol at different temperatures.[II]

4.3.3   The effect of pH

As already seen in Table 1, the pH has a dramatic effect on the activity of the studied system. The only compound which did not benefit from the increase in pH was complex **6**, which remains inactive in the whole pH range from 4 to 13. Figure 14 shows the improvement in activity of Co(salen)(**1**) when raising the initial pH of the reaction solution from 11 to 12.8. It is also interesting to note that once the pH is raised above 11 it is no longer necessary to use an additional axial base, such as pyridine. In fact, at pH 12 activity is somewhat higher without pyridine.[II]

During the reaction pH decreases, which means that the OH⁻ ions are consumed in the reaction. After a certain time the reaction is stopped, but adding another portion of NaOH can restart it. Figure 15 shows that the 48 h reaction gives the same results as the 24 h reaction unless more NaOH is added to the solution after the first 24 h period.

After the reaction has stopped and pH has decreased to less than 9, the deactivated Co(salen) compound precipitates out of solution. This solid can be separated and characterized and it was observed in MS that it is indeed Co(salen). This compound can be used again as a catalyst if added to the solution at pH 12. This was tested by dividing the leftovers of one reaction in two parts and both were dissolved in water. NaOH was added to the other solution whereas the other solution was used for reaction as such. The complex at pH 12 was able to continue catalyzing the oxidation of veratryl alcohol, whereas the other portion remained inactive. This means that the catalyst is deactivated by the decrease in pH and it can be regenerated by the addition of NaOH. Another point

24

in this experiment is that it shows that the catalyst can be removed from the reaction mixture if pH is allowed to decrease below pH 9.
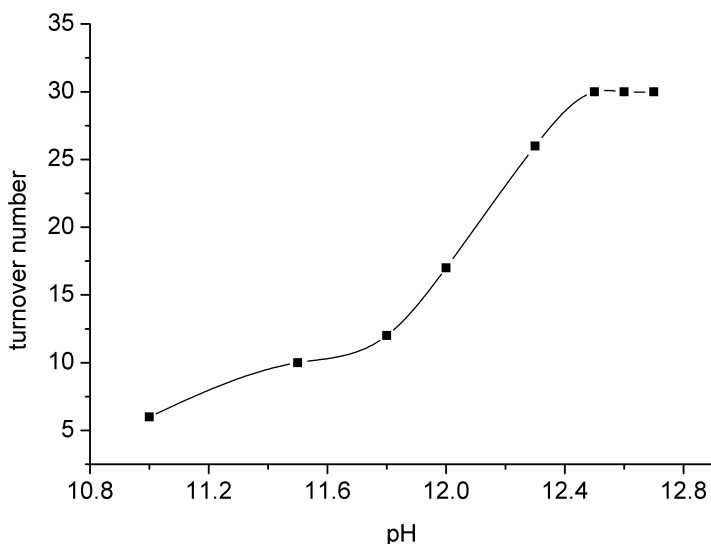
Figure 14. The effect of pH on the activity of Co(salen) catalyzed oxidation of veratryl alcohol at 80°C in water.[II] Each point in the graph represents the activity of Co(salen) in a 24 h oxidation reaction vs. the initial pH of the reaction solution.
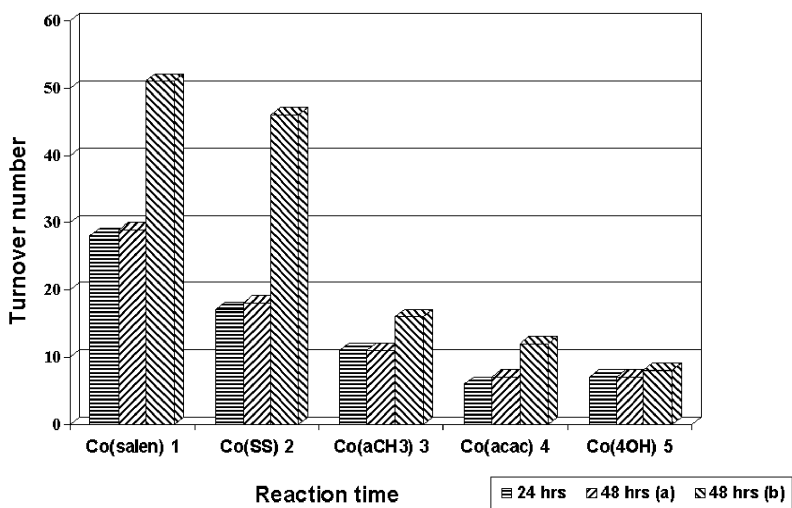
Figure 15. The oxidation activity of complexes **1-5** in the oxidation of veratryl alcohol in the 24 h reaction (left columns), 48 h reaction (middle columns) and the 48 h reaction during which another portion of NaOH was added after the first 24 hours (right columns).[II]

There seems to be a clear correlation between turnover numbers reached and the amount of hydroxide-ions consumed (Figure 16).[II] However, the molar ratio of formed aldehyde and OH⁻-ions consumed varies from tens to hundreds (Figure 17).[IV] This indicates that actually only a few substrate molecules are deprotonated by OH⁻ ions or that a big part of the OH⁻-ions are recovered during the reaction cycle. It is also plausible that all of the OH⁻-ions consumed during deprotonation are recovered, but there is another competing mechanism, which consumes hydroxide ions, and a consequent drop in pH causes the deactivation of the catalytic system.
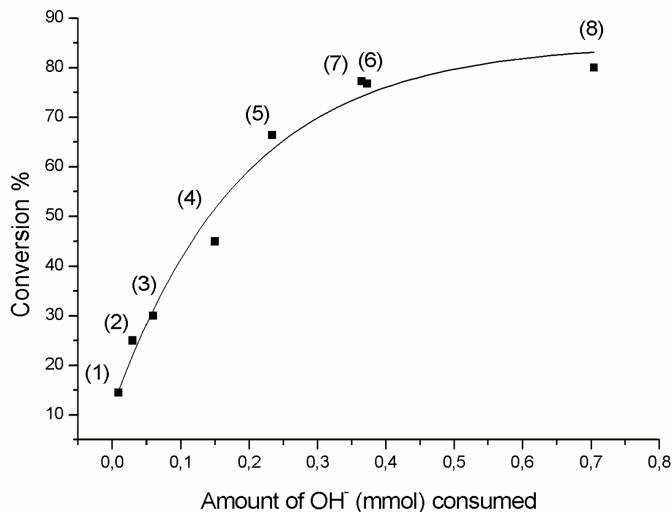
Figure 16. Conversion of veratryl alcohol as a function of consumed OH⁻- ions. Numbers in parentheses correspond to the entry numbers in Table 1 in article II. (The line is to guide eye only.)
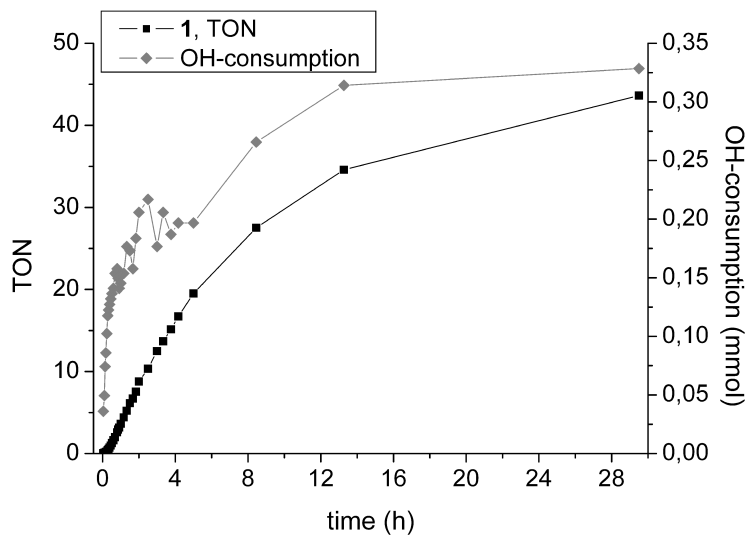
Figure 17. The activity and the change in pH in a Co(salen) catalyzed oxidation of veratryl alcohol as monitored by taking samples from the reactor at certain intervals. (89.6 mg Co(salen) and 4 ml of veratryl alcohol in 200 ml of water at 80 °C and under 10 bar oxygen pressure).[IV]

The need of high pH can be due to many reasons. In the case of alcoholic substrates, the base is assumed to deprotonate the substrate, which makes it more susceptible to further reaction.[16,20,82-83] However, no direct proof for deprotonation has been given. Another reason for the need of high pH can be that the catalytic species is only present under these conditions. For example, product distribution studies for the Co(salen)-MePy-O_2 system in aerobic water:dioxane solution show formation of binuclear peroxo-bridged species at pH values higher than 6 reaching a maximum at pH 10. At pH 12 and above a hydroxo- or dihydroxo chelate complex starts to dominate.[70] It is plausible that such a species is required for the reaction to start.

Summarizing, it seems that in this reaction NaOH has two roles. The reaction does not start before the addition of NaOH, and therefore OH⁻ ions must be directly involved in generating the active species. It is also likely that OH⁻ ions are needed to deprotonate the alcoholic substrate. The deprotonation step would consume OH⁻ ions, which causes the need of NaOH addition during the reaction to keep the catalyst in its active form. This shows that the deactivation of the catalyst at low pH is not irreversible as the activity can be revived with the addition of base. It is likely that as the pH gets lower the catalyst changes into a "dormant" state, from which it can be "awakened" by re-adjustment of pH to 12. This could be occuring via the formation of a dimeric, doubly bridged μ-hydroxo-μ-peroxo-species, which is said to be very stable.[8] The readjustment of pH to 12 or above could force this species to reform the hydroxo- or dihydroxo complex. Nevertheless, after a period of about 96 hours the catalytic activity cannot be recovered anymore.

4.3.4   The effect of axial base

Co(salen) type complexes usually need an additional ligand, which can bind to the axial position and act as a Lewis base. This axial base is needed to keep the cobalt in a low spin state, to pull the metal somewhat from the plane, and to facilitate electron donation from the metal to dioxygen.[69] All these features enforce oxygen binding to the cobalt center. In the case of Co(salen), the most commonly utilized base is pyridine.[14,65]

In the beginning of this study, pyridine was used as an axial base with a 10:1 ratio compared to the cobalt complex. Consequently it was observed, that if a lower amount of pyridine was added, the activity of the system increased. On a more detailed study, it was shown that 1:1 ratio of Co(salen) to pyridine gives the best result when experiments are performed at pH 11. It has been shown in the literature, that if an axial base is added with a 2:1 ratio to the cobalt, one base molecule can bind to both axial coordination sites and either the oxygen molecule[68] or substrate[73] can no longer enter the coordination sphere. This explains the inhibiting effect of an excess amount of pyridine. However, at higher pH values than 11 pyridine is no longer needed, but in fact its presence somewhat decreases the activity. It seems apparent, that pyridine is only needed at lower pH but at higher pH values OH⁻ ions can act as an axial base.[II] The amount of pyridine is so small, that its effect on the pH is negligible.

Other bases than pyridine were also tested (Figure 18). Pyridine and diethyleneamine both promoted the reaction at pH 11. However, the bases with two nitrogens inhibited the reaction.[I]

Two explanations are likely for this behaviour. The bases with two nitrogens might be binding to cobalt too strongly and either oxygen or substrate cannot replace them and this causes the inactivity of the system. Another explanation, which has been given for cobalt(II) porphyrins and their reactions with axial bases and oxygen, is that an oxygen complex is formed but it is too stable. This is caused by enhanced π acceptor strength of these bases, which increases the π bonding from coordinated oxygen to the axial base stabilizing the cobalt-oxygen bond.[35] As a result there is no catalytic reactivity. Also, for Co(acacen) it has been shown that the stability of the cobalt-oxygen bond is increased with the increased basicity of the axial base.[100]

pyridine   diethyleneamine   imidazole   ethylenediamine
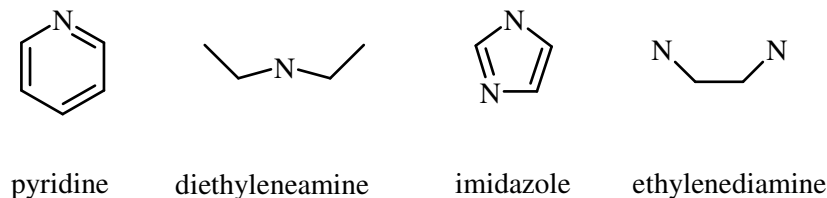
Figure 18. Schematic structures of the different axial bases used in this study.

4.3.5   The effect of concentration

The effect of the catalyst concentration on the oxidation activity and catalyst lifetime was explored in article II. At first, the amount of other reagents was kept the same and the Co(salen) amount was varied. In the case of an auto-oxidation mechanism, the outcome of each reaction should be the same, i.e. independent of Co(salen) concentration. Results of these experiments are summarized in Table 2.

Table 2. Results of oxidation experiments performed with different concentrations of Co(salen) **1**. The experiments were performed in water at 80°C and pH 12.5. (Modified from article II)

Entry	$n_{substrate}$ /mmol	$n_{complex}$ /mmol	Ratio Cat : Subst	$V_{solvent}$ /ml	t / h	Selectivity %	TON
1	5	0.3	1: 16.7	15	24	84	14
2	5	0.15	1: 33.3	15	24	81	27
3	5	0.045	1: 111	15	24	60.5	67
4	5	0.03	1: 167	15	24	58.8	98
5	5	0.006	1: 833	15	24	22.4	187
6	50	0.06	1: 833	150	24	24.6	205
7	35.7	0.006	1: 5950	0	24	5.5	330

It turned out that at lower concentrations the catalyst is able to perform more turnovers. This suggests that either the rate of deactivation is decreased when cobalt concentration is decreased, or that at higher cobalt concentrations the main part of the cobalt complexes is inactive from the start and limited by the amount of other reagents. In the latter case an activity, which is expressed in turnover numbers, gives an unrealistic picture of the real activity of the catalyst. Nevertheless, if we cannot monitor the activity of each catalyst particle separately, expression of activity in turnover numbers (or frequencies, TOF = turnover numbers per hour) together with conversions is still the best expression we have.

In further experiments the amount of other reagents was kept the same, but the substrate amount varied (Figure 19 and entries 5 and 7 in Table 2). It turned out that the ratio of substrate to catalyst has an enormous impact on oxidation activity.
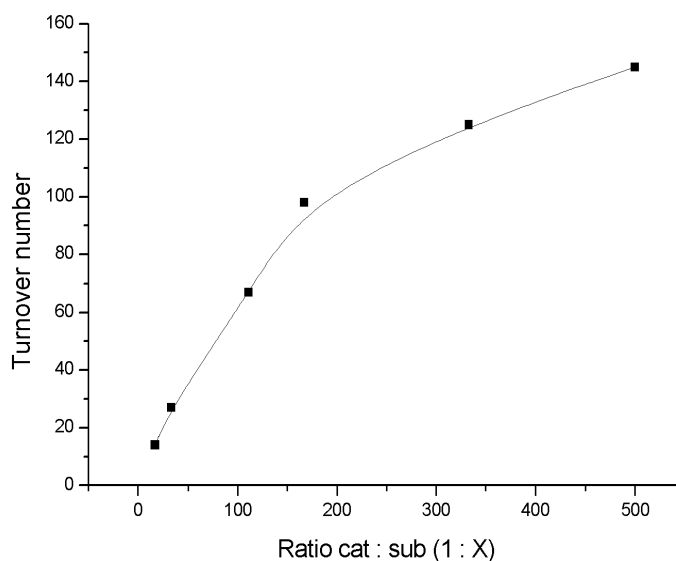
Figure 19. Activity of Co(salen) catalyzed oxidation of veratryl alcohol with an increasing substrate to catalyst ratio. (0.06 mmol of Co(salen) in 15 ml of water at 80°C and pH 12)

According to these results it seems that the replacement of a coordinated pyridine- or hydroxide molecule by the substrate molecule in the coordination sphere of cobalt might be prerequisite for the efficient oxidation to occur. In other words, substrate coordination to the cobalt center is evidently a key step in this reaction.

The enormous effect of the increased substrate concentration also suggests that the reaction is promoted by the substrate, that is, perhaps the substrate itself is a better axial base than OH^- or pyridine.[56] It has already been suggested for *lignin peroxidase* that veratrylalcohol protects the enzyme against deactivation.[101] It has also been proposed for similar systems that an excess of alcohol prevents the further oxidation of the product aldehyde to carboxylic acid. This reaction consumes OH^- ions and thus lowers the pH of the solution, which causes the catalytic system to deactivate. Thus, if the carboxylic acid formation is prevented by excess substrate, the lifetime of the catalytic species is longer.

4.3.6   The effect of pressure

High pressure is usually used in oxidation reactions to improve the yield by increasing the oxygen concentration in the solvent which in water or basic NaOH solutions is moderately low.[102-104]

In article I the effect of pressure is explored in the Co(salen) catalyzed reaction at rather concentrated solution. At these conditions the increased oxygen pressure linearly increases the oxidation activity (Figure 20).
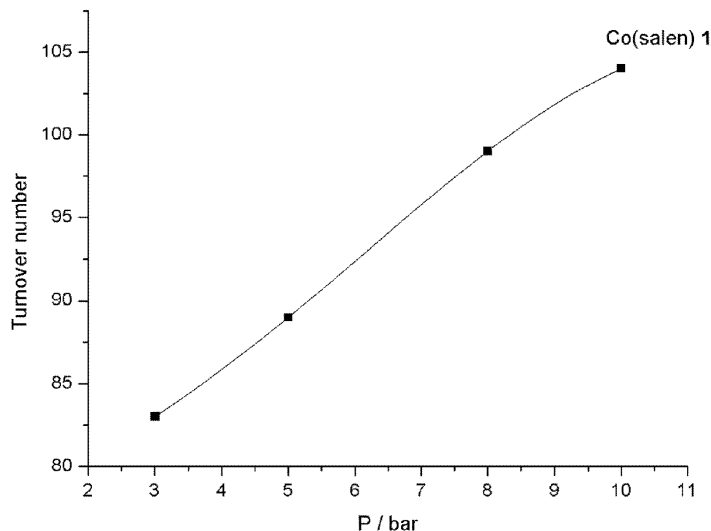
Figure 20. The effect of pressure on the oxidation of veratryl alcohol by complex **1**. (7.5 mM Co(salen), 7.5 mM pyridine and 40 mM of veratryl alcohol in water at pH 12.5 and 80 °C, reaction time 70 h).[II]

However, it was later noticed that at low catalyst concentrations the increase in oxygen pressure did not improve the oxidation results. Therefore, to study the influence of oxygen pressure on the reaction at high and low concentrations, reaction-monitoring experiments were performed with a set-up from which samples can be taken during the experiment under higher oxygen pressures. Figure 21 summarizes the results of these experiments. At low concentrations the reaction rate is about the same under 1 and 10 bar O_2 pressure, while at higher concentrations the increased oxygen pressure significantly enhances the reaction rate.[IV]

Obviously, at higher Co(salen) concentrations a higher amount of oxygen is needed to react with higher amount of reagents. However, higher catalyst activity at low concentrations and low impact of added oxygen pressure on the catalytic system at low concentrations imply that a μ-peroxo (2:1 ratio of Co:O_2) species is involved in the catalytic cycle.[35]

Figure 21. Oxidation activity (expressed as TON = turnover number, the moles of product per one mole of catalyst) at (1) 0.14 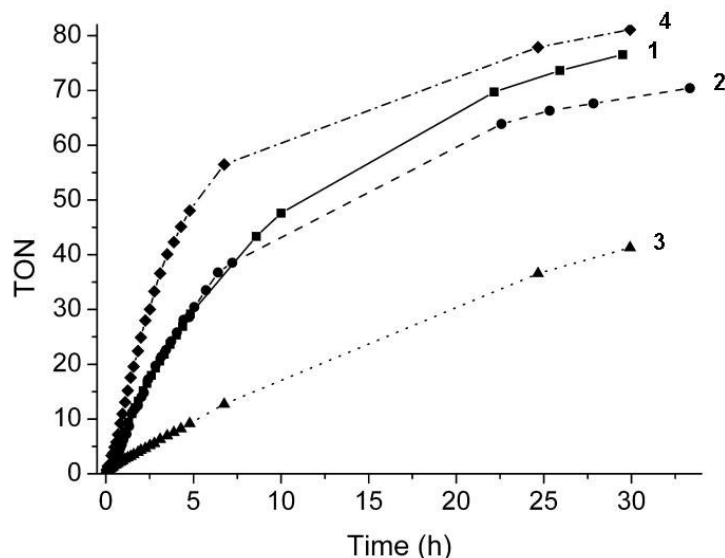mM Co(salen), 14 mM veratryl alcohol and 1 bar O_2, (2) 0.14 mM Co(salen), 14 mM veratryl alcohol and 10 bar O_2, (3) 0.41 mM Co(salen), 41 mM veratryl alcohol and 1 bar O_2 and (4) 0.41 mM Co(salen), 41 mM veratryl alcohol and 10 bar O_2.[IV]

4.4 Summary of Part I

Part I of this study describes a Co(salen) catalyzed oxidation reaction, which is most active in water at pH values over 12 and at temperatures over 70°C. Additional axial base is not needed for this catalytic system, as hydroxyl-ions or the substrate itself can act as an axial base. Low catalyst concentration prolongs the catalyst lifetime, although in longer experiments NaOH needs to be added to keep the pH high enough for the system to stay active. High substrate to cobalt ratio increases the reaction rate enormously.

The unsubstituted Co(salen) (**1**) is the most active of the tested complexes and for example Co(N-Me-salpr) (**6**), which is claimed to be the most active complex of this type in the oxidation of phenolic substrates, is practically inactive. Co(N-Me-salpr) (**6**) and Co(acacen) (**4**) are said to form superoxo-complexes more easily than Co(salen).[97-100] Superoxo-complexes have usually been suggested to be the catalytically active species in cobalt-catalyzed oxidation reactions.[14,20] Nevertheless, the above mentioned results suggest that superoxo-species is not the active catalyst in the reaction studied in this thesis.

The required reaction conditions for the maximum activity support the presence of a dinuclear cobalt-complex as the active species. The effects of axial base and substrate to cobalt ratio imply that substrate coordination could be a key step in the catalytic cycle. To gain more insight into what is really taking place in this reaction and why the above-mentioned reaction conditions promote activity, spectroscopic measurements of the reaction solution seemed like a very attractive next experimental step.

31

5 PART II: IN-SITU SPECTROSCOPIC STUDY OF THE REACTION MECHANISM OF CO(SALEN) CATALYZED OXIDATION OF VERATRYL ALCOHOL

Much research has been done on characterizing the different oxygen-species formed by cobalt complexes with dioxygen. The most common methods in characterizing cobalt-oxygen complexes have been X-ray crystallography, EPR-, Raman- and absorption spectroscopy. To study a certain system thoroughly, a combination of different spectroscopic techniques should be used. For this study, UV-Vis, IR and Raman spectroscopic techniques were chosen. The results of the *in situ* spectroscopic studies are described in articles III, IV and V.

5.1 ATR-IR spectroscopy

Molecular vibrations give rise to absorption bands throughout most of the infrared region.[105] Both, Infrared and Raman spectroscopy, involve vibrational and rotational energy levels. They are not duplicates of each other but rather complementary. For infrared spectroscopy one of the selection rules states that in order to absorb infrared radiation, a molecular vibration must cause a change in the dipole moment of the molecule. Thus, non-symmetrical vibrations are more intense in infrared spectra than in Raman spectra.[105]

Aldehydes exhibit a strong C=O vibration in an IR spectrum.[105-106] Therefore IR-spectroscopy is an attractive choice to study the formation of veratraldehyde in this system. However, IR-spectroscopy of aqueous solutions is demanding due to the strong absorption of water, which may interfere with the IR absorption of the sample. It has been common to use very thin layers of solutions (0.01-0.05 mm) of rather high concentrations (5-20 %) which are then placed between two plates of water-insoluble crystals, such as CaF_2 and KRS-5 (TlBr/TlI).[107] Such a system is obviously not well suited for online *in situ* measurements.

In the Attenuated Total Reflection (ATR) technique, the penetration depth of the IR-laser is in the order of micrometers and therefore interference from the absorptions of water can be reduced. In other words, with this technique the sample thickness is automatically very low.[108] As a result, ATR-IR technique can be used to study *in situ* the mechanism of Co(salen) catalyzed oxidation reaction in an aqueous solution.

5.1.1 Experimental

The ATR-IR measurements were conducted on a ReactIR 1000 spectrometer from Mettler Toledo (Figure 22). A more detailed description of the set-up and of the experimental procedure of the measurements is presented in article III.

The oxidation experiments were performed as closely as possible to the same procedures as those described in article I and II but some limitations were set by this

spectroscopic technique. First of all, the concentration of the compounds must be reasonably high and therefore it is not possible to perform the experiments with low catalyst concentrations. This is certainly unfortunate, as the lifetime of the catalyst has been observed to be higher at lower concentrations. Thus, in a standard reaction 0.45 mmol (150 mg) of Co(salen) and 14-21 mmol (2-3 ml) of veratryl alcohol were dissolved in 90 ml of solvent. The concentration of the catalyst is about the same as in the initial oxidation experiments of this thesis described in article I. As a result the maximum turnovers that can be expected for these reactions are in the range of 30-40 during 24 h.

Another change to the experimental procedure is due to the poor solubility of the product in water. It was observed that the produced aldehyde can form a film on the ATR-IR probe, which then prevents other species to be seen in the spectra. To circumvent this problem 1,4-dioxane was introduced as a co-solvent, which does not affect the activity of the system.

Figure 22. The experimental set-up used for *in situ* ATR-IR spectroscopy.

5.1.2 Reference spectra

Veratraldehyde in water at pH 12 exhibits several peaks, which are listed here with tentative assignments (in cm^{-1}): 1017 (m) arises from the C-O bond of the functional group (this vibration is similar to the C-O of the alcohol; it seems that due to hydrogen bonding a similar vibration, but weaker, is observed in the aqueous solutions of the aldehyde), 1140, 1160 (m), and 1272 (s) arise from the methoxy-group, 1428 (w) and 1468 (m) come from the methyl C-H bonds, 1513 (m) and 1588 (d, m) exhibit the aromatic ring vibrations and 1679 (m) comes from the aldehyde C=O vibration and 2960 (w) and 2854 (w) arise from the methoxy C-H bonds.[105-106]

The reference peaks for veratrylic acid and veratryl alcohol are listed in the notes of articles III and IV, respectively. The vibrations of the methoxy-groups and the aromatic ring only shift slightly within the alcohol, the aldehyde and the acid, and therefore all reference peaks are not listed here. Main differences in the spectrum of veratrylic acid are the vibrations at 1694 cm^{-1} (m), 1378 cm^{-1} (m-s) and 1546 cm^{-1} (m).

The first is the C=O bond and the last two imply the presence of a hydrogen-bonded carboxylato-dimer (spectrum taken at pH 12).[105]

The co-solvent 1,4-dioxane shows vibrations at (in cm^{-1}) 2961 and 2919 (CH_2 stretch), 1284 (CH_2 wag), 1126 (C-O stretch) and 867 (C-H bend).

5.1.3 Results and discussion

Aldehyde formation is clearly observed by ATR-IR spectroscopy as a vibration arising at wavenumber 1675 cm^{-1} (Figure 23). No other peaks are formed at the carbonyl area, which suggests that carboxylic acid is not formed or its amount is too low to be seen in the ATR-IR spectra.
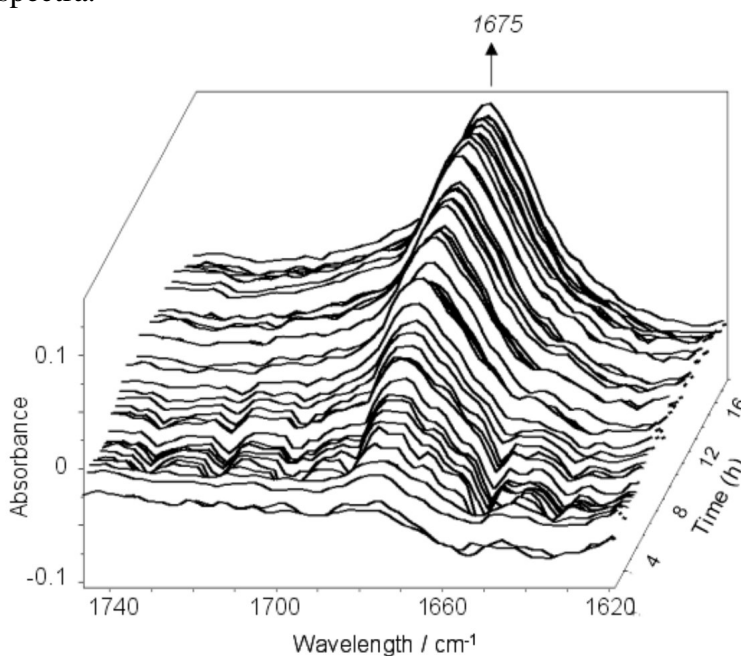

Figure 23. 3D plot of the carbonyl region in time-resolved ATR-IR spectra of veratryl alcohol oxidation by Co(salen). (150 mg Co(salen) and 3 ml of veratryl alcohol in 90 ml of water:dioxan (5:1) mixture at 80°C and pH 12).[III]

In addition to the aldehyde C=O vibration at 1675 cm^{-1}, a second strong vibration peak which increases with reaction time was observed at 993 cm^{-1} (Figure 24). The rate of formation of the peak at 993 cm^{-1} is faster than that of the peak at 1675 cm^{-1}, indicating that they belong to two different species. Thus the peak at 993 cm^{-1} is not arising from the product, but is due to a reaction intermediate or a side-product.

When only Co(salen) is stirred at pH 12 in the absence of oxygen, a weak vibration peak at 984 cm^{-1} is observed to appear, but after the substrate is added, a strong vibration at 993 cm^{-1} forms and the 984 cm^{-1} peak can no longer be observed (Figure 25).[IV] The 984 cm^{-1} vibration is assigned to bis-μ-hydroxo[Co(salen)]$_2$ species, as this species should be formed in a solution of Co(salen) under these reaction conditions.[70] Also, a similar bridging hydroxo group in the bis-μ-hydroxo[Cu(bipy)$_2$] type complex exhibits a vibration at 955 cm^{-1}.[107,109] The peak at 993 cm^{-1}, on the other hand, seems to depend on the presence of veratryl alcohol.
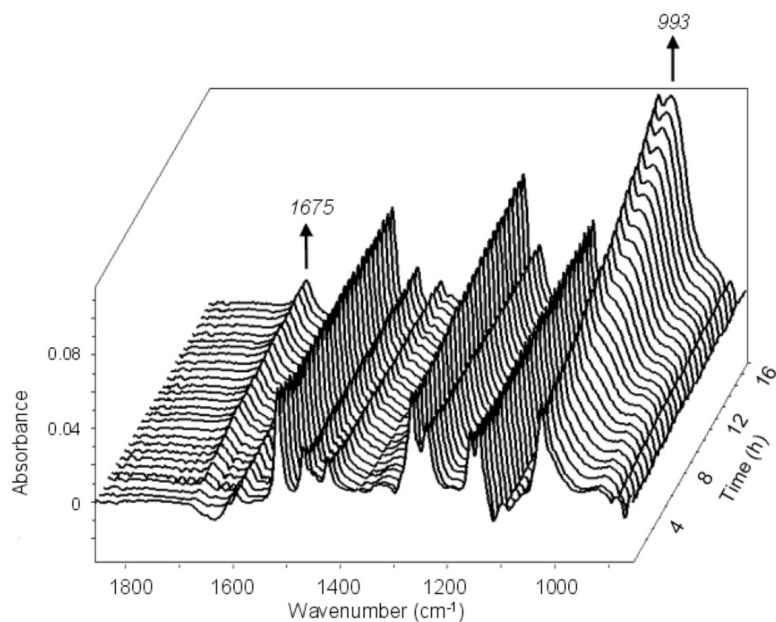
Figure 24. 3D plot of time-resolved ATR-IR spectra of the veratryl alcohol oxidation by Co(salen) and dioxygen in water at 80°C and pH 12. (150 mg Co(salen) and 3 ml of veratryl alcohol in 90 ml of water:dioxan (5:1) mixture).[IV]
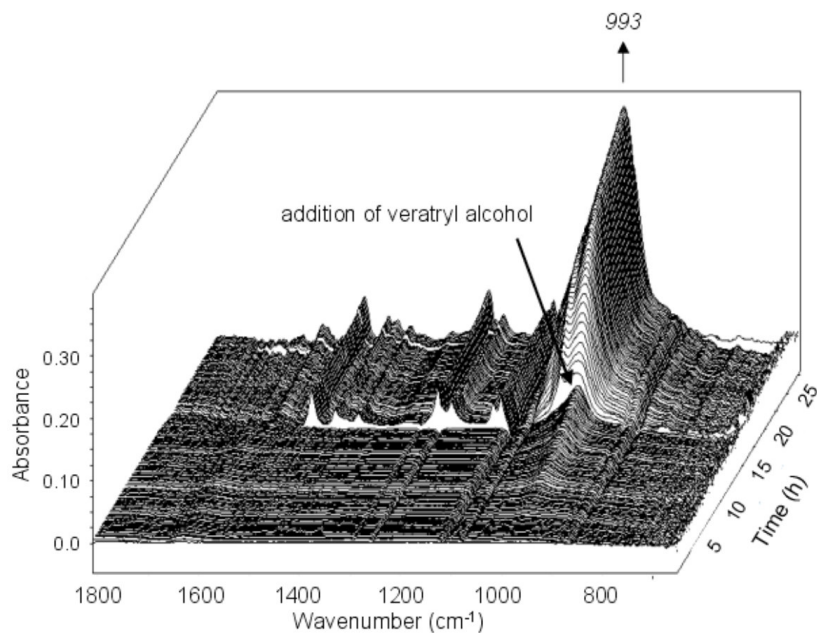

Figure 25. 3D-plot of the ATR-IR spectra of a reaction before and after the addition of veratryl alcohol. (150 mg Co(salen) and 3 ml of veratryl alcohol in 90 ml of water:dioxan (5:1) mixture at 80°C and pH 12 under argon).

Metal-bound alkoxides (M-OR) exhibit ν(CO) at ca. 1000 cm^{-1}.[107] As the vibration peak at 993 cm^{-1} is not formed in the absence of Co(salen) or veratryl alcohol, it has been assigned to a cobalt-alkoxo intermediate (**B**), in which the substrate is coordinated as an alkoxo-group to the cobalt center (Figure 26).[IV]

The intermediate **B** is not forming at low pH or at temperatures lower than 70°C, which implies that these reaction conditions are needed for the formation of this species. It is very plausible that higher temperature and pH are required to deprotonate the substrate, which can then form the alkoxo-species. It is also possible that these reaction conditions are required to form the bis-μ-hydroxo[Co(salen)]$_2$ species (**A**), which is able to deprotonate the substrate. It is very difficult to prove which of the two steps happens first, substrate coordination or substrate deprotonation.
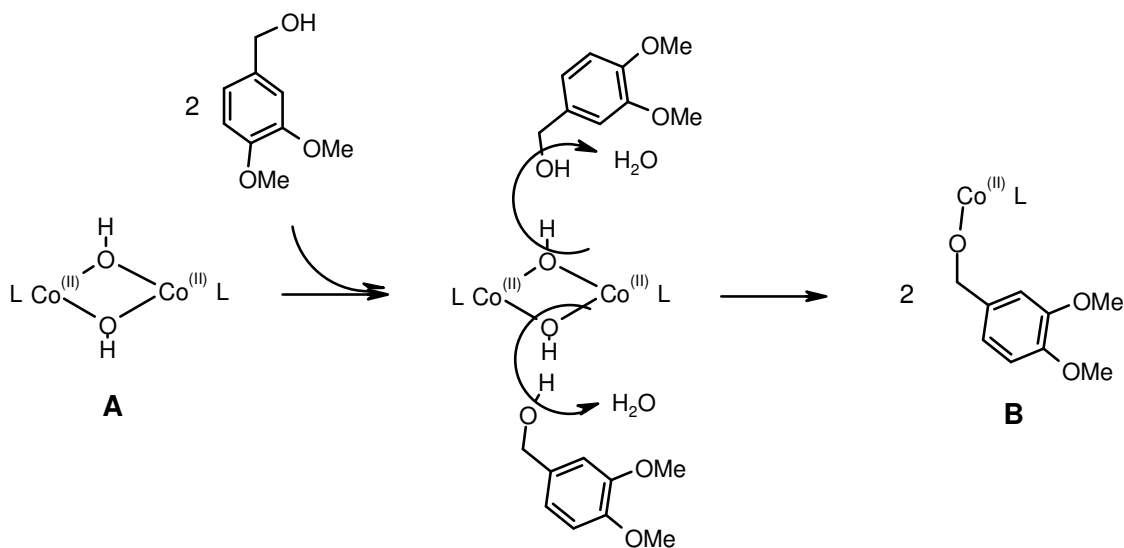

Figure 26. Suggested mechanism for the formation of a cobalt-alkoxo intermediate (**B**).

The cobalt-alkoxo intermediate **B** is formed in the absence of oxygen directly after Co(salen) is added into the solution of veratryl alcohol at 80°C and pH 12. The rate of formation of the vibration peak at 993 cm^{-1} slows down after introduction of oxygen to the reaction mixture (Figure 27). The introduction of oxygen initiates the aldehyde formation. This suggests that when the aldehyde production starts, the accumulation rate of the intermediate **B** decreases. In a standard reaction, in which all reagents are present from the start, the 993 cm^{-1} peak accumulates as well. This implies that the rate of alkoxo-intermediate (**B**) formation is faster than the rate of the following reaction steps.

Co(salen) cannot oxidize benzyl alcohol to benzaldehyde under the reaction conditions in which veratryl alcohol is oxidized. Nevertheless, the vibration peak at 993 cm^{-1} indicating a cobalt-alkoxo intermediate is forming in the reaction of benzyl alcohol with Co(salen) (Figure 28). Within 14 h of reaction the alcohol C-O vibration at 1025 cm^{-1} is replaced by the cobalt-bound C-O at 993 cm^{-1}. No aldehyde formation is observed. Thus, it seems that benzyl alcohol can also form an alkoxo-intermediate with Co(salen). This alkoxo-intermediate is more stable than with veratryl alcohol and the reaction seems to stop at this step. Therefore it is apparent that either oxygen cannot coordinate to the benzyl alkoxo-Co(salen) species or the formed oxygen complex is too stable. The latter

explanation seems more likely, as it is plausible that the coordinated oxygen cannot abstract a hydrogen from a benzyl alkoxo-species. It can be concluded that the abstraction of a β-hydrogen leading to the formation of aldehyde seems to be enhanced by the methoxy-substituents in veratryl alcohol.
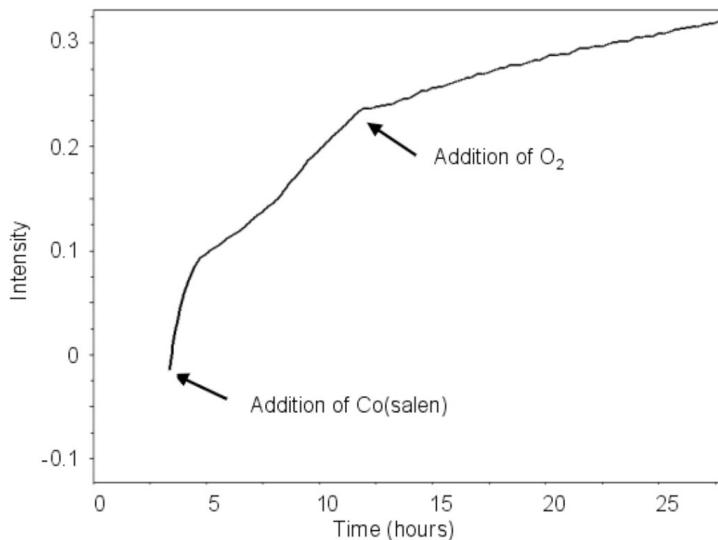
Figure 27. Appearance and increase in the integrated area of the vibration peak at 993 cm^{-1} in a Co(salen) reaction in the absence and presence of oxygen. (150 mg Co(salen) and 3 ml of veratryl alcohol in 90 ml of water:dioxan (5:1) mixture at 80°C and pH 12 initially under argon).[IV]
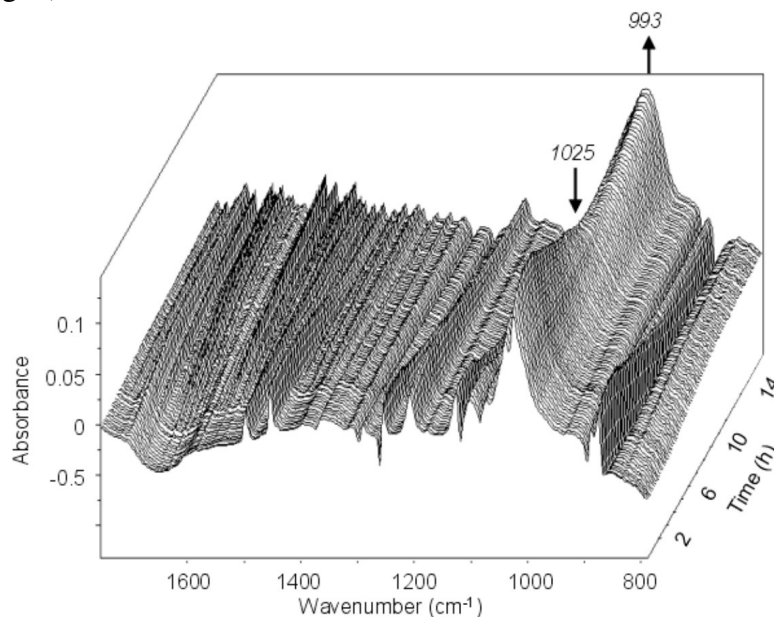

Figure 28. Vibration peak at 993 cm^{-1} replaces the vibration peak at 1025 cm^{-1} during the reaction of benzyl alcohol with Co(salen) at 80°C and pH 12.

Summarizing, aldehyde formation is not observed in the ATR-IR spectra at pH lower than 10, in the absence of oxygen or at temperatures lower than 70°C. A cobalt-alkoxo intermediate exhibiting a vibration at 993 cm^{-1} appears at the temperature and pH range of an active system and forms faster in the absence of oxygen. It is very likely that this temperature and pH range is required to form the alkoxo-intermediate. The rate-limiting step is either oxygen coordination to the cobalt-alkoxo intermediate or product detachment from the Co(salen)-alkoxo-oxygen complex. This step is aided by the methoxy-substituents in veratryl alcohol.

5.2   Raman spectroscopy

Many oxygen bridges in metal complexes have high symmetry and are therefore they exhibit low IR activity. In order for a molecular vibration to be Raman active, the vibration must be accompanied by a change in the polarizability of the molecule. In other words, symmetrical molecules are more often Raman active. Consequently, Raman spectroscopy is frequently used for the study of metal oxygen complexes.[112-116]

The vibrational spectra of cobalt oxygen species have usually been recorded at a solid state. The $\nu(O_2)$ in cobalt oxygen complexes falls into the typical range of $\nu(O_2)$ of superoxo- and peroxo-type complexes. The superoxo (O_2^-) type exhibits $\nu(O_2)$ in the 1200-1070 cm^{-1} region, while the peroxo (O_2^{2-}) type exhibits $\nu(O_2)$ in the 930-740 cm^{-1} region.[107,110,112] The $\nu(O_2)$ frequency is somewhat sensitive to the nature of the base ligand B. For example, for B = pyO, DMF or py, the $\nu(O_2)$ changes from 910, 897 to 888 cm^{-1}, respectively. In the absence of an axial base ligand, [Co(salen)]$_2$O$_2$ exhibits $\nu(O_2)$ at 1011 cm^{-1}, which falls between superoxo- and peroxo bridge regions.[110] These different oxygen species should be observable by Raman spectroscopy in aqueous solution as water hardly interferes with other bands in the Raman spectra. In this study Raman spectroscopy was used to verify whether cobalt-oxygen species can be observed at the applied reaction conditions.

5.2.1   Experimental

Raman spectroscopy is even less sensitive than ATR-IR, and therefore a high concentration of reagents had to be used (7.7 mM Co(salen), 0.32 M veratryl alcohol). Due to the high concentration, precipitation of the product on the probe is a real problem in Raman measurements if using an insertion probe. Therefore a set-up was used, in which Raman scattering was measured through the reaction flask (Figure 29). This method worked very well. Otherwise a standard procedure for oxidation experiments was used.[I, II, III]

Figure 29. Set-up for *in situ* Raman spectroscopy.

5.2.2   Results and discussion

Figure 30 shows, that the only changes observed after an overnight measurement are the formation of a weak carbonyl vibration at 1675 cm^{-1} and shifts in the vibration peaks of the substrate. Thus no peroxo- or superoxo bridges are observed in the Raman spectra of the Co(salen) catalyzed reaction at these conditions.

It is expected that a superoxo- or peroxo species is involved in the reaction mechanism and therefore at a first thought it is surprising that no O-O vibrations are observed in either ATR-IR or Raman spectra. However, this turns out to be due to the high concentrations of reagents used in these experiments. As was noted in the results of the ATR-IR spectroscopic studies, a metal-alkoxo intermediate accumulates during the reaction. Thus, at these reaction conditions the reaction rate depends on the oxygen insertion or the aldehyde formation, steps, which seem to occur very fast compared to the alkoxo-intermediate formation. As a result, the peaks arising from the metal-alkoxo intermediate or the product aldehyde dominate the ATR-IR and the Raman spectra.
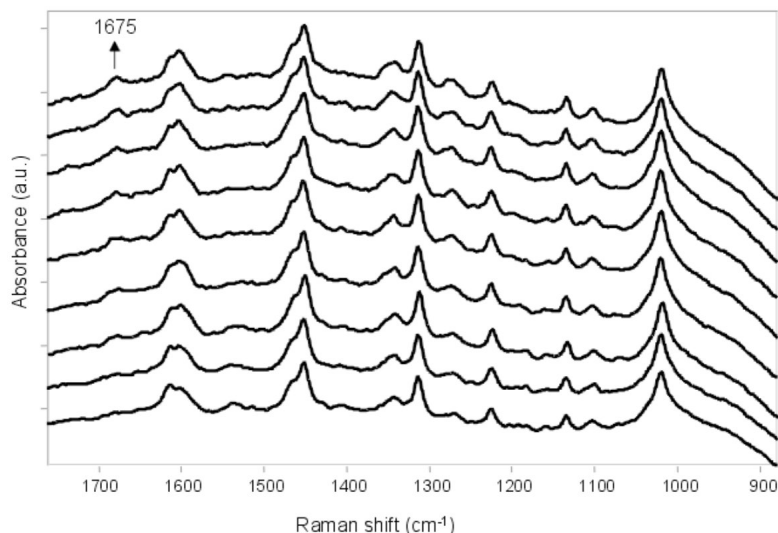
Figure 30. Raman spectra of Co(salen) catalyzed veratryl alcohol oxidation. Vibration at 1675 cm^{-1} corresponds to the C=O bond of the product. (200 mg Co(salen) and 5 ml veratryl alcohol in 90 ml of water:dioxan mixture (3:1) at 80°C and pH 12).[IV]

5.3 UV-Vis spectroscopy

Electronic transitions usually give rise to absorption or emission in the ultraviolet or visible regions of the electromagnetic spectrum. The oxygen-complexes of cobalt have been widely studied by UV-Vis spectroscopy.[17,48,50-52,114] The bridging superoxo complexes exhibit a single intense band in the electronic spectra in the region 25 000-33 000 cm^{-1} (400-300 nm). This band has been assigned to a charge-transfer transition from the π_h^* orbital to an appropriate d_σ^* level on the metal center. Another absorption band falls in the region 13 000-20 000 cm^{-1} (770-500 nm), most probably arising from the $d\pi \rightarrow \pi_v^*$ (MLCT) charge-transfer transition.[51]

A bridging nonplanar peroxo species has two absorption bands of similar intensity at about 30 000 cm^{-1} (320 nm) and 25 000 cm^{-1} (400 nm) assigned to ligand to metal charge-transfer (LMCT) transitions. The deviation from planarity gives rise to two equally strong absorption bands as there is no distinction between π_h^* and π_v^* levels and as a result two equal $\pi^* \rightarrow d_{\sigma^\star}$ (LMCT) transitions are observed.[48,50,52] Sometimes a planar peroxo-bridge can form between two cobalt centers. The electronic situation resembles the superoxo-case and two LMCT bands appear, one strong and one weak.

A doubly bridged μ-hydroxo-μ-peroxo (OH, O_2^{2-}) has one intense LMCT band at about 26 500 cm^{-1} (375 nm) and a shoulder at higher energies (about 34 000 cm^{-1}, 290 nm).[51] The distortion from planarity should be greater in this species than in the simple peroxo-bridged species or in a doubly bridged superoxo species. The intensities of the two LMCT bands depend upon the degree of distortion of the $Co(O_2)(OH)Co$ ring.[51] Cobalt histidine complexes have been shown to form a doubly bridged μ-hydroxo-μ-peroxo species from a peroxo-bridged complex when adding NaOH to the solution. This

transformation is seen in the UV-Vis spectra of the Co-histidine solution as the absorption bands of the peroxo-species at about 325 nm and 390 nm are replaced by a single absorption band at about 370 nm and a shoulder at higher energies (about 290 nm).[49]

A shoulder at 480-490 nm is often observed in the spectra of cobalt complexes, which is assigned to d-d transitions.[51,115] The intensity of this shoulder decreases on oxidation of Co(II) to Co(III) in Co(salen) type complexes indicating a removal of an electron from the d_{z^2} orbital of cobalt.[114]

5.3.1 Experimental

An opposite limitation is met when using UV-Vis spectroscopy to study this system than when using ATR-IR or Raman spectroscopy. The UV-Vis detector gets overloaded with signal already at a concentration range of 2-4 mM Co(salen) due to an intense absorption band at around 300 nm in the UV region, which means that if the UV-range is wished to be explored, the concentration of cobalt must be kept very low. Moreover, the produced aldehyde exhibits an n → π* transition arising from the carbonyl oxygen,[116] which appears as an intense absorption peak at 308 nm.

Consequently, the UV-Vis measurements were conducted at very low concentrations, typically in the range of 0.8-1.0 mM of Co(salen). The measurements were performed on a Varian CARY50 spectrometer with an optical fibre probe, which could be immersed directly into the reaction mixture. The pathlength of the UV light can be varied by changing the tip of the probe. In a typical experiment, the solvent was heated to 80°C before recording the baseline. In most experiments, the substrate veratryl alcohol was included in the baseline as it was added in excess to the other reagents.

5.3.2 Reference spectra

The commercial veratraldehyde exhibits absorption maxima at 268 nm and 308 nm with a shoulder at 290 nm. Veratrylic acid shows an absorption maximum at 250.4 nm with shoulders at 295 nm and 330 nm. Salen ligand exhibits absorption bands at 256 nm, 327 nm and 372 nm. All reference spectra were measured in water.

5.3.3 Results and discussion

Results of the UV-Vis measurements are summarized in Table 3. According to the UV-Vis spectra, substrate can replace the hydroxyl-group from the first coordination sphere of the cobalt center. This is seen as shifts of the absorption bands at 316 nm and 375 nm to 336 nm and 390 nm after the addition of veratryl alcohol to the solution of Co(salen) at pH 12 (Table 3, entries 3 and 6). The absorptions at 336 nm and 390 nm are resembling the absorptions of Co(salen) dissolved in ethanol (Table 3, entry 2). Similar bands are also present in the solution of Co(salen) and veratryl alcohol at low pH under argon (Table 3, entry 7). This suggests that veratryl alcohol is located in the coordination sphere of cobalt also at low pH.

Table 3. UV-Vis absorption maxima of Co(salen) in different solutions. (sh = shoulder)

Entry	Compound	Solvent	Other parameters	nm	nm	nm
1	Co(salen)	H_2O		310sh	372	480sh
2	Co(salen)	Ethanol		333	391	480sh
3	Co(salen)	H_2O	pH 12	316	375	490 sh
4	Co(salen)py	H_2O		322sh	378	480sh
5	Co(salen)py	H_2O	pH 12	316	375	480sh
6	Co(salen)py, veratryl alcohol	H_2O	pH 12	336	390	485sh
7	Co(salen), veratryl alcohol	H_2O	under argon	339	392	490sh
8	Co(salen), veratryl alcohol	H_2O	pH 12 under argon	339	392	490sh
9	Co(salen), veratryl alcohol	H_2O	pH 12 with O_2	324	378	
10	Co(salen), veratryl alcohol	H_2O	pH 12 with O_2, in time	324sh (decreased)	378	
11	Co(salen), veratryl alcohol	H_2O	with O_2	300sh	378	
12	Co(salen), veratryl alcohol	H_2O	with O_2 pH 12	308 (growing)	378	

When oxygen is added to this solution, the absorption bands shift to 300 nm (shoulder-like) and 378 nm and the shoulder at 490 nm disappears (Table 3, entry 11). This type of spectrum resembles a doubly-bridged μ-hydroxo-μ-peroxo species, although the presence of only one major absorption band can also suggest a mono-bridged species with a symmetric ligand field.[48,51] The disappearance of the 490 nm absorption suggests that Co(II) is being oxidized to Co(III), which also indicates coordination of dioxygen to cobalt.[36] Aldehyde production does not start in this solution before the addition of NaOH. This is seen as the formation and growth of the absorption band at 308 nm. The absorption band at 380 nm does not shift (Figure 31).

When oxygen is added to the solution of Co(salen) and veratryl alcohol at pH 12 under argon, the absorption bands at 339 nm and 392 nm shift to 324 nm and 378 nm and the shoulder at 490 nm disappears (Table 3, entries 8 and 9 and Figure 32). These shifts suggest the formation of a monobridged, nonplanar μ-peroxo complex.[48,52] With time, the absorption band at 324 nm diminishes (Table 3, entry 10 and Figure 32), which could

mean that a second bridge is forming between the cobalt centers, as doubly-bridged species exhibit only one absorption maximum.[48,51]
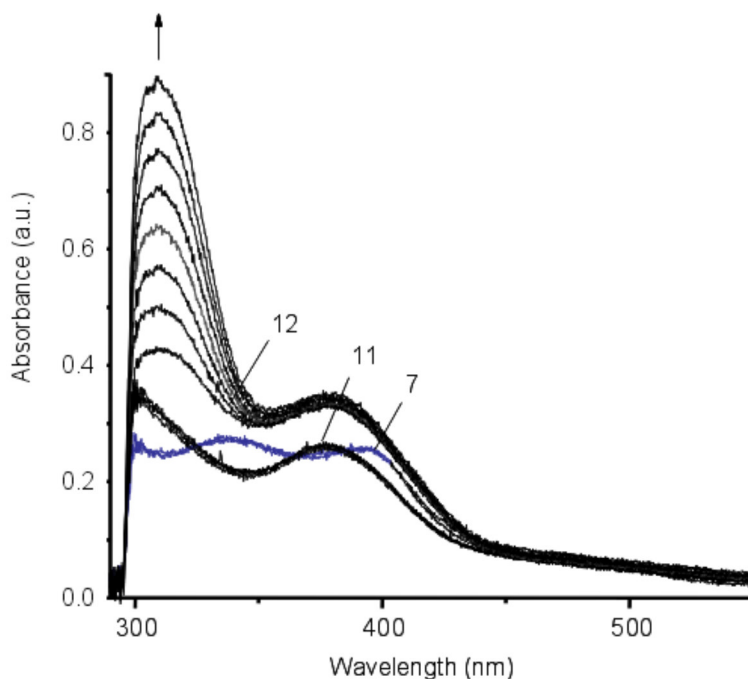

Figure 31. UV-Vis spectra of a solution of Co(salen) and veratryl alcohol in water at 80°C under argon (7), after the addition of oxygen (11) and after increasing the pH value to 12 with NaOH (12). (10 mg of Co(salen) and 2 ml of veratryl alcohol in 120 ml of water at 80°C)[IV]

Summarizing, the UV-Vis spectra clearly indicate that oxygen coordinates to Co(salen) at these reaction conditions. The absorption bands observed after addition of oxygen to the reaction mixture imply that an O-O bridge is formed between two cobalt atoms and that Co(II) is oxidized to Co(III) in this process. Interestingly, the UV-Vis results suggest that at low pH a doubly-bridged species is formed when oxygen is introduced to the solution of veratryl alcohol and Co(salen). At high pH a monobridged species is formed first, but is transformed into a doubly bridged species over time.

It is also plausible that the planarity of the oxygen-bridge changes with pH and therefore the intensities of the two absorption bands change in relation to each other. The difference can also be caused by the effect of high pH on the substrate. At low pH the substrate is coordinated as an alcohol group to the cobalt center, whereas at high pH it is coordinated as an alkoxyl group, which has a radical-type character. Therefore the oxygen-bridge, which is formed at high pH, is less symmetric as there is a charge transfer from the alkoxyl group to the bridge. In the catalytic cycle the oxygen bridge abstracts a proton from the substrate but also electron transfer occurs. One electron and one proton from each substrate is transferred to the oxygen bridge, causing the $O\text{-}O^{2-}$ bond to break and two hydroxyl-bridges are formed between the cobalt centers, regenerating the bis-μ-hydroxo[Co(salen)]$_2$ species (Figure 26). This step is illustrated in Figure 33.
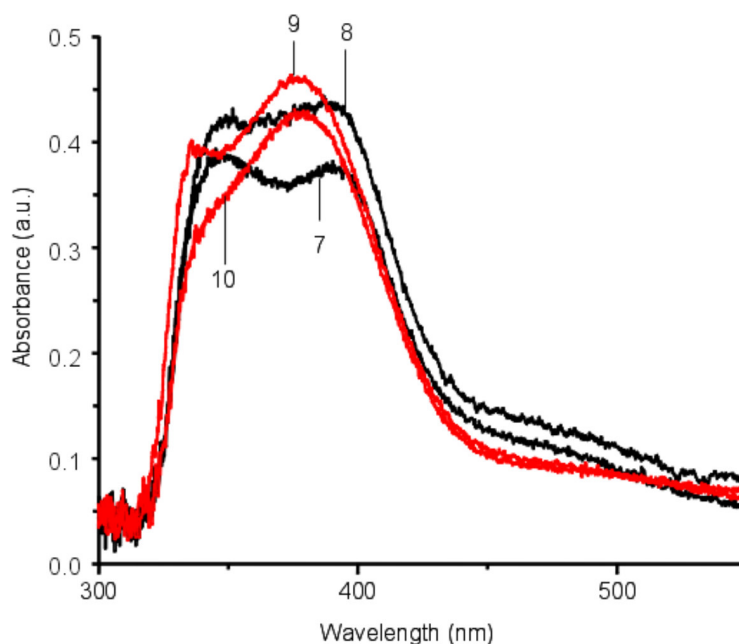
Figure 32. UV-Vis spectra of the solution of Co(salen) and veratryl alcohol in water under argon (7), at pH 12 after the addition of NaOH (8), directly after the introduction of oxygen (9) and in time reacting with oxygen (10). (10 mg of Co(salen) and 2 ml of veratryl alcohol in 120 ml of water at 80°C).[IV]
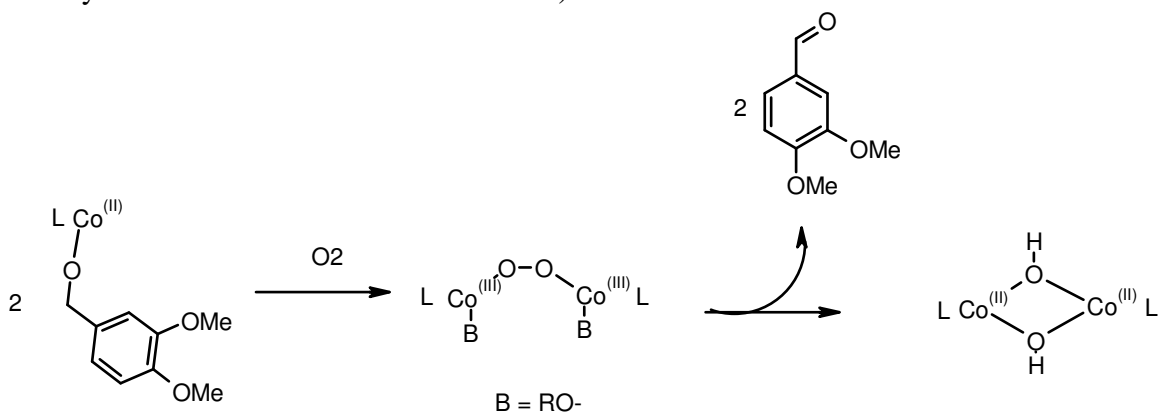
Figure 33. The proposed mechanism of oxygen insertion to a Co(salen)alkoxo-intermediate and consequent oxidation of the alkoxo-groups to aldehydes and reduction of the peroxo-bridge into two hydroxyl-groups.

5.4   Three spectroscopic techniques in one set-up approach

It is an intriguing idea to monitor the reaction mixture simultaneously with several spectroscopic techniques.[117] The observations from different techniques could be correlated to each other within the same reaction. In addition, the results from one technique could be checked by the other, i.e. whether the spectroscopic technique itself causes changes to the reaction.[118] In general spectroscopy of reaction solutions encounters a philosophical dilemma: Are we altering the reaction we study with the method we study it with? Multiple techniques can help to solve this dilemma by checking with one technique the possible damage caused by another. This approach was tested in an experiment in which all three probes, from the UV-Vis-, Raman and ATR-IR spectrometers, were inserted into the same reaction mixture in a set-up illustrated in Figure 34.

However, this approach is hampered by the different sensitivities of the chosen techniques. The detector of the UV-Vis set-up is overloaded with signal at concentrations which are tens of times too low for the Raman or ATR-IR measurements. Therefore the same reaction solution cannot be studied with all of these three techniques. This notion brings up another dilemma. If we are not able to measure the same reaction solution with different techniques, is the reaction which we study separately with different techniques, the same? Thus, as we study the same reaction with different techniques at different concentrations, we must keep in mind that the mechanisms of these reactions could actually be different from each other.

Figure 34. The set-up to perform UV-Vis, Raman and ATR-IR spectroscopic measurements simultaneously.

5.5   EPR spectroscopy

EPR spectroscopy has been commonly used to confirm the presence or absence of Co(III)superoxo-complexes.[48] The mononuclear and binuclear Co(III)superoxo-species have an EPR signal whereas the binuclear Co(III)peroxo-species is EPR silent. Measuring an EPR spectrum in an aqueous solution can be problematic due to the interference from water. EPR spectra can, however, also be measured from ice. This is in any case more convenient, as the EPR spectra of cobalt must be measured at low temperatures, preferably as low as possible. In these experiments, the EPR spectra were measured on a Bruker spectrometer at 77 K. This is certainly not the temperature of the active catalytic reaction and therefore the procedure for as *in situ* measurements as possible was to run the reaction in a standard way (see article II) and take samples via a 1 ml syringe, which was directly thrown into liquid nitrogen. The reaction stops immediately by cooling it to liquid nitrogen temperature, at which the measurements were taken.

Unfortunately the signal observed was a very broad one, which implies that there are many species present in the reaction mixture and it is very difficult to distinguish the signals between them. No conclusions could be drawn about the presence or absence of the Co(III)superoxo species according to these results and therefore the EPR measurements were not continued.

5.6   *In situ* ATR-IR spectroscopic study on a copper system

Veratryl alcohol oxidation has also been studied by using several copper complexes as catalysts.[119] These complexes are more active than Co(salen) under high oxygen pressures. The reactions in which Cu(phen) was used as a catalyst were monitored by using *in situ* ATR-IR spectroscopy. These experiments are explained in more detail in article V. The measurements on the copper system were useful for the study of Co(salen) catalyzed reactions, as the spectra of the two systems could be compared. The product in both systems is veratraldehyde and this could clearly be seen as the formation of the vibration of the aldehyde carbonyl at 1675 cm^{-1} and other vibrations related to veratraldehyde (Figure 35). However, the other major vibration which appears in the Co(salen) catalyzed reaction at 993 cm^{-1} was totally absent in the Cu(phen) system. This already proved that the vibration peak at 993 cm^{-1} is not simply product related, but depends on Co(salen).

The appointment of the peak at 993 cm^{-1} as C-O bond of a cobalt-alkoxo intermediate and the absence of such vibrations in the Cu(phen) catalyzed reaction suggest that either such a species is not formed in the copper system or that this species cannot be observed in the copper system. It is very likely that the reaction mechanism of Cu(phen) is different from the mechanism of Co(salen). It is plausible that an alkoxo-copper intermediate is formed but it is not observed to accumulate, as the next steps in the reaction are faster compared to the cobalt-catalyzed reaction. For example, the formed

oxygen bridge in the copper complex can be more reactive than in the cobalt complex and consequently the metal-alkoxo intermediate cannot be seen.

It is also possible that substrate coordination is not required in the copper catalyzed reaction, but this seems unlikely according to the literature references on similar copper systems.[16,21,83] A metal-coordinated alkoxyl group is suggested to be a key intermediate in the alcohol oxidation by CuCl/TEMPO. Nevertheless, direct evidence for the formation of this species as part of the CuCl/TEMPO catalytic cycle has not been given. However, as the CuCl/TEMPO system is quite similar to the Cu(phen) catalyst studied in this work, it is possible that such a Cu-alkoxyl-intermediate is so short-lived, that it could not be observed with spectroscopic methods.
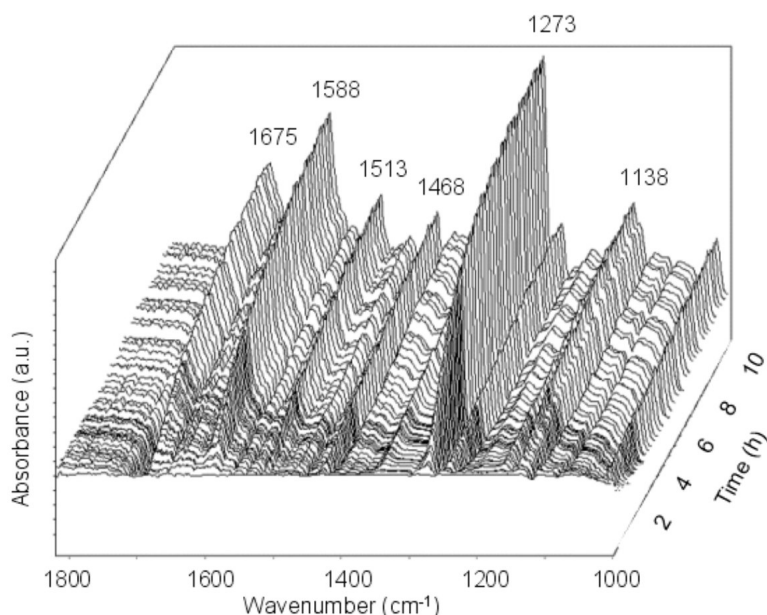
Figure 35. ATR-IR spectra of Cu(phen) catalyzed oxidation of veratryl alcohol. The depicted peaks arise from the product aldehyde.[V]

5.7   Summary of Part II

In situ spectroscopy proved to be a powerful method to study the Co(salen) catalyzed oxidation of veratryl alcohol. Combination of several spectroscopic techniques allowed for more precise identification of the observed species and broadened the scope of detectable intermediates. The spectroscopic fingerprints of different species detected by UV-Vis, ATR-IR and Raman spectroscopy for the Co(salen) system are summarized in Table 4. A detailed discussion of the suggested mechanism (Scheme 1) is given in article IV.

Table 4. Spectroscopic fingerprints of species **A-D**. (sh = shoulder)

| Species	Definition	ATR-IR (cm^{-1})	Raman (cm^{-1})	UV-Vis (nm)
A	bis-μ-hydroxo[Co(salen)]$_2$	984	-	316, 375, 490sh
B	Co(salen)alkoxo-species	993	-	339, 392
C	μ-peroxo[Co(salen)alkoxo]$_2$	-	-	324 , 378
D	Veratraldehyde	1675	1677	308

6 CONCLUSIONS

In this thesis, a catalytic system was developed, which oxidizes veratryl alcohol selectively to veratraldehyde with molecular oxygen in water reaching a turnover frequency of 15-20 h^{-1} at 80°C and pH 12 at ambient oxygen pressure. Furthermore, the mechanism of this reaction was thoroughly investigated by carefully monitoring the effect of reaction conditions with several *in situ* spectroscopic techniques.

Based on the results of this thesis, the oxidation of veratryl alcohol in water catalyzed by Co(salen) and oxygen is suggested to proceed via the steps described in Scheme 1. The spectroscopic methods, which have been used to observe a certain species, are also indicated in Scheme 1. A more detailed discussion of the mechanism is given in article IV.

Summarizing, the cycle of veratryl alcohol oxidation starts with a bis-μ-hydroxo[Co(salen)]$_2$complex **A**, which can deprotonate a substrate molecule at temperatures higher than 60°C forming an alkoxo-intermediate **B** and water. In the absence of oxygen, this species accumulates in the reaction.

An oxygen molecule forms a non-planar μ-peroxo-bridge between two Co(salen)-substrate units. This is the intermediate **C**. The peroxo-bridge of species **C** abstracts a proton from each coordinated substrate molecule and veratraldehyde is formed as a product (**D**). In the overall reaction, one activated oxygen molecule oxidizes two veratryl alcohol molecules to veratraldehyde, water is produced as the sideproduct and the initial Co(salen)-hydroxo complex is regenerated in the cycle. The rate-limiting step seems to be the proton transfer from substrate to the peroxo-bridge followed by the detachment of the product. The methoxy-substituents in the aromatic ring of veratryl alcohol seem to aid this step.
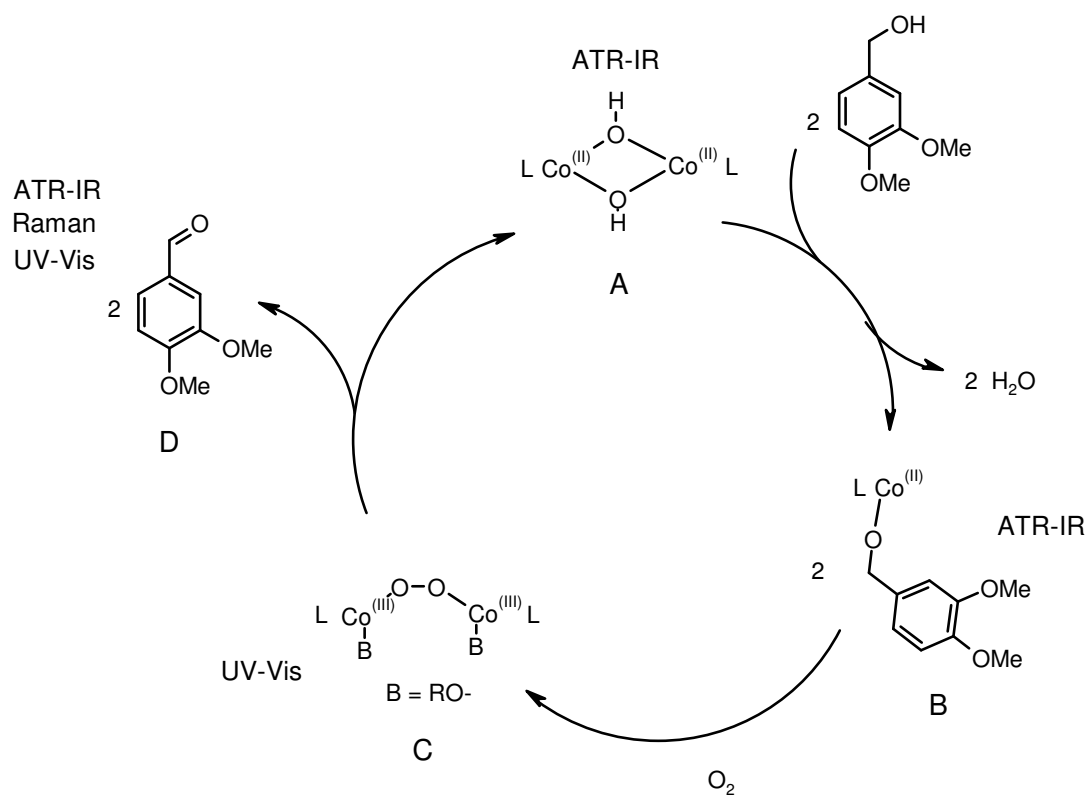
Scheme 1. The suggested mechanism for veratryl alcohol oxidation by Co(salen).

As the reaction mechanisms of transition metal complexes in oxygen activation are not well understood, each elucidated mechanism takes the research in this area a step further. New methods of studying a reaction can benefit other groups working in this field. Comparison of results with other existing systems proves valuable as differences in reactivities can be explained. All this effort hopefully helps the development of new, green, oxygen activating catalysts.

7 REFERENCES

1. J. Ebner and D. Riley in Active Oxygen in Chemistry, J. S. Valentine, A. Greenberg and J. F. Liebman, Eds., Chapman and Hall, London, vol.1, 1995.
2. I.P. Skibida and A. M. Sakharov, *Catal. Today 27* (1996) 187.
3. R. A. Sheldon, I. W. C. E. Arends and A. Dijksman, *Catal. Today 57* (2000) 157.
4. D. Riley, M. Stern and J. Ebner, in *The Activation of Dioxygen and Homogeneous Catalytic Oxidation*, D. H. R. Barton, A. E. Martell and D. T. Sawyer, Eds., Plenum Press, New York, 1993.
5. W. Kaim and B. Schwederski, Bioinorganic Chemistry: Inorganic Elements in the Chemistry of Life, John Wiley & Sons, 1994.
6. S. Lippard and J. Berg, *Principles of Bioinorganic Chemistry*, University Science Books, 1994.
7. R. Sheldon, *Metalloporphyrins in Catalytic Oxidations*, Marcel Dekker, Inc., New York, 1994.
8. R. D. Jones, D. A. Summerville and F. Basolo, *Chem. Rev. 79* (1979) 139.
9. M. Costas, M. P. Mehn, M. P. Jensen and L. Que, Jr., *Chem. Rev. 104* (2004) 939.
10. R. A. Sheldon, in *The Activation of Dioxygen and Homogeneous Catalytic Oxidation*, D. H. R. Barton, A. E. Martell and D. T. Sawyer, Eds., Plenum Press, New York, 1993.
11. *Bioinorganic Chemistry of Copper*, K. Karlin and Z. Tyeklár, Eds., Chapman&Hall, 1993.
12. Y. Cui, R. Patt, R. Chen and J. Gratzl, *J. Mol. Catal. A: Chemical 144* (1999) 411.
13. R. Hage, J. E. Iburg, J. H. Koek, R. Martens, J. Kerschner, E. L. M. Lempers, R. J. Martens, U. S. Racheria, S. W. Russell, T. Swarthoff, M. R. P van Vliet, J. B. Warnaar, L. van der Wolf and B. Krijnen, *Nature 369* (1994) 637.
14. R. Sheldon and J. Kochi, *Metal-Catalyzed Oxidations of Organic Compounds*, Academic Press, 1981.
15. A. Lubineau and J. Augé, in *Aqueous-Phase Organometallic Catalysis*, B. Cornils, and W. A. Herrmann, Eds., Wiley-VCH, Weinheim, 1998.
16. R. A. Sheldon and I. W. C. E. Arends, in *Catalytic Activation of Dioxygen by Metal Complexes*, L. I. Simandi, Ed., Kluwer Academic Publishers, Dordrecht, 1992.
17. G. McLendon, R. J. Motekaitis and A. E. Martell, *Inorg. Chem. 14* (1975) 1993.
18. A. Martell in *Oxygen Complexes and Oxygen Activation by Transition Metals*, A. Martell and D. Sawyer, Eds., Plenum Press, 1987.
19. R.A. Sheldon, I. W. C. E. Arends, G. -J. ten Brink, and A. Dijksman, *Acc. Chem. Res. 35* (2002) 774.
20. J. J. Bozell, J. O. Hoberg, D. Claffey, B. R. Hames and D. R. Dimmel, in *Green Chemistry*, P. T. Anastas and T. C. Williamson, Eds., Oxford University Press, Oxford, 1998.

21. C. X. Zhang, H.-C. Liang, K. J. Humpreys and K. D. Karlin, in *Catalytic Activation of Dioxygen by Metal Complexes*, L. I. Simandi, Ed., Kluwer Academic Publishers, Dordrecht, 1992.

22. *In-situ Spectroscopy of Catalysts*, Weckhuysen, B. M., Ed., American Scientific Publishers, Stevenson Ranch, 2004.

23. S. Haakana, The Activation of Oxygen Delignification and Hydrogen Peroxide Bleaching by Organometallic Catalysts, Licenciate Thesis, 2000, Helsinki University of Technology, Finland.

24. L. Kühne, J. Odermatt and T. Wachter, *Holzforschung 54* (2000) 407.

25. A. Dijksman, A. Marino-González, A. Mairata i Payeras, I.W.C.E. Arends, R.A. Sheldon, *J. Am. Chem. Soc. 123* (2001) 6826.

26. A. Che, K. Cheng, M.C.W. Chan, T. Lau, C. Mak, *J. Org. Chem. 65* (2000) 7996.

27. L. De Luca, G. Giacomelli, A. Porcheddu, *Org. Lett. 3* (2001) 3041.

28. T. Iwahama, Y. Yoshino, T. Keitoku, S. Sakaguchi, Y. Ishii, *J. Org. Chem. 65* (2000) 6502.

29. R. Ben-Daniel, P. Austers, R. Neumann, *J. Org. Chem. 66* (2001) 8650.

30. G. Csjernyik, A. H. Éll, L. Fadini, B. Pugin and J.-E. Bäckvall, *J. Org. Chem. 67* (2002) 1657.

31. B. A. Steinhoff, S.R. Fix, S.S. Stahl, *J. Am. Chem. Soc. 124* (2002) 766.

32. B. A. Steinhoff, I. A. Guzei and S. S. Stahl, *J. Am. Chem. Soc. 126* (2004) 11268.

33. M. D. Sollewijn Gelpke, J. Lee and M. H. Gold, *Biochemistry 41* (2002) 3498.

34. R. Y. N. Ho, J. F. Liebmanand J. S. Valentine, in *Active Oxygen in Chemistry*, J. S. Valentine, A. Greenberg and J. F. Liebman, Eds., Chapman and Hall, London, vol.1, 1995.

35. E. Niederhoff, J. Timmon and A. E. Martell, *Chem. Rev. 84* (1984) 137.

36. *Homogeneous Catalysis: The Applications and Chemistry of Catalysis by Soluble Transition Metal Complexes*, G. W. Parshall and S. D. Ittel, Eds., John Wiley & Sons, New York, 1992.

37. *A*. Bigotto, G. Costa, G. Mestroni, G. Pellizer, A. Puxeddu, E. Reisenhofer, L. Stefani and G. Tauzher, *Inorg. Chim. Acta* (1970) 41.

38. *Inorganic Chemistry: Principles of Structure and Reactivity*, J. E. Huuhey, E. A. Keiter, R. A. Keiter, Eds., HarperCollins College Publishers, New York, 1993.

39. L. Cavallo and E.N. Jacobsen, *Inorg. Chem. 43* (2004) 2175.

40. P.J. Pospisil, D.H. Carsten and E.N. Jacobsen, *Chem. Eur. J. 2* (1996) 974.

41. M. Costas, K. Chen and L. Que Jr., *Coord. Chem. Rev. 200-202* (2000) 517.

42. E.I. Solomon, T.C. Brunold, M.I.Davis, J.N. Kemsley, S.K. Lee, N. Lehnert, F. Neese, A.J. Skulan, Y.S. Yang and J. Zhou, *Chem. Rev. 100* (2000) 235.

43. A. Werner and A. Mylius, Z. *Anorg. Allg. Chem. 16* (1898) 245.

44. R. Drago and B. Corden, *Acc. Chem. Res. 13* (1980) 353.

45. *Comprehensive Coordination Chemistry: the synthesis, reactions, properties and applications of coordination compounds*, G. Wilkinson, Ed.; Vol. 4, Pergamon Press, 1987

46. B. S. Tovrog, D. J. Kitko and R. S. Drago, *J. Am. Chem. Soc. 98* (1976) 5144.

47. A. Sobkowiak and D. Sawyer, *Polish J. Chem. 69* (1995) 1531.

48. S. Fallab and P. Mitchell, *Adv. Inorg. Bioinorg. Mech. 3* (1997) 311.
49. S. Bagger and K. Gibson, *Acta Chem. Scand.26* (1972) 3788.
50. *Inorganic Electronic Spectroscopy*, A. B. P. Lever, Ed., Elsevier, Amsterdam, 1986.
51. A. B. P. Lever and H. B. Gray, *Acc. Chem. Res. 11* (1978) 348.
52. W. M. Miskowski, J. L. Robbins, I. M. Treitel and H. B. Gray, *Inorg. Chem. 14* (1975) 2318.
53. S. Hikichi, M. Akita and Y. Moro-oka, *Coord. Chem. Rev. 198* (2000) 61.
54. S. Hikichi, H. Komatsuzaki, N. Kitajima, M. Akita, M. Mukai, T. Kitagawa and Y. Moro-oka, *Inorg. Chem. 36* (1997) 266.
55. S. Hikichi, M. Yoshizawa, Y. Sasakura, M. Akita and Y. Moro-oka, *J. Am. Chem. Soc. 12* (1998) 10567.
56. T. Punniyamurthy, B. Bhatia, M. M. Reddy, G. C. Maikap and J. Iqbal, *Tetrahedron 53* (1997) 7649.
57. T. Tsumaki, *Bull. Chem. Soc. Jpn 13* (1938) 252.
58. H. Diehl and C. C. Hach, *Inorg. Synth. 3* (1950) 1962.
59. M. Calvin, R. H. Bailes and W. K. Wilmarth, *J. Am. Chem. Soc. 68* (1946) 2254.
60. C. H. Barkelew and M. Calvin, *J. Am. Chem. Soc. 68* (1946) 2257.
61. W. K. Wilmarth, S. Aranoff and M. Calvin, *J. Am. Chem. Soc. 68* (1946) 2263.
62. M. Calvin and C. H. Barkelew, *J. Am. Chem. Soc. 68* (1946) 2267.
63. E. W. Hughes, W. K. Wilmarth and M. Calvin, *J. Am. Chem. Soc. 68* (1946) 2273.
64. G. McLendon and A. E. Martell, *Coord. Chem. Rev. 19* (1976) 1.
65. J. J. Bozell, B. R. Hames and D. R. Dimmel, *J. Org. Chem. 60* (1995) 2398.
66. L. I. Simandi, in *Catalytic Activation of Dioxygen by Metal Complexes*, L. I. Simandi, Ed., Kluwer Academic Publishers, Dordrecht, 1992.
67. D. Chen and A. E. Martell, *Inorg. Chem. 26* (1987) 1026.
68. E. G. Jäger, J. Knaudt, M. Rudolph and M. Rost, *Chem. Ber. 129* (1996) 1041.
69. I. Sasaki, D. Pujol, A. Gaudemer, P. Thuery, R. Claude and J. Zarembowitch, *New. J. Chem. 13* (1989) 843.
70. R. J. Motekaitis and A. E. Martell, *Inorg. Chem. 27* (1988) 2718.
71. H. M. van Dort and H. J. Guerson, *Rec. Trav. Chim. Pays-Bas 86* (1967) 520.
72. A. Nishinaga, H. Tomita, K. Nishizawa and T. Matsuura, *J. Chem. Soc., Dalton Trans.* (1981) 1504.
73. M. Frostin-Rio, D. Pujol, C. Bied-Charreton, M. Perree-Fauvet and A. Gaudemer, *J. Chem. Soc., Perkin Trans. I* (1984) 1971.
74. E. Bolzacchini, C. Canevali, F. Morazzoni, M. Orlandi, B. Rindone and R. Scotti, *J. Chem. Soc., Dalton Trans.* (1997) 4695.
75. T. Elder and J. J. Bozell, *Holzforschung 50* (1996) 24.
76. A. Zombek, R. S. Drago, B. B. Corden and J. H. Gaul, *J. Am. Chem. Soc. 103* (1981) 7580.
77. E. Bolzacchini, A. M. Brambilla, M. Orlandi and B. Rindone, *Life Chemistry Reports 13* (1995) 71.
78. I. E. Marko, P. R. Giles, M. Tsukazaki, I. Chelle-Regnaut, C. J. Urch and S. M. Brown, *J. Am. Chem. Soc. 119* (1997) 12661.

79. G. J. ten Brink, I. W. C. E. Arends and R. A. Sheldon, *Science 287* (2000) 1636.
80. Y. Wang, J. L. DuBois, B. Hedman, K. O. Hodgson and T. P. D. Stack, *Science 279* (1998) 537.
81. P. Caudhuri, H. Hess, T. Weyhermüller and K. Wieghardt, *Angew. Chem. Int. Ed. 274* (1999) 1095.
82. M. M. Whittaker and J. W. Whittaker, *Biochemistry 40* (2001) 7140.
83. P. Gamez, I. W. C. E. Arends, J. Reedijk and R. A. Sheldon, *Chem. Commun.* (2003) 2414.
84. M. Fabbrini, C. Galli, P. Gentili and D. Macchitella, *Tetrahedron Lett. 42* (2001) 7551.
85. M. E. Arias, M. Arenas, J. Rodriguez, J. Soliveri, A.S. Ball and M. Hernandez, *Appl. Environ. Microbiol. 69* (2003) 1953.
86. M. Y. Balakshin, C.-L. Chen, J. S. Gratzl, A. G. Kirkman and H. Jakob, *Holzforschung 54* (2000) 171.
87. M. Tien and D. Ma, *J. Biol. Chem. 272* (1997) 8912.
88. K.D. Valli, H. Wariishi and M.H. Gold, *Biochemistry 29* (1990) 8535.
89. M. Bietti, E. Baciocchi and S. Steenken, *J. Phys. Chem. A 102* (1998) 7337.
90. E. Baciocchi, M. Bietti, M. F. Gerini and O. Lanzalunga, *Biochem. Biophys. Res. Commun. 293* (2002) 832-835.
91. W. Langenbeek and K. Oehler, *Chem. Ber. 89* (1956) 2455.
92. A. E. Martell, P. J. McCarthy, R. J. Hovey and K. Ueno, *J. Am. Chem. Soc. 77* (1955) 5820.
93. G. T. Morgan and J. D. M. Smith, *J. Chem. Soc.* (1925) 2030.
94. R. M. McAllister and J. H. Weber, *J. Organomet. Chem. 77* (1074) 91.
95. M. Hariharan and F. L. Urbach, *Inorg. Chem. 8* (1969) 556.
96. J. Manassen, *Inorg. Chem. 9* (1970) 966.
97. D. Chen, A. Martell and Y. Sun, *Inorg. Chem. 28* (1989) 2647.
98. B. B. Corden, R. S. Drago and R. P. Perito, *J. Am. Chem. Soc. 107* (1985) 2903.
99. C. Floriani and F. Calderazzo, *J. Chem. Soc.* (1969) 946.
100. A. L. Crumbliss and F. Basolo, *J. Am. Chem. Soc. 92* (1970) 55.
101. R. S. Koduri and M. Tien, *J. Biol. Chem. 270* (1995) 22254.
102. Å. Broden, R. Simonson, *Svensk Papperstidning* (1978) 541.
103. Å. Broden, R. Simonson, *Svensk Papperstidning* (1979) 487.
104. R. Battino, T.R. Rettich and T. Tominaga, *J. Phys. Chem. Ref. Data 12* (1983) 163.
105. N. B. Colthup, L. H. Daly and S. E. Wiberley, *Introduction to Infrared and Raman Spectroscopy*, Academic Press, Inc., San Diego, 1990.
106. G. Socrates, *Infrared Characteristic Group Frequencies*, John Wiley & Sons, Chichester, 1980.
107. *Infrared and Raman Spectra of Inorganic and Coordination Compounds, Part B: Applications in Coordination, Organometallic and Bioinorganic Chemistry*, K. Nakamoto, Ed., John Wiley and Sons, Inc., New York, 1997.
108. *Internal Reflection Spectroscopy,* F. Mirabella, Ed., Marcel Dekker, Inc., New York, 1993.
109. J. R. Ferraro and W. R. Walker, *Inorg. Chem. 27* (1965) 1382.

110. M. Suzuki, T. Ishiguro, M. Kozuka and K. Nakamoto, *Inorg. Chem. 20* (1981) 1993.
111. C. G. Barraclough, G. A. Lawrence and P. A. Lay, *Inorg. Chem. 17* (1978) 3317.
112. N. N. Greenwood and A. Earnshaw, *Chemistry of the Elements*, Pergamon Press, Oxford, 1984, p. 720.
113. E. M. Nour and R. E. Hester, *J. Mol. Struct. 62* (1980) 77.
114. B. Ortiz and S.-M. Park, *Bull. Korean Chem. Soc. 21* (2000) 405.
115. M. A. Hitchman, *Inorg. Chem. 16* (1977) 1985.
116. *Spectroscopic Methods in Organic Chemistry*, D.H. William, and I. Fleming, Eds.; McGraw-Hill Book Company, London, 1989.
117. S.J. Tinnemans, J.G. Mesu, K. Kervinen, T. Visser, T. A. Nijhuis, A. Beale, A.M.J. van der Eerden and B.M. Weckhuysen, accepted in *Catal. Today*
118. J. G. Mesu, A.M.J. van der Eerden, F.M.F. de Groot and B.M. Weckhuysen, accepted to *J. Phys. Chem. B*
119. Korpi, H., Lahtinen, P., Sippola, V., Krause, O., Leskelä, M. and Repo, T., *Appl. Catal. A, General 268* (2004) 199.