Leibniz-Institut für Katalyse e. V. an der Universität Rostock

METAL-CATALYZED OXIDATION AND REDUCTION REACTIONS OF OXYGENATED ORGANIC COMPOUNDS

Dissertation

zur

Erlangung des akademischen Grades

Doctor rerum naturalium (Dr. rer. nat.)

der Mathematisch-Naturwissenschaftlichen Fakultät

der Universität Rostock

vorgelegt von

Konstanze Kiersch (geb. Möller)

geboren am 15.April 1984 in Bernburg

aus Rostock

Rostock, 28.06.2011

urn:nbn:de:gbv:28-diss2011-0188-7

Für
meine kleine
Familie

Die vorliegende Arbeit entstand in der Zeit von September 2008 bis Juni 2011 am Leibniz–Institut für Katalyse e.V. an der Universität Rostock.

Vollständiger Abdruck der von der Mathematisch-Naturwissenschaftlichen Fakultät der Universität Rostock zur Erlangung des akademischen Grades eines Doktors der Naturwissenschaft genehmigten Dissertation.

Gutachter der Dissertation:	1) Prof. Dr. Matthias Beller, Leibniz-Institut für Katalyse e.V. an der Universität Rostock Albert-Einstein Str. 29a, 18059 Rostock (Germany) 2) Prof. Dr. Peter Langer, Institut für Chemie der Universität Rostock Albert-Einstein Str. 3a, 18059 Rostock (Germany)
Termin des Rigorosums:	23. September 2011
Prüfungsvorsitzender:	Prof. Detlef Heller Leibniz-Institut für Katalyse e.V. an der Universität Rostock
Prüfer Hauptfach: (Organische Chemie)	Prof. Dr. Matthias Beller, Leibniz-Institut für Katalyse e.V. an der Universität Rostock
Prüfer Nebenfach: (Einführung in die BWL)	Prof. Dr. Stefan Göbel, Wirtschafts- und Sozialwissenschaftliche Fakultät Universität Rostock
Wissenschaftliches Kolloquium:	08. November 2011

Danksagung

Herrn Professor Matthias Beller danke ich an dieser Stelle herzlich für die Aufnahme in seine Arbeitsgruppe, die ausgezeichneten Arbeitsbedingungen, seinen unerschöpflichen Ideenreichtum sowie für sein großes Interesse am Gelingen dieser Arbeit.

Besonders bedanken möchte ich mich bei *Frau Dr. Kathrin Junge* für die herzliche Aufnahme in die Redoxgruppe und für die Unterstützung in den letzten drei Jahren. Danke für die gewährte Freiheit und für das Vertrauen in meine Arbeit.

Weiter möchte ich der Oxidationsgruppe in Warnemünde und der Reduktionsgruppe in der Südstadt für die gute Zusammenarbeit und ihre Hilfsbereitschaft danken. Insbesondere *Dr. Benoît Join*, Dr. *Kristin Schröder, Dr. Yuhui Li, Shoubhik Das, Gerrit Wienhöfer* und *Felix Westerhaus* danke ich für die schöne Zeit und die sehr gute Atmosphäre.

Ferner gilt mein Dank meinen Kolleginnen und Kollegen am LIKAT, insbesondere
Katharina Vlach, Andreas Dumrath, Dr. Irene Piras, *Dr. Daniele Addis, Karolin Kral, Christa Lübbe, Bianca Wendt* und vielen mehr.
Dem Analytikteam des LIKAT danke ich für die zahlreichen Analysen, die für mich während meiner Zeit am Institut durchgeführt wurden. Im Besonderen möchte ich *Dipl.-Ing. Andreas Koch* für die stete Unterstützung, Geduld und Hilfe in Warnemünde und bei verschiedensten Messungen danken.

Für die Zeit neben der Dissertation danke ich meinen Freunden, insbesondere *Alice Voß, Dr. Heike Wächtler, Christin Meyer, Martin Jacobsen, Katrin Kaune und Stefanie Wenda,* die mich in all meinen Vorhaben unterstützt haben.

Mein ganz besonderer Dank gebührt meiner Familie und meinem Ehemann Kristian für die Unterstützung, die sie für meine Arbeit während der letzten Jahre aufgebracht haben und das Vertrauen, das sie in mich während meiner gesamten Zeit in Rostock gesetzt haben.

Abstract

This thesis describes the development of novel catalytic oxidation and reduction reactions. More specifically, the synthesis of alcohols, aldehydes, epoxides, ketones, quinones has been developed based on Fe, Re, Ru, and Zn catalysts. In general, the described oxidations as well as reduction reactions provided high reactivity and good to excellent selectivity. In addition to catalytic studies mechanistic investigations were also performed. A major focus of the work has been on the synthesis of quinones, whereby excellent results in catalysis were realized.

Zusammenfassung

Die vorliegende Dissertation beschäftigt sich mit der Entwicklung neuer katalytischer Oxidations- und Reduktionsmethoden. In diesem Rahmen wurden verschiedene Alkohole, Aldehyde, Epoxide, Ketone und Chinone in Gegenwart von Fe, Re, Ru, Zn Katalysatoren synthetisiert. Die beschriebenen Oxidations- als auch die Reduktionsreaktionen führten zu sehr guten Umsätzen und Selektivitäten. Neben katalytischen Studien wurden auch mechanistische Untersuchungen erfolgreich durchgeführt. Der Schwerpunkt dieser Arbeit lag jedoch auf der Synthese von Chinonen, wobei sehr gute Ergebnisse in der Katalyse realisiert wurden.

Table of Contents

Table of Contents

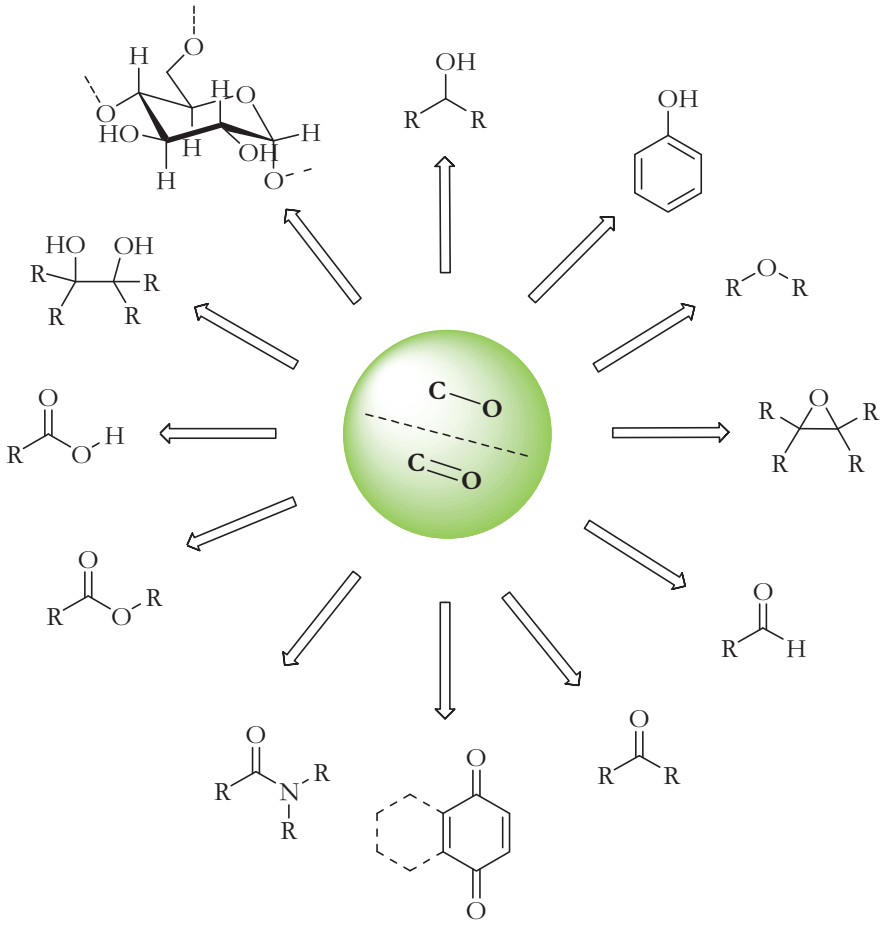
Abbreviation

ADP	adenosindiphosphat
AHQ	alkyl anthrahydroquinone
AQ	alkyl anthraquinone
ATP	adenosintriphosphat
aq.	aqueous
CT-complex	charge transfer complexes
conv.	conversion
cyt	cytochrome
D	primary donor chlorophyll (P680)
DHS	3-dehydroshikimic acid
DMF	dimethylformamide
E	electrode potential
E°	standard electrode potential
ee	enantiomeric excess
e.g.	exempli gratia
ESI	electrospray ionisation
equiv.	equivalents
etc.	et cetera
FePcS	tetrasulfonic phthalocyanine
HPPO	hydrogen peroxide propylene oxide
H_2pydic	pyridine 2,6-dicarbocylic acid
In	initiator
KIE	kinetic isotopic effect
log	logarithm
m	meta
Me	methyl
MOM	methoxymethyl
MS	mass spectroscopy
MTO	methyltrioxorhenium
MTBE	methyl *t*-butyl ether
NAD(H)	nicotinamide adenine dinucleotide
NMR	nuclear magnetic resonance
o	ortho
p	para

PET	polyethylenterephthalat
Ph	phenyl
phen	phenanthroline
PKS	polyketide synthases
PMHS	polymethylhydrosiloxane
PSII	photosynthesise II
PTC	phase transfer catalysts
py	pyridine
PVC	polyvinylchloride
Q9	plastoquinone
Q10	ubiquinone
QA	quinic acid
Q_A	primary quinone acceptor
Q_B	the secondary quinone acceptor
QH	ubisemiquinone
QH_2	ubihydroquinone
Q_i	cytosolic side
rac	racemate
ROS	reactive oxygen species
r.t.	room temperature
SA	shikimic acid
select.	selectivity
t-	tertiary-
THAHQ	5,6,7,8-tetrahydroalkyl-anthrahydroquinone
THAQ	5,6,7,8-tetrahydroalkyl-anthraquinone
TMB	1,3,4-trimethylbenzene
TMBQ	2,3,5-trimethylbenzoquinone
TMP	2,3,6-trimethylphenol
wt	weight

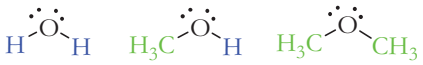
Preface

Oxygenated compounds are of major scientific and technical importance. In addition, they play also an important role in everyday life. In organic chemistry oxygen is one of the most important elements beside carbon, hydrogen and nitrogen. It forms a variety of important functional groups, with carbon-oxygen single or double bonds (carbonyl group). Scheme 1 presents some important organic compounds which include C-O and / or C=O bounds.



Scheme 1: Some important organic compounds with C-O bond or carbonyl group.

The simplest carbon-oxygen single bond compounds are alcohols, which have a hydroxy group. Therefore they are derivates of water and it is possible to act as acid (proton donator) or base (proton acceptor) like water. After changing one hydrogen atom against a carbon group it becomes ether (Figure 1).[1]



water methanol dimethylether

Figure 1: Structure of water, methanol and dimethylether.

Cyclic ethers with three ring atoms are named oxiranes (epoxides, Figure 2). This ring approximately forms an equilateral triangle, which makes it highly strained. The strained ring makes epoxides more reactive than other ethers. The industrially dominant epoxides are ethylene oxide and propylene oxide.[2]

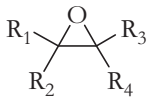
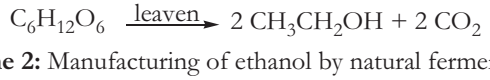


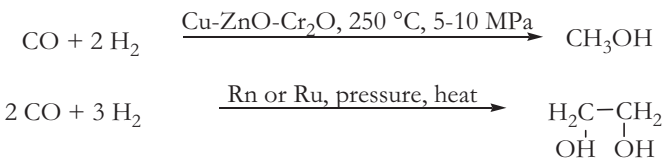
Figure 2: Epoxide.

Alcohols are distributed ubiquitous in nature and are used for numerous applications (isopropanol: production of acetone, glycol: anti-freezing agent, and so on). Ethanol is used as "drinking alcohol" since millennia and can be produced from carbohydrates by natural fermentation (Scheme 2).[3]



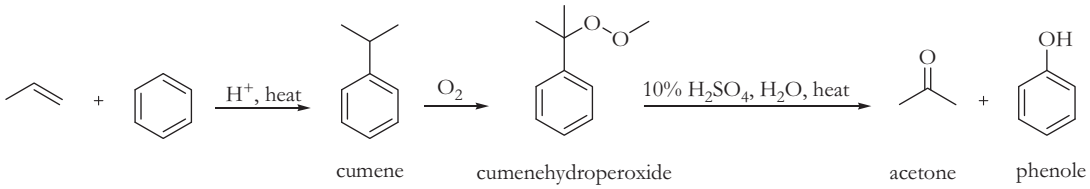
Scheme 2: Manufacturing of ethanol by natural fermentation.

Alcohols are used e.g. as solvents and the technical production of simple aliphatic alcohols (mainly methanol) proceeds from synthesis gas (CO and H_2) (Scheme 3).[1]



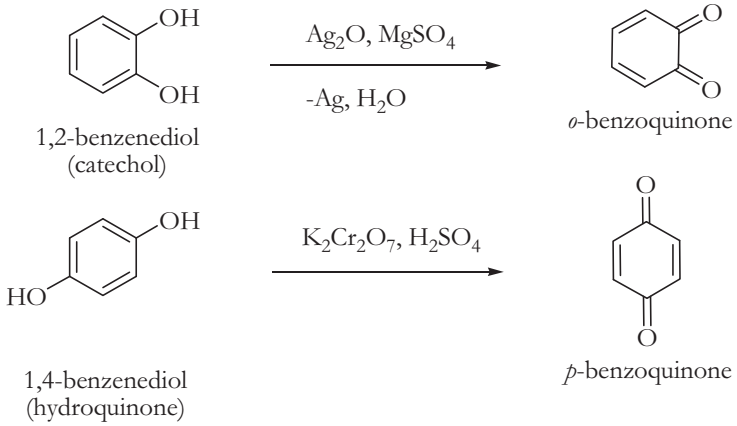
Scheme 3: Synthesis of methanol or ethylene glycol using synthesis gas and different catalysts.

Aromatic alcohols are known as phenols. The syntheses of phenols are quite different compared to the synthesis of aliphatic alcohols. The most common industrial production of phenol is the cumene process (Hock process) (Scheme 4).[2,4]



Scheme 4: Cumene process.

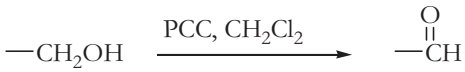
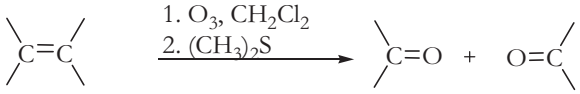
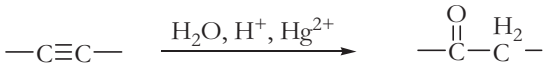
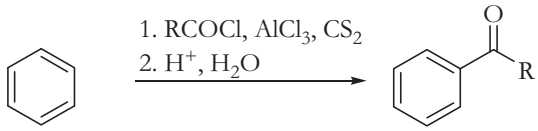
Substituted phenols are applied in medicine (topical anaesthetic, ear drops, scelerosing agent or neurolytic agent), as herbicides and as industrial intermediates (bisphenol A, caprolactam). Oxidation of phenols is the most common method to obtain quinones (Scheme 5), which are involved in important oxidation-reduction processes in nature (photosynthesis, respiration chain, and so on).



Scheme 5: Synthesis of *o* - and *p*-benzoquinone.

Aldehydes and ketones are most common carbonyl compounds which are used as flavour and aroma chemicals for the food industry.[5] Formaldehyde and acetone, are produced on million ton scale and used for various bulk applications. The former one is industrially produced by oxidation of methanol and used for phenolic resins production or as bactericidal or fungicidal disinfectant as an aqueous solution (formalin).[6] Acetone is a side product of the cumene process (*vide* supra, Scheme 4) and is used as solvent and in the chemical industry as raw material for other compounds. Table 1 summarizes four options for laboratory-scale synthesis of aldehydes or ketones.[6]

Table 1: Synthesis of aldehydes and ketones.

Reaction	Formula
1. oxidation of alcohols	
2. ozonolysis of alkenes	
3. hydration of alkynes	
4. Friedel-Crafts-Alkylation	

The combination of a single and double carbon-oxygen in one carbon atom is called carboxylic acid group and is shown in Figure 3.

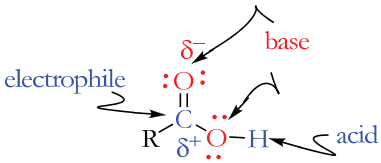
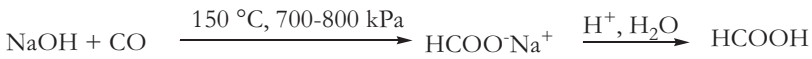


Figure 3: Carboxylic acid.

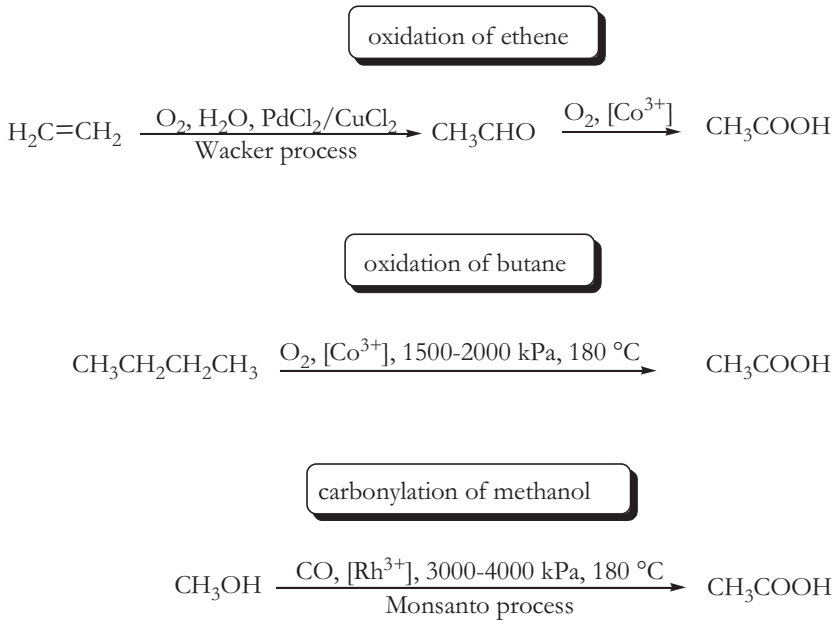
The two simplest acids are formic acid and acetic acid. Both are synthesized on a large industrial scale.[7] The former is used for the tanning of leather and in the manufacture of latex.[8] It is produced by powdered sodium hydroxide with carbon monoxide under high pressure at 150 °C (Scheme 6).[9]



Scheme 6: Synthesis of formic acid.

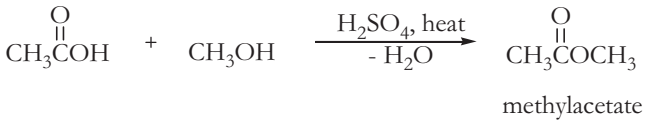
In nature acetic acid is formed via enzymatic oxidation of ethanol. The acetic acid and anhydride are industrially important chemicals, which are used for production of monomers for the polymerization. Additionally, they are used as precursors in the synthesis

of pharmaceuticals, dyes and pesticides. The industrial processes used for production are oxidation of ethene, oxidation of butane and carbonylation of methanol (Scheme 7).[9]



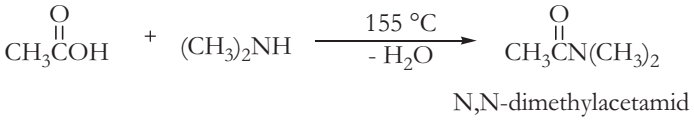
Scheme 7: Synthesis of acetic acid.

Important carboxylic acid derivatives are amides and esters. They are widely distributed in nature (fat, oils, beeswax) and have many practical applications (e.g. PET, PVC, insecticide, medicines and so on). The formation of esters proceeds by reaction of carboxylic acids and alcohols under acid-catalyzed conditions (Scheme 8).[10]



Scheme 8: Synthesis of esters.

In the same way amides can be produced by reaction of carboxylic acids and amines instead of the alcohol, whereby an addition-elimination reaction takes place (Scheme 9).[11]



Scheme 9: Synthesis of amides**.**

The amide structure can be found in many natural materials including peptides, which are regarded as an important class of compound in nature.

The present dissertation highlights recent achievements in metal-catalyzed (Fe, Re, Ru, Zn) oxidation and reduction reactions to several oxygenated compounds. Thereby quinones, aldehydes, ketones, epoxides, and alcohols were synthesized with different catalytic reactions. The main focus of the work is set on the class of quinones. For this reason in the next chapter the occurrence, application and synthesis of different quinones are presented. At the end of this dissertation further oxidation and reduction reactions are summarized. This dissertation is presented as a cumulative collection of publications which have been already published or are accepted for publication in international peer-reviewed journals.

1. Introduction – Quinone

Quinones are organic compounds that are considered as oxidation products of aromatic substances. Oxidations of arenes or phenols to quinones constitute biological processes,[12] which have important roles in living organism (photosynthesis, respiratory chain). In addition, they have a wide variety of applications in industry for example as catalyst of hydrogen peroxide production or pulping (*vide* infra).

Typically, quinones have two carbonyl groups and two carbon-carbon double bonds in a 6-membered ring, forming a system of conjugated double bonds (a quinoid structure or system) (Figure 6) causing a specific reactivity of these compounds.[1]

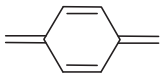
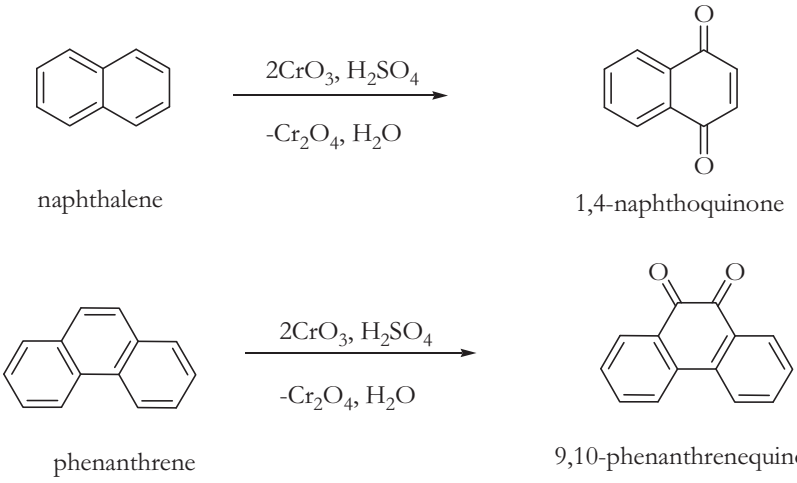


Figure 4: Quinoid structure.

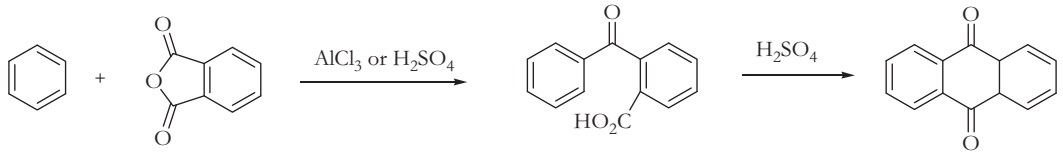
The base body of the quinones are derived from benzene, 1,2 - and 1,4-benzoquinone or rather called *o*- and *p*-quinone (*vide* supra, Scheme 5). These compounds are intensive red or yellow colored, pungent odorous substances resulting from oxidation of catechol and hydroquinone (*vide* supra, Scheme 5).[13] The occurrence of electron-donating substituents at aromatic rings increases their nucleophilicity and contributes to a large redox potential needed to break their aromaticity. Other quinones are 1,4-naphthoquinone and 9,10-anthraquinone, which are the basis of many colors.



Scheme 10: Synthesis of 1,4-naphthoquinone and 9,10-phenanthrenequinone.

They can be produced by oxidation of arenes, which is the most general methodology for formation of quinones from naphthalene-, anthracene and phenanthrene compounds (Scheme 10).[1]

Linear condensed quinones such as 9,10-anthraquinone can be prepared by electrophilic acylation of arenes with phthalic anhydride (Scheme 11).[1]



Scheme 11: Fiedel-Crafts-Acylation of arene with phthalic anhydride.

Basically all quinones have two common characteristics: First, they are almost all colored and secondary, they show a typical standard redox potential (Table 2).[14,15,16,17] The latter ability to compose a reversible oxidation-reduction cycle finds applications at electron carriers in energy metabolism in nature (photosynthesis or respiratory chain), but also in industry (photography or quinhydrone electrode).

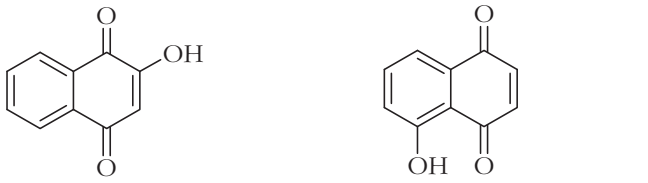
One advantage in the application of quinones is the significant change of standard redox potential by substituents (halogen, cyano, alkyl, hydroxyl groups, and so on).[18,19] The potential is decreased by introduction of electron-donating groups such as OH (Table 2), and increased by electron-withdrawing groups such as Cl or NO_2 (Table 2)).

Table 2: Standard redox potential of different quinones.

Quinone	Standard redox potential
1,4-benzoquinone[18]	+0.715 V
nitro-1,4-benzoquinone[14]	+0.765 V
1,2-benzoquinone[14]	+0.810 V
3-hydroxy-1,2-benzoquinone[14]	+0.677 V
1,4-naphthoquinone[17]	+0.484 V
1,2-naphthoquinone[17]	+0,576 V
1,2-naphthohydroquinone [15]	+0.578 V
9,10-anthraquinone[16]	+0.154 V
3,4-phenanthrenequinone [15]	+0.623 V
dichlorodicyanoquinone (DDQ) [19]	+1.150 V

1.1 Occurrence

Due to the unique characteristics of quinones, they are diverse in nature and play important roles in living organisms. They all have a quinoid structure, but an exchange of substituents or their position can change occurrence and/or application, e.g., lawsone (2-hydroxyl-1,4-naphthoquinone) and juglone (5-hydroxyl-1,4-naphthoquinone)(Figure 5).



2-hydroxyl-1,4-naphthoquinone
lawsone

5-hydroxyl-1,4-naphthoquinone
juglone

Figure 5: Lawsone and juglone, 1,4-naphthoquinone derivates.

Lawsone, is a brown colored powder, which can be isolated from the leaves of the henna plant (*Lawsonia inermis*) as well as jewelweed (*Impatients balsamica*). Since ancient times it was used at the Indian Subcontinent for decorating and dyeing hands, soles, beard and hair and to impart beautiful shades of dark red color.[20] The second hydroxyl-naphthoquinone is a chemical released by walnut trees (*Juglans nigra*), which can be toxic at various levels to several plant species.[21] It is used as herbicide, coloring agent for foods and cosmetics and as a dye for cloth and inks.[

More than 120 naphthoquinones have been isolated from plants.[22] In nature, quinones are particularly common in dyes, from fungi, bacteria or flowers, in photosynthesis (plastoquinone Q9) and respiratory chain. In the latter one ubiquinone (Q10) plays a big role as an electron carrier.

Also in insects, e.g. bombardier beetles, rather in their defensive secretions, primarily benzo- and toluquinone are found. Some vitamins have a quinoid structure including vitamin K (phylloquinone, menaquinone, menandione) (Figure 10, *vide* infra) and vitamin E (Figure 12, *vide* infra) (α-tocopherol). Vitamin K_1 is found in plant foods, for example, in soybeans, milk and milk products, flesh, tomatoes, rose hips, green vegetables and potatoes. In contrast to that, vitamin K_2 is synthesized by intestinal bacteria.[23] Nevertheless the vitamin K_3 is a synthetic vitamin.

1.2 Application

Quinones are used in wide variety of applications in industries and are applied especially for drug construction in medicine, because a variety of quinone compounds including naturally occurring compounds, especially the naphthoquinone derivatives have wide variety of bioactivities.

The best known natural naphthoquinones with bioactivities are vitamin K_1 and K_2 (phylloquinone, menaquinone). They are known as antihemorrhage vitamins. Atovaquone is another important naphthoquinone derivative, which is used as a malaria drug (Figure 6) and has also an anti HIV activity. Other compounds with naphthoquinone structure have been developed as key composition of wide variety of medicine.

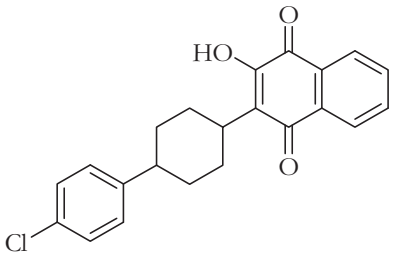
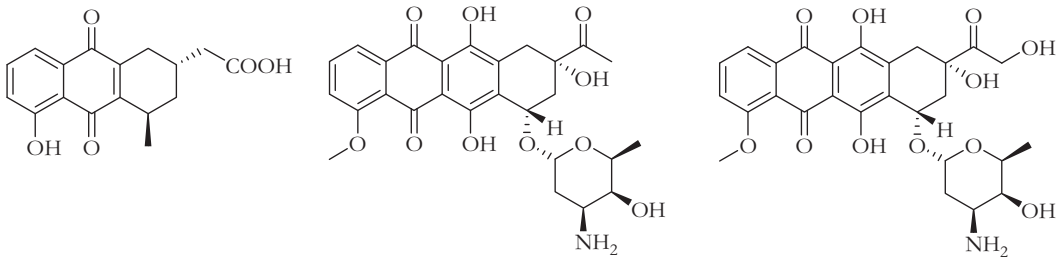


Figure 6: Atovaquone.

Quinones such as nanomycin, daunomycin and adriamycin, (Figure 7) are used for the manufacture of antibiotics. Originally, the latter two have been developed as anticancer drug.



nanomycin A daunomycin or daunorubicin adriamycin or hydroxydaunorubicin

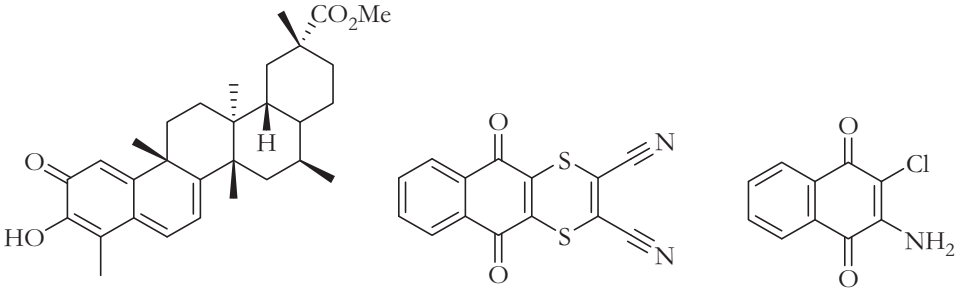
Figure 7: Nanomycin, daunomycin and adriamycin.

Quinones also have potential for application as anti-inflammatory agent, anti-allergic agent and hypotension.[24] They can be used for the production of infection drugs as anti-fungal agents, anti-virus medicines and antibacterial agents against gram-positive bacteria, gram-negative bacteria, and so on. In the field of animal drugs, menadione (vitamin K_3, Figure 10, *vide* infra) is used as a hemostatic, a feed additive.

There are other applications mainly used for human. Quinone derivatives are used in the cosmetic. For example vitamin E (Figure 12, *vide* infra) is an antioxidant and is used for sun cream. Additionally, they are extensively used in the dye, chemical, tanning, and textile

industries, while in the pulp and paper industry quinone compounds find application as cooking additive.[25] Other application fields are the manufacturing industries and chemical laboratories associated with protein fiber, photography, hydrogen peroxide (anthraquinone) and gelatine making.[26]

Another important area is the agricultural usage. Here chemicals were used or developed to raise the productivity of farm products by improving or controlling their physiological functions and protect crops by ridding of pathogenic fungi, harmful insect, weeds and rats. There are some types such as insecticides (pristimerin), fungicides (delan), herbicides (mogeton), plant growth regulators, anti-fouling agent, bird repellents (Figure 8).[27]



pristimerin delan mogeton

Figure 8: Figures of **p**ristimerin, delan and mogeton.

In addition quinones are good oxidants and can used for redox reaction for example in the electrochemistry as electrode.

In the next sections detailed applications of selected quinones are shown and explained in detail.

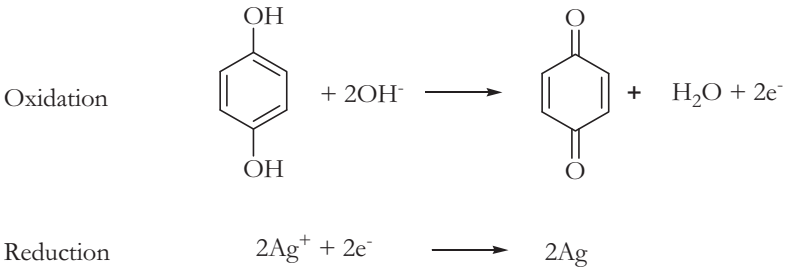
1.3 Hydroquinone

Hydroquinone has a variety of applications. For example, it can be used in medical applications, as monomer inhibitors, for making dyes and pigments, as agricultural chemicals, and so on. Some applications and the important roles of the hydroquinone are discussed here more in detail.

1.3.1 Application

1.3.1.1 Photography

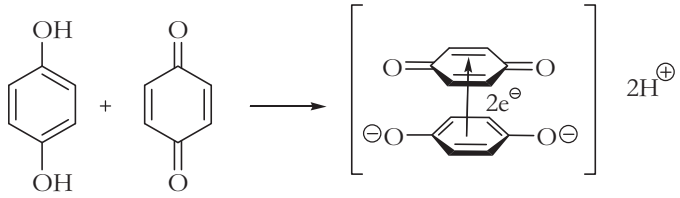
Hydroquinone is a dihydroxybenzene and can easily be oxidized to quinone. This reducing effect is exploited in the photography. During the expose the small silver halide grains which are suspended in the photosensitive layer accumulate development nucleus. The developer (hydroquinone) attacks at the nucleus and reduces the silver ions to black, silver metallic. During the fixation the unexposed silver halide grains are usually extracted with sodium thiosulfate, to make the left layer light-resistant (Scheme 12).



Scheme 12: Reactions during the photography.

1.3.1.2 Charge transfer complex

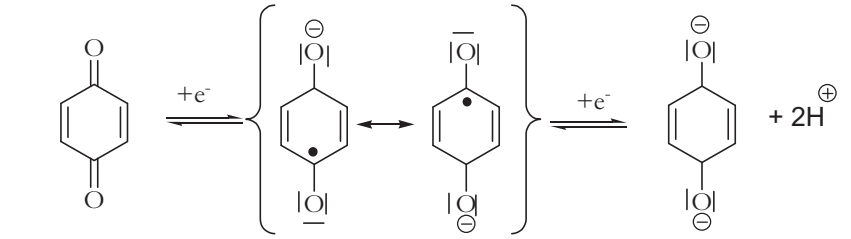
The reduction of 1,4-benzoquinone (yellow) to hydroquinone (colorless) develops a reactive intermediate the so called quinhydrone (dark green/brown). It can also be obtained by mixing equivalent quantities of *p*-benzoquinone and hydroquinone. In the presence of light, an electron is transferred from hydroquinone (donor) to *p*-benzoquinone (acceptor) giving the quinhydrone the very characteristic purple color. 1:1-adducts with this property are called "charge transfer complexes" (CT-complex) or "donor-acceptor-complex" (Scheme 13).[1]



Quinhydrone
Charge-Transfer-Komplex

Scheme 13: Charge transfer complex.

The +M-effect of the two OH groups of the hydroquinone increased the electron density in the aromatic six-membered ring, so it can act as electron rich donor. The benzoquinone is the acceptor, his six-membered ring show an electron deficiency due to the -I-effect of the two oxygen substituents.



p-benzoquinone semiquinone-radical-anion hydroquinone-dianion

Scheme 14: Semiquinone-radical-anion.

The interaction of π-electrons leads to a facilitated excitability by electromagnetic radiation. For this reason all CT-complexes show demonstrative staining. Thereby, the electron exchange takes place in two steps over the detectable resonance stabilized semiquinone radical anion (Scheme 14).

1.3.1.3 Electrochemistry: quinhydrone electrode

The redox system hydroquinone / benzoquinone in the molar ratio 1:1 is used in the pH-measurement as the so called quinhydrone electrode. Thus, pH measurements in acidic and neutral solutions can be realized. It consists of a platinum plate (inert metal electrode), which dips into the saturated quinhydrone (quinone:hydroquinone, 1:1) analysis solution.[28] Here, the electrode charged to a particular potential, which is measured by a reference electrode. The electrode half-reaction is shown in Formula 1 (**2**). The electrode-potential E of this organic half cell can described in accordance with the equation:

$$\hat{E} = E^{o} + 0.059 \cdot \log \frac{\left[C_6H_4O_2\right]^{\frac{1}{2}} \cdot \left[H^+\right]}{\left[C_6H_4(OH)_2\right]^{\frac{1}{2}}}. \quad (\mathbf{1})$$

with $\frac{\left[C_6H_4O_2\right]}{\left[C_6H_4(OH)_2\right]} = 1$;

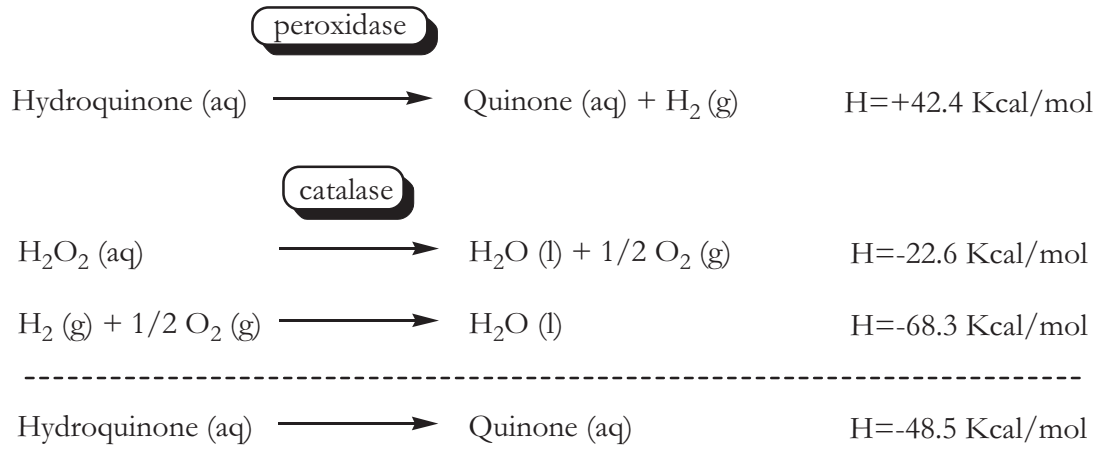
$$E = E^{o} + 0.059 \cdot \log\left[H^+\right] \quad (\mathbf{2})$$

Formula 1: Electrode potential of the quinhydrone electrode.

The equation allows a fast and easy determination of the hydrogen ion concentration of any solution. However, the disadvantage of the electrode is the limitation to an acidic or neutral medium. In an alkaline solution the hydroquinone behaves like a very weak acid and absorbs hydroxyl ion, so a too high hydrogen ion concentration is determined. Additionally, the hydroquinone will be oxidized quickly to organic acids.

1.3.1.4 Bombardier beetle

In nature hydroquinone plays an important role in the animal world of insects. The so called bombardier beetle (*Carabidae, Brachinini*) uses hydroquinone in the defence mechanism of arthropods. These insects respond to disturbance by ejecting a quinoid secretion from a pair of glands that open at the tip of the abdomen.[29] They aim their discharge by revolving the abdominal tip and direct their spray with accuracy toward any region of the body subjected to assault.[30] The discharges are accurately aimed [30,31] and they occur with audible detonations, hence the name 'bombardiers'. The active component of the secretion is 1,4-benzoquinone[29], a compound known to be potently irritating[32].
The defensive reaction takes place in the middle of the beetle. The beetle has two glands where the chemicals ordinarily stored separately. Each gland consists of two confluent compartments. In the major compartment (the reservoir or storage chamber) are hydrogen peroxide and hydroquinone and the other (the reaction chamber) contains a mixture of enzymes (catalase, peroxidase).[33]In the moment of defense, several reactions take place. The quinone is generated explosively at the moment of ejection by the mixing of two sets of chemicals[34] (Scheme 15).[35]



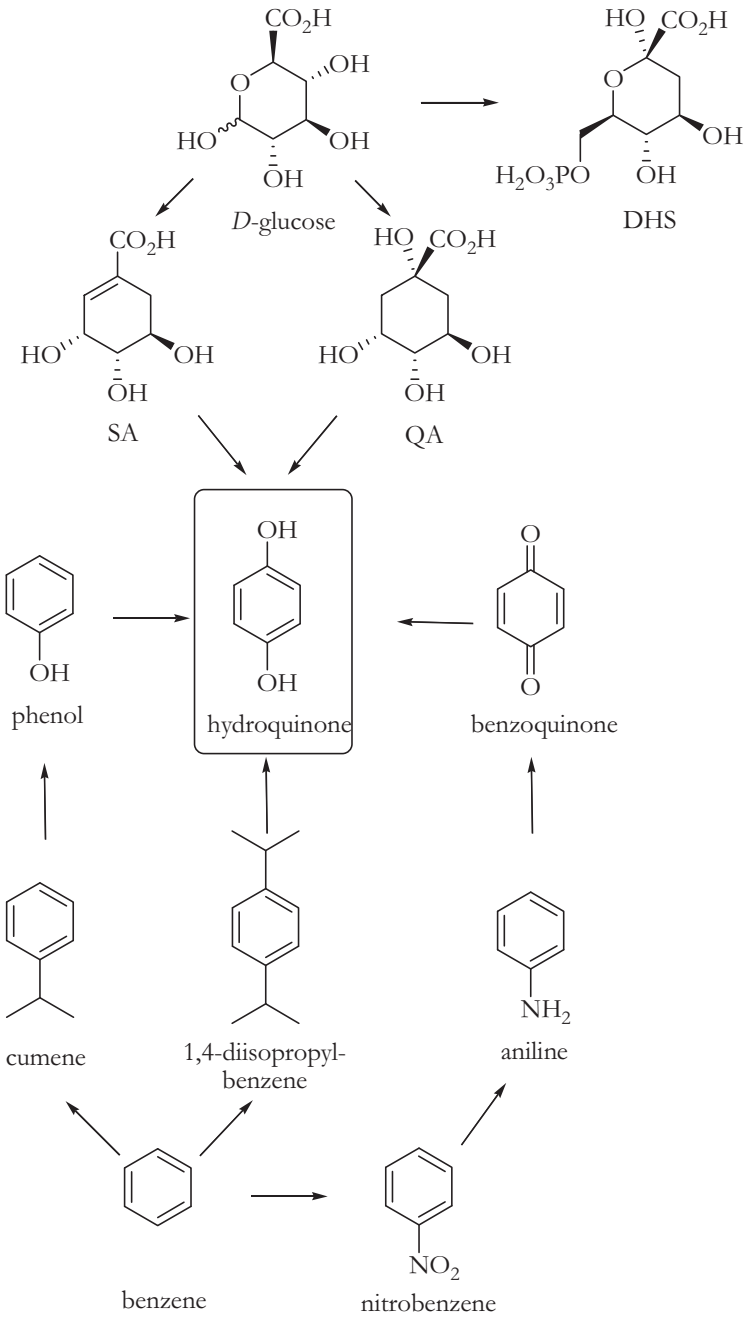
Scheme 15: Defensive reaction of the bombardier beetle.

When combined, the reactants undergo a violent exothermic chemical reaction, (Scheme 15) and their temperature raising near to the boiling point of water (100 °C).[36]

To activate the spray, the beetle squeezes fluid from the reservoir into the reaction chamber. This results in the instantaneous liberation of oxygen from hydrogen peroxide, and the oxidation of the hydroquinones to quinones by the freed oxygen. The corresponding pressure buildup forces the entrance valves from the reactant storage chambers to close, thus protecting the beetle's internal organs. The boiling, foul-smelling liquid partially becomes a gas and is expelled through an outlet valve into the atmosphere with a loud popping sound.[29,35,37] An audible detonation accompanies the discharge. The spray is an effective deterrent to predators.[38] The flow of reactants into the reaction chamber and subsequent ejection to the atmosphere occurs cyclically at a rate of about 500 times per second and with the total pulsation period lasting for only a fraction of a second.

1.3.2 State-of-the-art Synthesis

All current routes for the synthesis of hydroquinone utilize benzene as the starting material (Scheme 16). The manufacture of hydroquinone is now dominated by oxidation of phenol and 1,4-diisopropylbenzene.[39] The first route begins with Friedel-Crafts alkylation of petroleum-derived benzene to afford cumene. Subsequent Hock-type, air oxidation of the cumene leads to formation of acetone and phenol. Additionally this is currently the predominant method used in the production of phenol, which amounts to $5x10^9$ kg annually.[40] The phenol is then oxidized using 70% hydrogen peroxide either in the presence of transition metal catalysts or in formic acid solution where performic acid is the actual oxidant. The generated catechol and hydroquinone mixture is separated into its pure components by distillations.

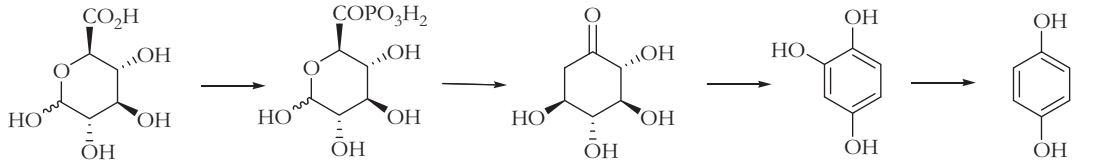


Scheme 16: Synthesis of hydroquinone.

The second synthesis way, which is also manufactured, is the reaction with propene and benzene to 1,4-diisopropylbenzene, which reacts afterwards to the hydroquinone.[41] Nevertheless there are more than this two synthetic routes.

Benzene reacts to nitrobenzene by using HNO_3 and H_2SO_4 and after that to the corresponding aniline. Next, benzoquinone is synthesized by a route employing stoichiometric amounts of MnO_2 to oxidize aniline, followed by iron catalyzed reduction to the corresponding hydroquinone.[42] While benzene is a volatile carcinogen derived from non-renewable fossil fuel feedstocks, an alternative way to hydroquinone has been

elaborated (Scheme 16).[43] Glucose is nonvolatile, nontoxic, and derived from renewable plant polysacharrides and plays an important role for these benzene free routes. From Glucose *Escheria coli* produce shikimic acid (SA), quinic acid (QA) and 3-dehydroshikimic acid (DHS).[44] Shikimic acid as well as quinic acid are known for the hydroquinone synthesis (Scheme 16). In 1995 the manufacture of hydroquinone and catechol has been elaborated that utilize *D*-glucose as the starting material and biocatalysts, a genetically modified microbe, *Escheria coli*.[43c)] Here the shikimic acid was the precursor for the quinones. Furthermore the synthesis of hydroquinone by an alternative benzene free route was published in 1838. Woskresensky synthesized the quinone from quinic acid.[45] In 1992 Drahts et al. reported about the production of quinic acid from glucose with *Escheria coli*.[46] They also published the oxidation of quinic acid with stoichiometric amounts of MnO_2 to benzo- and hydroquinone in low to modest yield. Next Ran and co-workers developed a new catalytic route from quinic acid to hydroquinone.[47] They used stoichiometric amounts of NaOCl, $(NH_4)_2Ce(SO_4)_3$, V_2O_5 or catalytic quantities of $Ag_3PO_4/K_2S_2O_8$ to afforded 74% to 91% yield. One year later Hansen and Frost published a synthesis of 2-deoxy-scyllo-inososе from glucose which reacts to hydroxyhydroquinone (Scheme 17).[48]

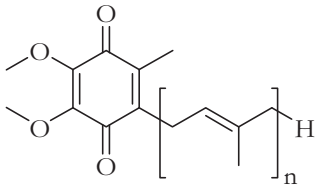


Scheme 17: Synthesis of hydroquinone, a benzene free route.

The latter is the starting material for the hydroquinone synthesis catalyzed by Rh/Al_2O_3, Rh/C, Pt/C, or Pd/C. The Rh on Al_2O_3 catalyst showed the best results (53% yield), whereas the Pd on carbon showed less activity (18% yield).

1.4 Ubiquinone

Some of the most well known quinones are called ubiquinones, also known as coenzymes Q or vitamin Q. Their structurally similarity is based on a 2,3-dimethyl-1,4-benzoquinone molecule with a side chain of isoprenyl units (Figure 9). They designated to the number of isoprenyl units of their side chain as Q1, Q2, and so on. In *Escherichia coli* Q1 to Q8 have been found, in fish Q9 and in rat Q11 and Q12. In most mammals including humans Q10 is predominant and, therefore, it has attracted most interest. All ubiquinones are naturally occurring, fat-soluble quinones that are localized in hydrophobic portions of cellular membranes. They serve as electron transferring compounds in the light dependent reaction of the photosynthesis and in respiration.



n=9: Ubiquinone
n=10: Plasroquinone

Figure 9: Ubiquinones Q9 and Q10.

1.4.1 Application

1.4.1.1 Photosynthesis

Photosynthesis was one of the driving evolution factors in the early earth's history, because it is responsible for the production of oxygen, which is required by aerobic organisms (Scheme 18). Additionally, it is the momentum behind most of the life on our planet, which occurs in plants, algae and some types of bacteria. In oxygenic photosynthesis, electron transport occurs in the thylakoid membrane and requires coordinated interactions between a large number of electron-carrier compounds and enzymatic proteins that facilitate the transfer of electrons (reducing power) from dissociated H_2O molecules to NADP.

light reaction:

$$12H_2O + 12NADP + 18(ADP + P) \xrightarrow{hv} 12NADPH_2 + 18ATP + 6O_2$$

dark reaction:

$$6CO_2 + 12NADPH_2 + 18ATP \longrightarrow C_6H_{12}O_6 + 6H_2O + 12NADP + 18(ADP + P)$$

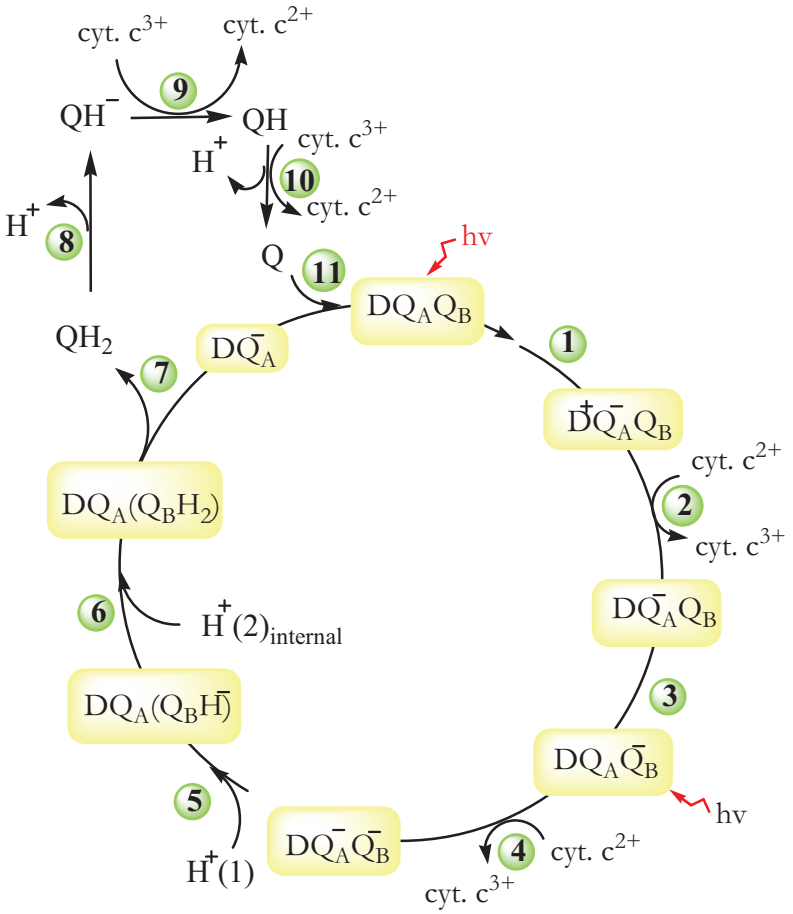
total:

$$6CO_2 + 12H_2O + hv \longrightarrow C_6H_{12}O_6 + 6O_2 + 6H_2O$$

Scheme 18: Reactions in the photosynthesis.

The electron-transport components are highly organized in the thylakoid membrane and facilitate the transfer of electrons laterally in the plane of the membrane from the grana regions (appressed) to the stroma-exposed (unappressed) regions. The redox map of photosynthesis of these organism can be described in terms of the well-known Z-scheme proposed by Hill and Bendall.[49] A photochemical reaction occurs at the photosynthetic reaction centre, which can be divided into 2 sections, photosynthesis I and II. The quinone plays an important role in the photosynthesis II. It is used as an electron transfer between pheophytin and plastocyanin over cytochrome b/f.

In photosystem II (PSII), light activates electron transfer from the primary donor chlorophyll (P680) D to the primary quinone acceptor Q_A and then to the secondary quinone acceptor Q_B, in the reaction centre. The tightly bounded Q_A is a one-electron carrier, whereas the loosely bounded Q_B can accept two electrons. [50,51] Scheme 19 shows the mechanism of the quinone in the photosynthesis.



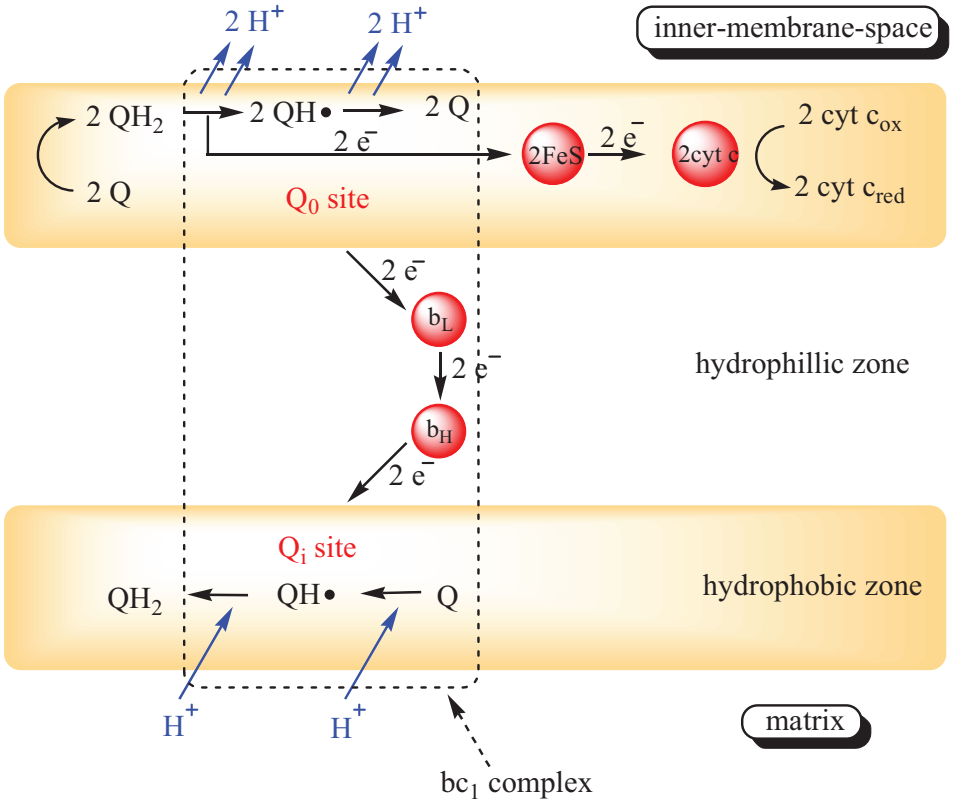
Scheme 19: Mechanism of the quinone in the photosynthesis.

In the first step **1** light activates the DQ_AQ_B complex and a charge couple $D^+Q_A^-Q_B$ is generated. After that the chlorophyll D^+ is reduced by a cytochrome cyt c^{2+} and the cyt c^{2+} was oxidized to cyt c^{3+} (step **2**). From the Q_A^- the electron is transferred to the secondary

quinone electron acceptor, Q_B (step **3**). The first two steps repeats (step **4**) and results in a two charged quinone. The first proton H^+(1) is taken up from solution and transferred to the reduced semiquinone Q_B^- before the second electron transfer (step **5**) to generate an uncharged quinone Q_A ($DQ_AQ_BH^-$) [52]. The second proton H^+ (2) is transferred internally (step **6**) and a hydroquinone Q_BH_2 ($DQ_AQ_BH_2$) is generated. The Q_BH_2 diffuses out of the reaction centre into an also membrane bound cytochrome bc_1 complex and is reoxidized to the quinone state. In steps **8** and **10** the protons were delivering. Due to the spatial arrangement of the protein complexes the protons are taken up in steps **5, 6** in the interior of the cell and expelled in steps **8, 10** to the periplasmic space. This process generates an electrochemical gradient across the cytoplasm membrane. The quinone cycle is closed by transfer of the quinone back to the cycle (step **11**).

1.4.1.2 Respiration

Ubiquinone serves in the respiration as an electron transferring compound. The quinone is important for the complex III in the respiration chain. This complex is a membrane-bound protein complex that conduces as electron acceptor from the hydroquinone (QH_2) and electron donator to cytochrome c (cyt c). It consists of three catalytic subunits (with cofactors): cytochrome *b* (two hemes), cytochrome *c*(1) (heme), and the Rieske iron-sulfur protein ([2Fe-2S] cluster).



Scheme 20: Mechanism of the quinone in the respiration chain.

The electron transfer mechanism is known as the bifurcated Q-cycle[53] and is shown in the Scheme 20. At first the ubiquinone Q reduced to the ubihydroquinone QH_2 by the complexes I and II. Now it is possible for the QH_2 to diffuse in the membrane and to deliver the absorbed 2 electrons. The hydroquinone tethers on the Q_0site in the complex III.

The Rieske protein first accepts an electron from a QH_2 molecule, and then donates the electron to cyt c.[52d),e)] The second electron is recycled to reduce the Q to ubisemiquinone QH in the cytosolic side (Q_i). In the Q_0site the QH_2 donate two hydrogens into the inner-membrane-space and reduce to the oxidized Q, which diffuse back to the ubiquinone pool. These reactions steps repeat again and again one cyt c and one semiquinone were produced. The semiquinone in the $Q_i$site, absorb two hydrogens from the matrix and reduce to the QH_2. The rate-limiting step occurs in the first electron transfer to the Rieske protein.[52d),e),54] The net reaction is to oxidize the hydroquinone to quinone, reduce two cytochromes c, release four protons into the inner-membrane-space, and transfer two protons across the membrane, against the proton gradient.

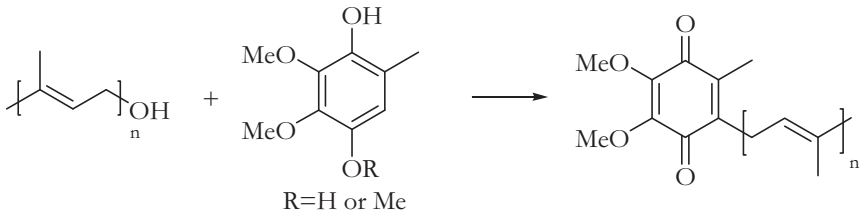
1.4.2 State-of-the-art Synthesis

Fortunately quantities of Q10 are available by well established fermentation [55] and extraction processes. Apparently more cost-efficient route in comparison to total synthesis is not available. Thus, the costs of these materials for research purposes are astonishingly high: e.g., Q9 is 119.00 €/g, and CoQ10 is 423.00 €/g [56].

First results of isolation of Q10 were published in 1957. Crane and co-workers isolated Q10 from mitochondria of beef heart.[57] Several approaches to synthesize ubiquinones have been developed the past 3-4 decades, attesting to the importance of these compounds. All side chains have to be confirmed to *trans*-configuration.[58] The first industrial approach by Hideaki Fukawa at Nisshin in 1974 [59] based on direct polyprenylation of hydroquinone monoacetate by Friedel-

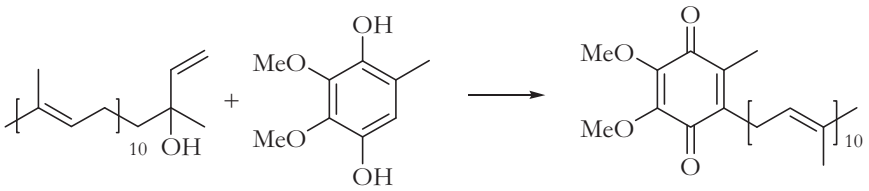
Crafts-type coupling is still exclusive for the partial synthesis of this vitamin. However, this process is, unfortunately, attended with some unwanted side reactions, especially partial cyclization to a chromanol type compound and (E)/(Z) isomerization during coupling. Moreover, the coupling yield is very low (20%).

As early as 1959 Isler et al. reported the first synthesis of ubiquinones Q9 and Q10 in about 20% and 71% yield by using 5-methyl-2,3-dimethoxy-hydroquinone and an isoprenoid alcohol (solanesol or decaprenol) in diethyl ether in the presence of $ZnCl_2$ as catalyst (Scheme 21). [60]



Scheme 21: Synthesis of ubiquinone.

This condensation step was advanced in the following years. In 1970 Fukawa et al. patented an improved method for ubiquinone coenzyme Q9-Q12 synthesis using $ZnCl_2$, $AlCl_3$ and BF_3 ether complex with 5-methyl-2,3-dimethoxy-hydroquinone or its 4-acyl derivative and the appending isoprenyl alcohols.[61] The application of another catalyst was reported in 1976. Kijima and co-workers used silica-alumina as catalyst to get after purification 25.8% yield of Q9 and 49.2% yield of Q10.[62] One year later they described the reaction of 2-methyl-4,5,6-trimethoxyphenol with boronic acid to obtain the corresponding borate which then reacts with a prenol or isoprenol hydrolyses and finally is oxidized to Q10.[63] Later Eto et al. used BF_3 OEt_2 as catalyst for the condensation and increased the yield to 51% (46% isolated yield).[64] The stereoselectivity was also increased to 92:2 (E/Z), respectively after purification >99:1. They also changed the compounds and used isodecaprenol which reacts with the hydroquinone in hexane/nitromethane (1:2, v/v) mixture as solvent to Q10 (Scheme 22).

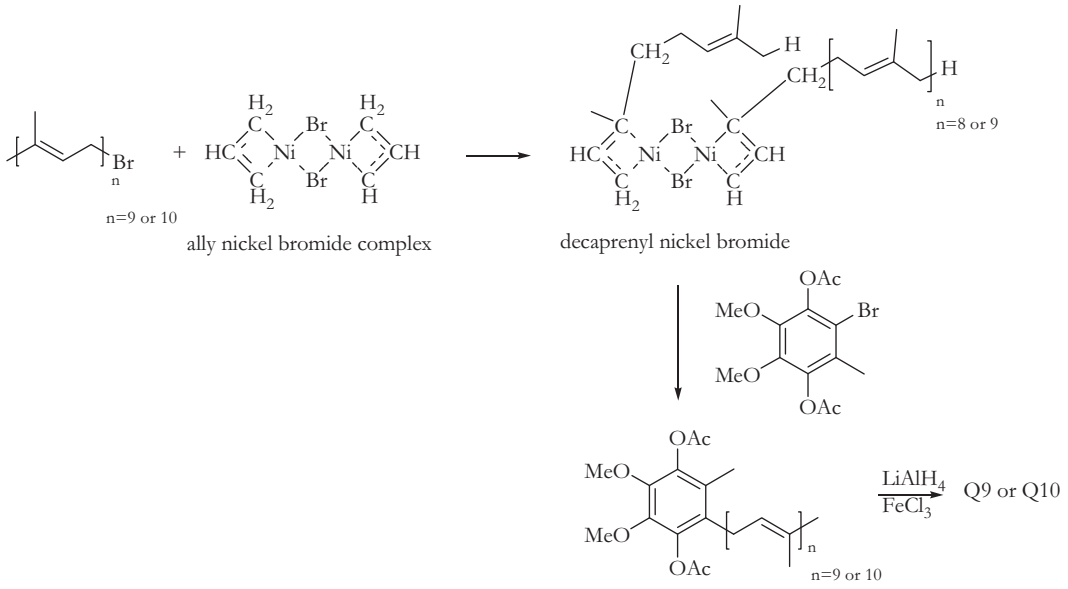


Scheme 22: Reaction with isodecaprenol to Q10.

Nevertheless, these processes are not useful for commercialisation due to large amounts of catalysts required for the condensation and/or their corrosive behaviour. Recently, Aquino et al. patented new results with this condensation method.[65] They synthesized Q9 and Q10 by using 2,3-dimethoxy-5-methylhydroquinone, prenol or isoprenol in the presence of a Brønsted-acid, a Lewis-acid, heteropolyacid, an NH- or a CH-acidic compound. The ubiquinone is obtained in good yield (36% to 50%) and E/Z-ratio (92:8 to 94:6) depends on the catalyst.

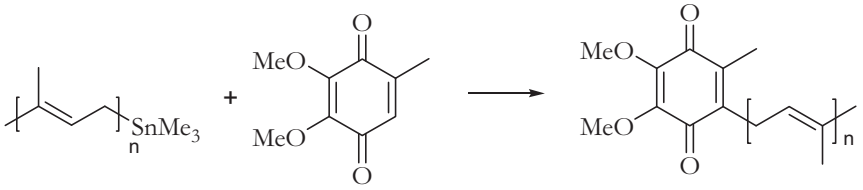
Also other methods for the synthesis of the coenzymes were developed. For example the synthesis of the quinone by using a π-allyl nickel bromide complex and protected quinones published by Sato et al. [66] They start manufacturing the coenzyme Q1 and later they adopted this procedure for the Q9 and Q10.[67] At first they synthesized the decaprenyl

nickel bromide with 9 or 10 units. These complexes react then with a protected bromo-quinone in phosphoramide at 70 or 75 °C to afford the protected Q9 or Q10 in 45% or 40% yield. This compound was then converted by removal of the acetate groups with $LiAlH_4$ and by subsequent oxidation by aq. $FeCl_3$ to the coenzymes Q9 or Q10 in a yield of 71% or 69% (Scheme 23).



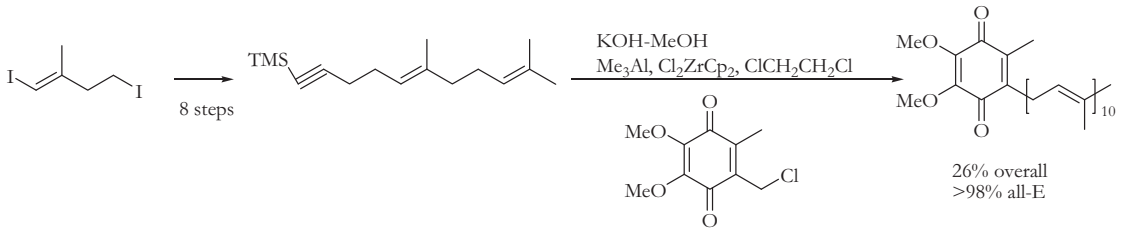
Scheme 23: Synthesis of Q9 or Q10 by π-ally nickel bromide complex.

The overall yield of the process is only 28%. Further drawbacks like the presence of only *cis* isomer and the high flammability of the formed nickel carbonyl make this process not suitable for industry. Another method is the reaction with unprotected quinone and allyl-stannyl compounds published in 1979 and 1980 (Scheme 24).[68]



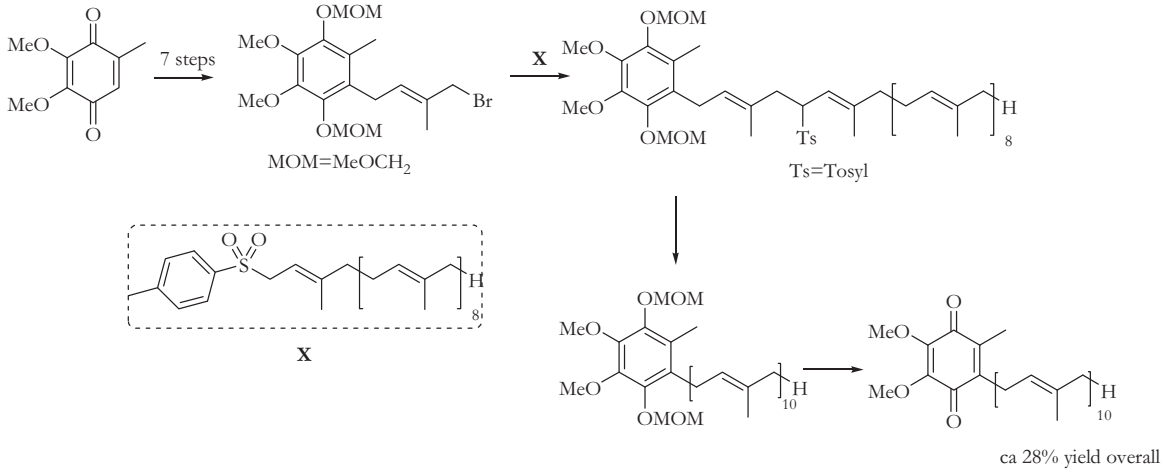
Scheme 24: Reaction with allyl-stannyl.

Naruta and co workers synthesized the stannyl reagent, which reacts with quinone and $BF_3{\cdot}OEt_2$ in a solvent mixture (CH_2Cl_2/hexane or CH_2Cl_2/isooctane) at -50 to -55 °C or -45 to -50 °C to the desired products Q9 or Q10 in both 51% yield (100% or 86% *trans*).
Another method of producing ubiquinones is the carboalumination of unactivated alkynes (Scheme 25). This procedure has been developed by Negishi [69] and later used by Lipshutz [70]. Starting from 3-butyn-1-ol the compound (E)-6,10-dimethyl-1-trimethylsilyl-5,9-undecadien-1-yne was synthesized followed by nine steps giving Q10 in 26% overall yield. No stereoisomeric separation was attempted in the synthesis of 98% (all-*E*).



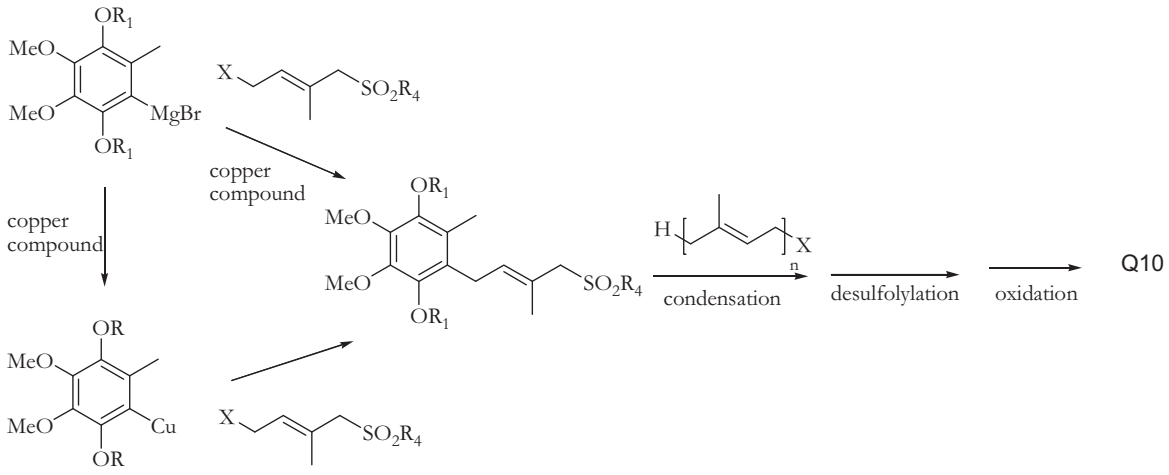
Scheme 25: 9 steps synthesis of Q10.

In 2005 Yu et al. synthesised Q10 in ten steps reaction (Scheme 26).[71] They used commercially available 2,3-dimethoxy-5-methylbenzoquinone which reacts after 6 steps to 1-[(2E)-4-bromobut-2-en-1-yl]-3,4-dimethoxy-2,5-bis(methoxymethoxy)-6-methylbenzene. This compound reacts in 9 steps and deprotection to the Q10 in approximately 28% yield overall.



Scheme 26: 10 steps reaction to Q10.

In 1981 Fujita and co-workers patented the reaction of ubiquinone with Grignard reagents.[72] The reactive sulfur compound is readily prepared by reaction of a Grignard reagent with a halo-sulfone and a copper compound, as follows:



Scheme 27: Synthesis of ubiquinone using Grignard reaction.

According to this procedure Q10 is obtained in 5% to 67% yield. Nearly two decades later a new synthesis using Grignard reagent was patented. [73] Upare et al. got Q9 and Q10 in 50-56% yield and purity of 98%.

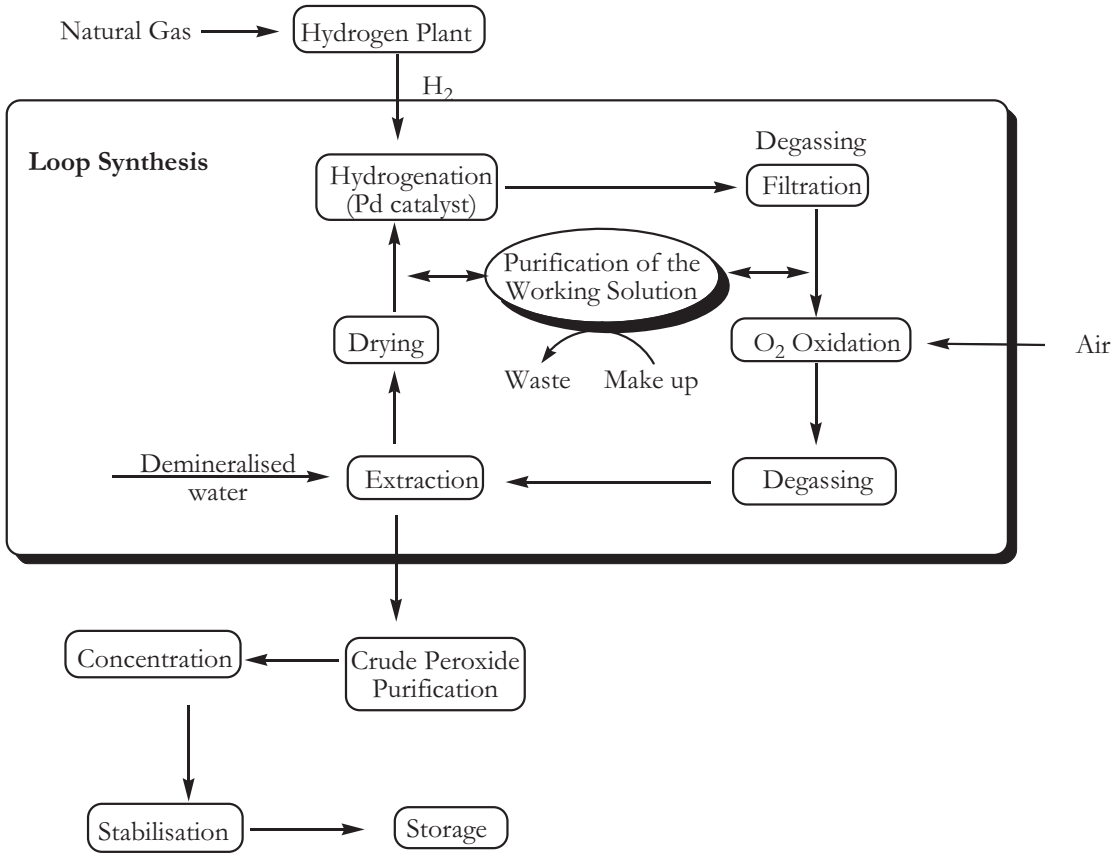
1.5. Anthraquinone

In nature anthraquinones occur in plants like fungi or in insects. It is an important substrate for the production of laxative, which is used in the medicine, production of dye stuff and paper fabrication. Nevertheless, the most important application is in the H_2O_2 manufacturing.

1.5.1 Application

1.5.1.1 Hydrogen peroxide manufacturing

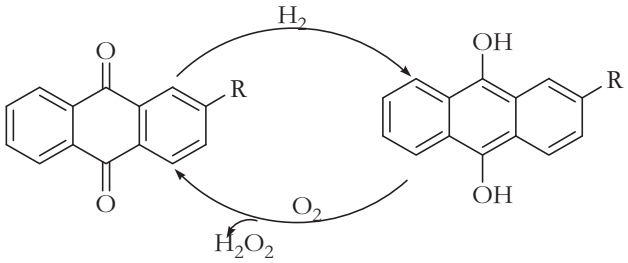
Hydrogen peroxide (H_2O_2) is a colorless liquid, miscible with water in all proportions and weakly acidic. The manufacturing process involves the reaction of H_2 with atmospheric O_2 to give H_2O_2. Hydrogen peroxide is manufactured using the anthraquinone process as a H_2 carrier.



Scheme 28: The Anthraquinone Process for H_2O_2 Manufacture

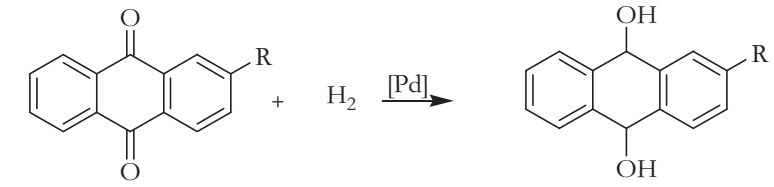
This process is a cyclic operation where an alkyl anthraquinone is reused. The synthesis loop consists of sequential hydrogenation, filtration, oxidation, hydrogen peroxide extraction and treatment of the working solution.[74] Scheme 28 shows a simplified flow diagram of the process steps. A number of ancillary processes are also involved.

The alkyl anthraquinone is important for the hydrogenation and oxidation step. In the step of the hydrogenation an alkyl anthraquinone AQ; usually 2-ethylanthraquinone, which is dissolved in appropriate solvent or mixture of solvents, one nonpolar and the other polar, is catalytically hydrogenated. The main reaction, which is known as the Riedl-Pfleiderer process[75] (Scheme 29), currently accounts for the largest part of hydrogen peroxide production (Scheme 30).

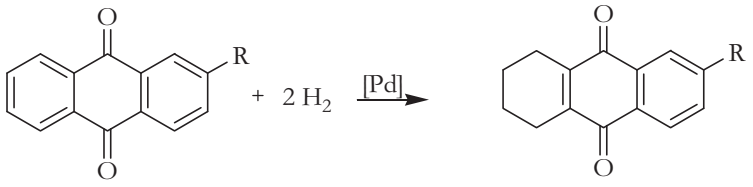


Scheme 29: Riedl-Pfleiderer process.

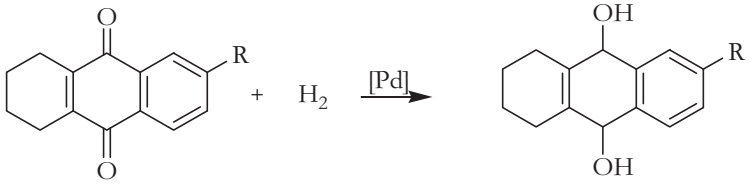
In the reaction solution AQ is hydrogenated at 4 bar using a simple palladium-on alumina catalyst.[72] Temperature is controlled to around 40-50 °C.



2-alkylanthraquinone **AQ** 2-alkylanthrahydroquinone **AHQ**



AQ 5,6,7,8-tetrahydroalkylanthraquinone **THAQ**

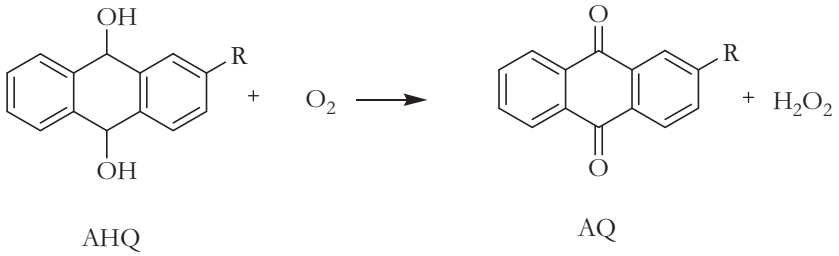


THAQ 5,6,7,8-tetrahydroalkylanthrahydroquinone **THAHQ**

Scheme 30: Hydrogenation steps of anthraquinone derivate.

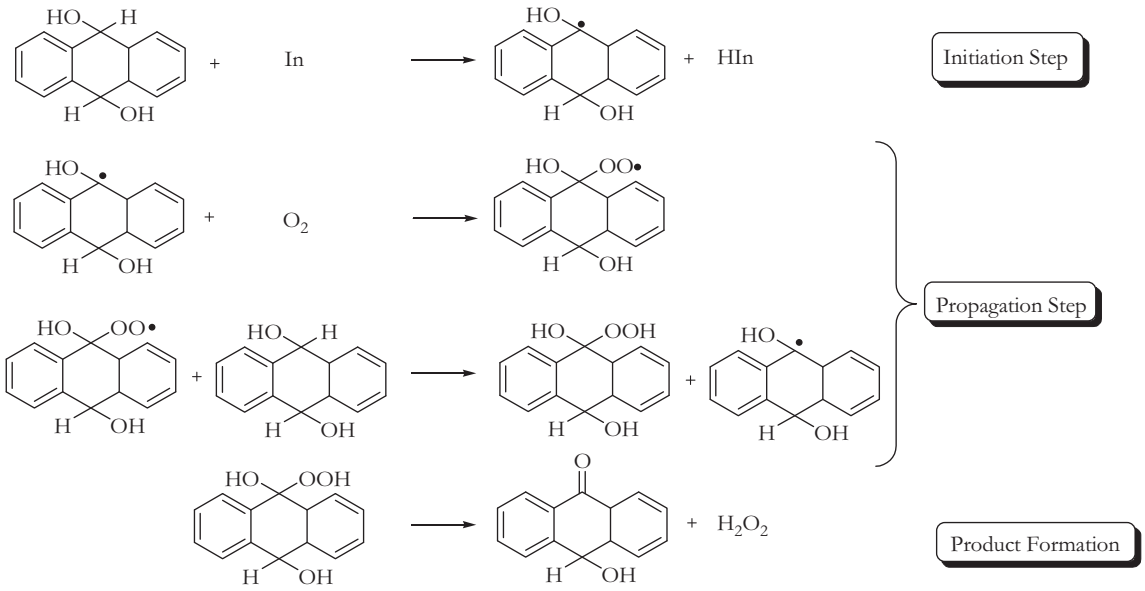
During hydrogenation AQ is converted to the alkyl anthrahydroquinone AHQ (Scheme 30). However, a side reaction is the hydrogenation of the unsubstituted aromatic ring to yield 5,6,7,8-tetrahydroalkyl-anthrahydroquinone THAHQ. The formation of this product is favoured because of the easier hydrogenation.

This by-product must be removed and treated periodically. The organic solvent employed is typically a mixture of an aromatic (a good solvent for the AQ) and a long-chain alcohol (a good solvent for the AHQ). After hydrogenation the solution AHQ is separated from the hydrogenation catalyst by the so called filtration process. The third step of the process involves the oxidation of the AHQ, regenerating the AQ, with oxygen (as air or oxygen). This uncatalyzed step produce simultaneously equimolecular amounts of hydrogen peroxide (Scheme 31).[76,77]



Scheme 31: Uncatalyzed oxidation of AHQ with O_2 to AQ and H_2O_2.

The solution is oxidized by blowing air through it at 30-60 °C and near atmospheric pressure. This reaction occurs by means of a well-documented free-radical chain mechanism (Scheme 32).[78]



Scheme 32: Free-radical chain mechanism.

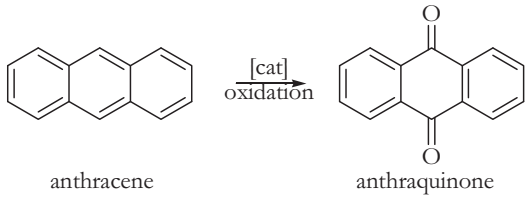
At first, an initiator (In), which can be an impurity in the hydrogen peroxide, can abstract a tertiary hydrogen atom of AHQ. After that the radical reacts with oxygen to form a hydroperoxyl radical and this reacts with a second AHQ molecule to give an instable alcohol hydroperoxide and an AHQ radical. In the third step the former product decomposes to a ketone and hydrogen peroxide, and the latter starts another propagation cycle. No catalyst is used and hence this step is often referred to as auto-oxidation.

After the oxidation step the hydrogen peroxide is stripped from the organic working solution by demineralised water in a counter current column to produce a solution that contains usually 30% by weight H_2O_2. Then, the aqueous H_2O_2 is distilled to remove impurities and increase the concentration to up to 70%, and the solvent/anthraquinone mixture is recycled.

There are advantages and disadvantages of the anthraquinone process. An advantage is the high yield of hydrogen peroxide per cycle. Nevertheless, there are two major drawbacks. On the one hand side reactions require regeneration of the solution and the hydrogenation catalyst. On the other hand a separation step to remove organic impurities from the hydrogen peroxide product is needed.

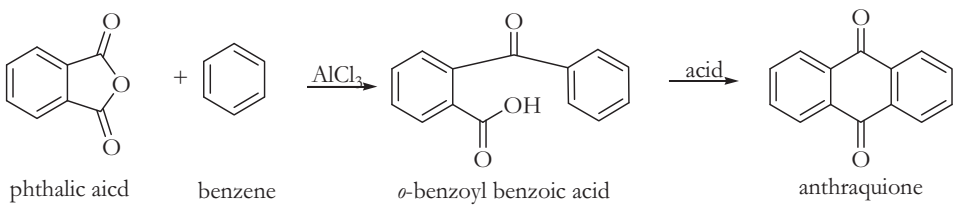
1.5.2 State-of-the-art Synthesis

The synthesis of anthraquinone and its derivates are well known. One of these methods is the oxidation of anthracene with various oxidizing agents such as molecular oxygen,[79] hydrogen peroxide,[80] ozone,[81] nitric acid,[82] chlorine,[83] and so on (Scheme 33).



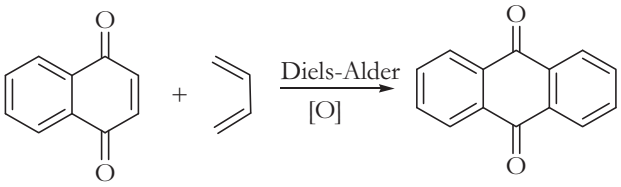
Scheme 33: Oxidation of Phenanthrene to the corresponding quinone.

The acylation of benzene with phthalic acid in the presence of aluminium chloride to obtain *o*-benzoyl benzoic acid is also published.[84] In the second step the acid is cyclized to anthraquinone in a medium such as concentrated sulphuric acid, polyphosphoric acid or hydrofluoric acid.



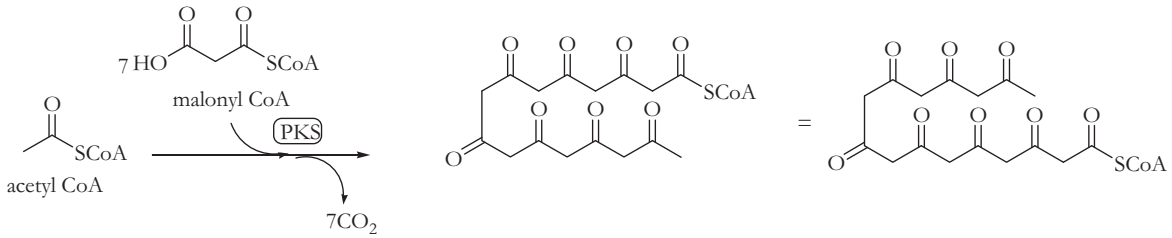
Scheme 34: Synthesis of the quinone from phthalic acid and benzene.

Furthermore, the quinone can be synthesised by a Diels-Alder reaction. In this case 1,4-naphthoquinone reacts with 1,3-butadien in an autoclave, followed by oxidation in air to the corresponding anthraquinone (Scheme 35).[85]



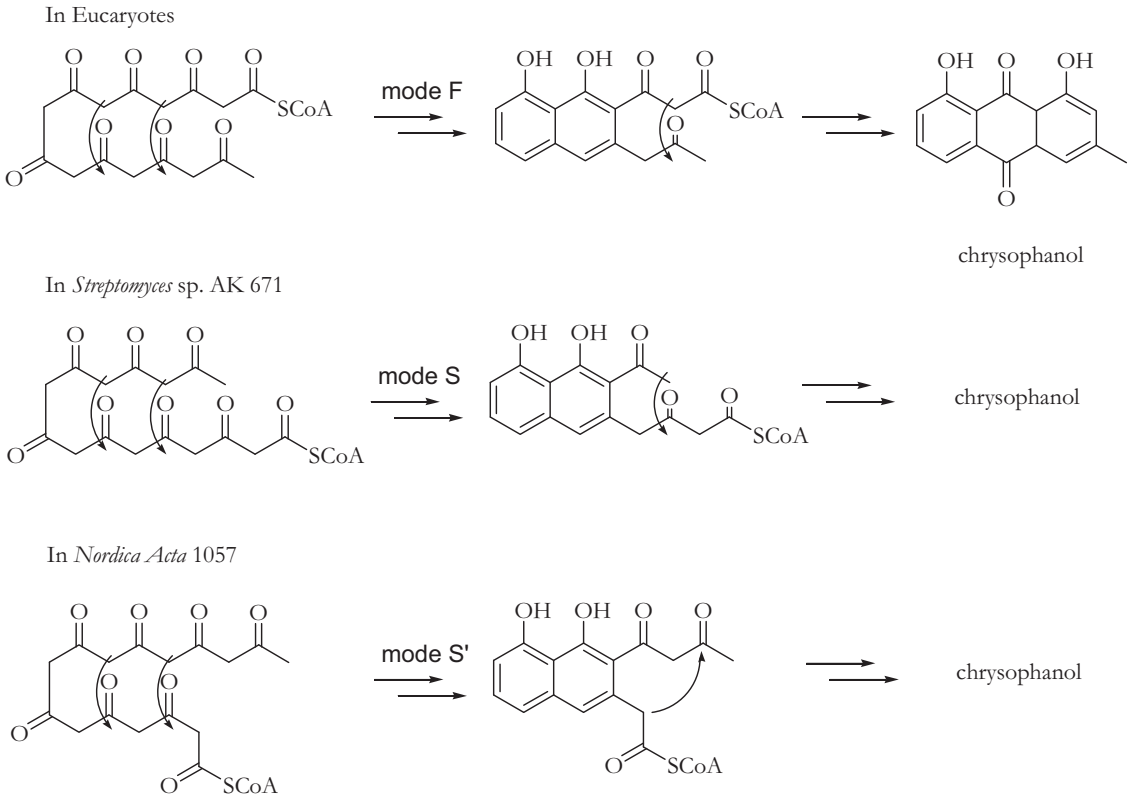
Scheme 35: Diels-Alder reaction.

In nature anthraquinone derivatives can be isolated from eukaryotic organism (fungi, higher plants and insects) and/or prokaryotes (bacterial organism).[86] In the last years the biosynthesis of these anthraquinone compounds were reviewed. Thus, it is known that anthraquinones like chrysophanol (Scheme 37) are biosynthesized via the polyketide pathways (Scheme 36).



Scheme 36: Polyketide pathways.

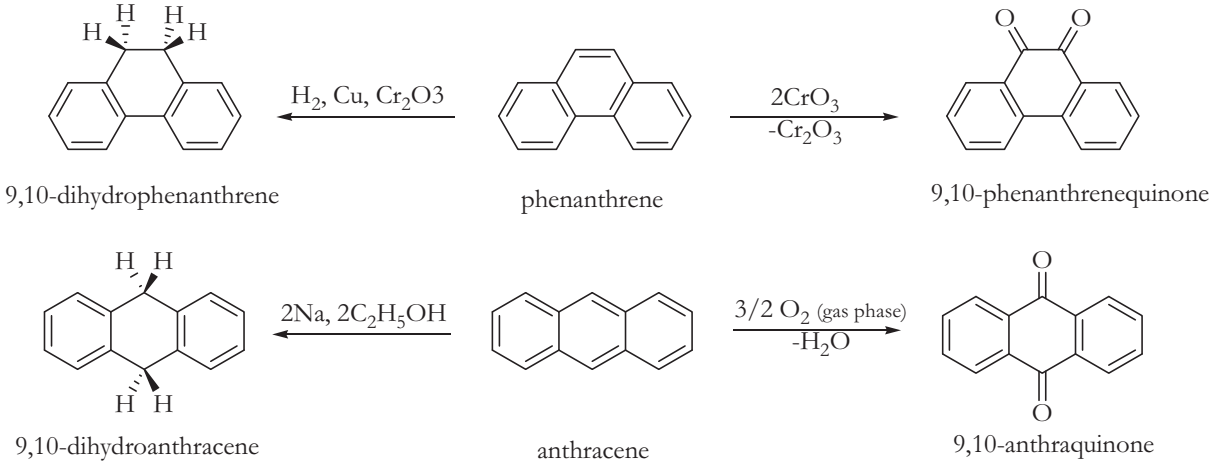
Until now three different pathways lead to chrysophanol in nature: one eukaryotic polyketide folding mode F (as initially established for fungi) and two different prokaryotic polyketide folding modes S (as expected for *Streptomyces*) and S'.[87] However, they always start from eight C2 units derivated from acetate and malonate (Scheme 35). Biosynthetically, polyketides are usually built up by successive Claisen condensation of an acyl-CoA starter unit with 7 molecules of malonyl-CoA catalyzed by polyketide synthases (PKS)[88] to provide an octa-β-keto-acyl chain (Scheme 36). Then the molecule gets diversely folded and reacts further in a divergent way, via three different series of intermediates and still, all of them finally provide the target molecule chrysophanol.



Scheme 37: Three different routs to chrysophanol in nature.

1.6 Phenanthrenequinone

Both phenanthrene and anthracene have preferential reaction centres at the meso-positions C-9 and C-10 thereby the two benzene-ring systems were sustained. Oxidation provides 9,10-quinone (Scheme 38).



Scheme 38: Reactions of phenanthrene and anthracene.

In comparison with similar reactions of the naphthalene they need mild reaction conditions. The most common photooxidation and biotransformation product of phenanthrene is phenanthrenequinone[89]. The quinone is a compound of substantial

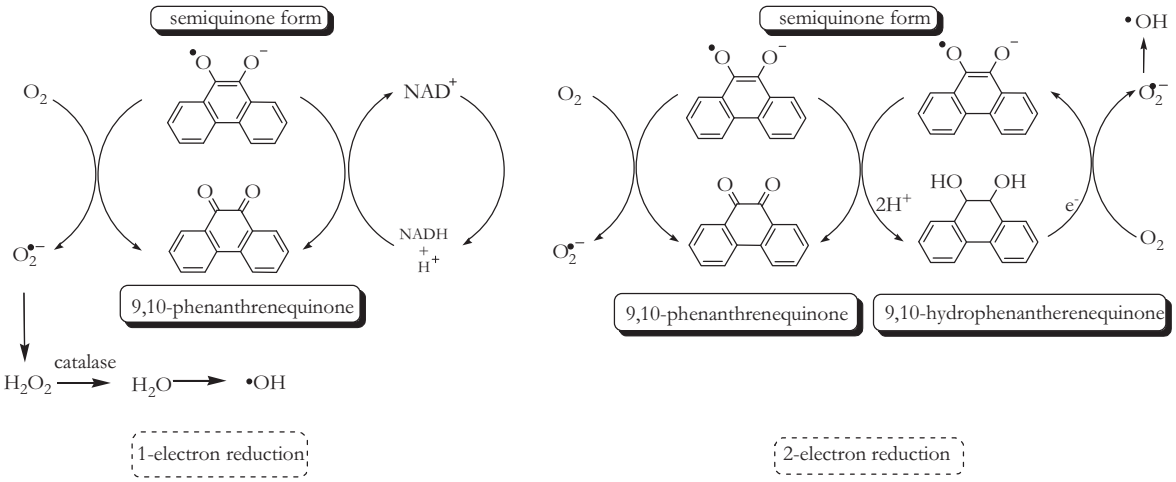
interest, because its toxicity to aquatic organisms can be much higher than in its parent chemical. Phenanthrenequinone act in the redox cycle in bacterial cells and transfer electrons to O_2.[90]

1.6.1 Application

1.6.1.1 Redox cycle

By virtue of their quinones, these agents can undergo a biochemical reduction by one or two electrons that are catalyzed by different enzymes such as cytochrome P450, cytochrome P450 reductase or flavoenzymes in the organism using NADPH as an electron donor.

This bioreductive process leads to the semiquinone and hydroquinone of anticancer drug.[91] The process of reductive activation is the first step in the process of redox cycle. The consequence of these enzymatic reductions is that the semiquinone (unstable) yields its extra electron to oxygen with the formation of superoxide radical anion ($O^{\cdot}_2^-$) and the original quinone (reactive oxygen species). This reduction by a reductase followed by oxidation (molecular oxygen) is known as redox-cycle and continues until the system becomes anaerobic (Scheme 39).



Scheme 39: 1- and 2-electron reduction.

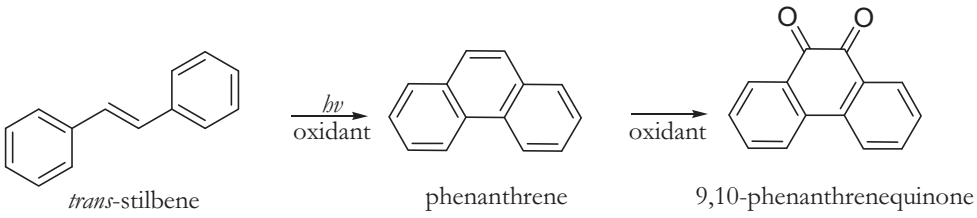
In the case of a 2-electron reduction, which is more complicated, the hydroquinone could become stable (Scheme 39). The 2-electron reduction leads to the formation of hydroquinone, which has a lower reactivity than semiquinone and as such, excreted by the organism in a detoxification pathway. It may also be due to autoxidation of hydroquinones to form reactive oxygen species (ROS).

In both pathways $O^{\cdot}_2^-$ were obtained. The formation of $O^{\cdot}_2^-$ is the beginning of a cascade that generates H_2O_2 and it also changed into the H_2O by catalase, generally referred to as ROS.[92] Chemicals are metabolized in the body to produce many kinds of ROS. The ROS is changed into •OH, through the Haber-Weiss reaction and the Fenton reaction processes. The •OH radical makes adducts with DNA to induce mutation.[93] It is known that all quinone-containing antitumor agents undergo redox cycling at different rates. The consequences of redox cycling may change with cell line, cellular pH, oxygen concentration, and with the type of tumor. [94]

1.6.2 State-of-the-art Synthesis

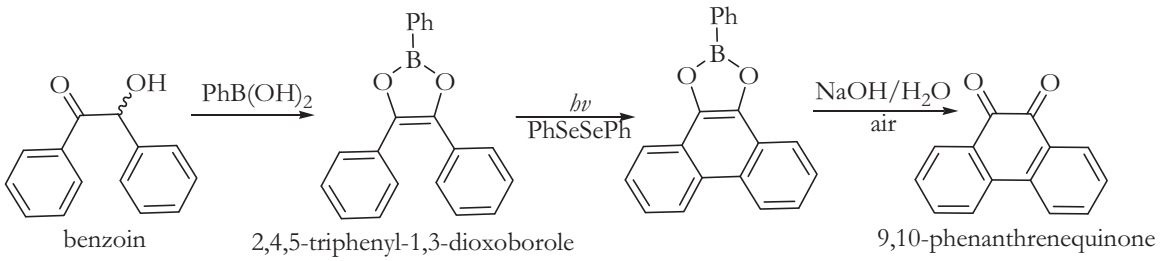
There are a number of synthetic routes available but the most used procedure involves the oxidation of phenanthrene. The catalytic oxidation of phenanthrene is one of the possibilities to obtain the corresponding quinone in high yields (*vide* supra).[95] Thereby a variety of catalyst systems are known. Recently our group published ruthenium catalyst oxidation of phenanthrene in 34% to 54% yields.[80]

However it is also feasible to achieve the 9,10-phenanthrenequinone and derivatives by photocatalytic reactions. Classically, this is done by oxidative photocyclization of stilbene followed by oxidation of the resulting phenanthrene [96] to 9,10-phenanthrenequinone (Scheme 40).



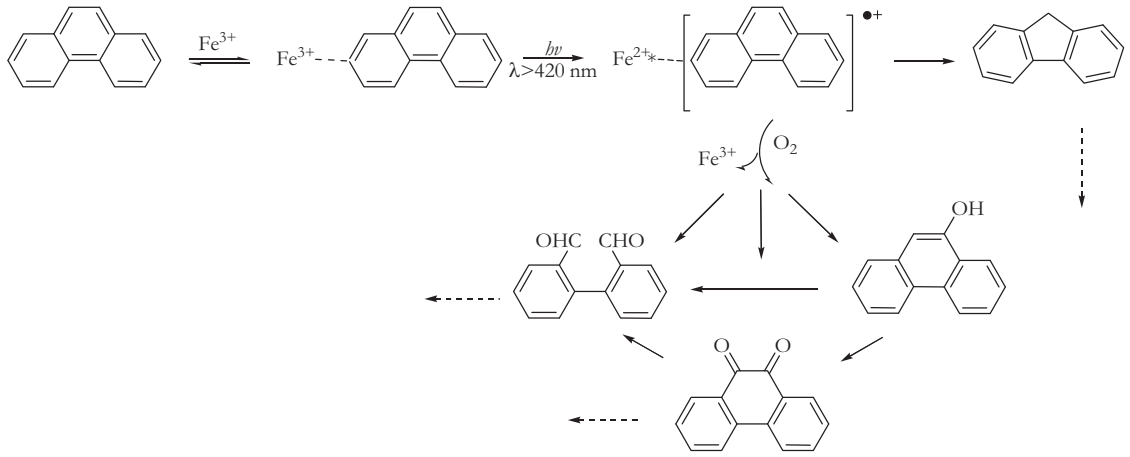
Scheme 40: Oxidative photocycization of stilbene to 9,10-phenanthrenequinone.

This route gives often low yield in the cyclization step due to competing *cis-trans* isomerization. It is also difficult to oxidize phenanthrene in high yields. In 1988 de Vries et al. found an alternative synthesis to resolve these problems.[97] They developed a route which converts benzoin into 9,10-phenanthrenequinone in 84% yield. For this two step-reaction they first used phenylboronic acid and benzoin which gave the 2,4,5-triphenyl-1,3-dioxoborole (Scheme 41). At this point the *cis-trans* isomerization is bypassed. However the next reaction step is the photocyclization of the dioxoborole in benzene with diphenyl diselenide as mild oxidant to produce a crystalline compound which react after hydrolysis to the 9,10-phenanthrenequinone.



Scheme 41: Reaction of benzoin to 9,10-phenanthrenequinone.

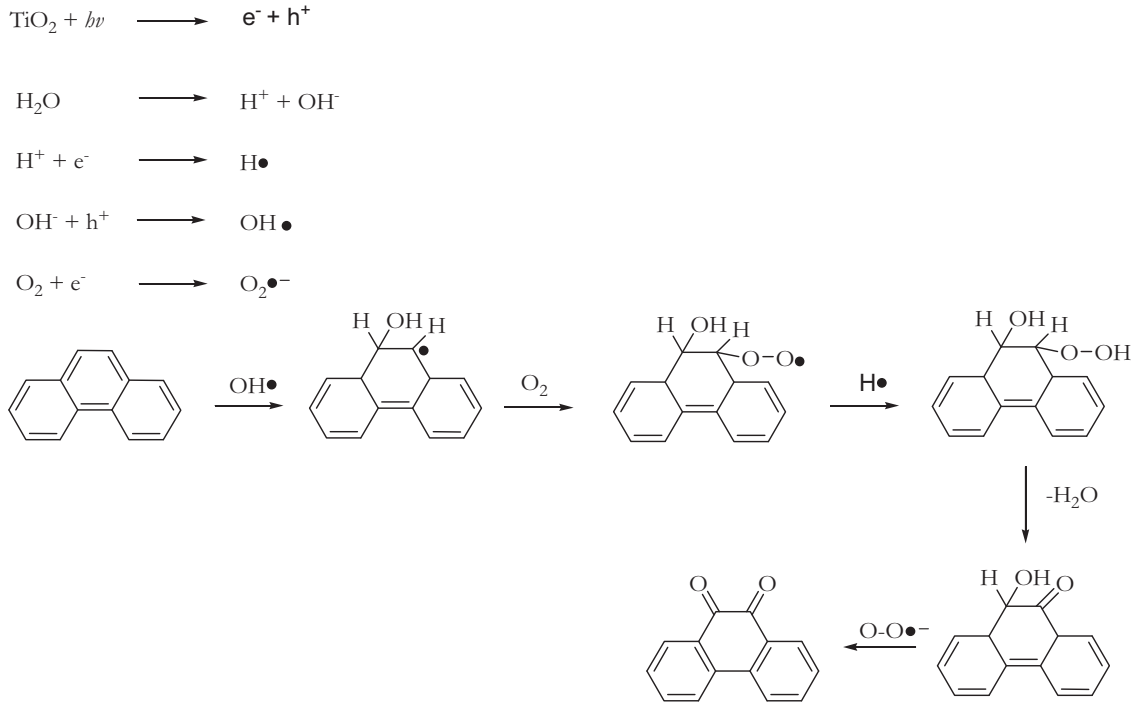
Togashi et al. used this method and tried to synthesised 9,10-phenanthrenequinone derivatives with electron donating (methoxy and methyl) and electron withdrawing (chloro) groups on the 3 and 6 position of the quinone.[98] The substituents used in this synthesis did not alter the rate or yield of cyclization, or the ease of hydrolysis. Ten years later Kou and co workers were interested in the influence of transition metal ions on the phenanthrene under visible light irradiation from 420 to 520 nm.[99] They applied transition metal salts ($FeCl_3$, $CuCl_2$, $MnCl_2$, $Cr(NO_3)_3$, $NiCl_2$, $ZnCl_2$, $CoCl_2$) by using a glass reactor. Only $FeCl_3$ showed some reactivity and 11 products were identified in the Fe^{3+}-acetone-water system.[100] The quinone and 2,2´-biphenyl-dicarboxaldehyde are the main products (Scheme 42) and the yield was 40.3% and 35.6%, respectively.



Scheme 42: Influence of *trans* metal ions to obtain 9,10-phenanthrenequinone.

Furthermore heterogeneous photocatalytic reactions are well known, too. In 2003 Lin et al. used a titania thin film of titania annular photocatalytic reactor for the degradation of phenanthrene in dilute water streams.[101] They postulated a mechanism of the conversion of phenanthrene to the corresponding quinone (Scheme 43). Whereas the e−/h+ couple generated by UV (<410 nm) illumination of titania will generate highly oxidizing species. However hydroxyl (•OH) and superoxide (O_2•−) radicals are the primary oxidizing species in heterogeneous photocatalytic processes. Scheme 43 show the postulated mechanism where the resulting hydroxyl radical attack on the 9-position of the phenanthrene and

subsequent reaction with oxygen and superoxide radical will lead to the formation of the corresponding quinone.



Scheme 43: Postulated mechanism of the synthesis from phenanthrene to the quinone.

With this reaction condition seven intermediates were identified. Photocatalytic reaction using TiO_2 powder, acetonitrile and water (1:1) as eluent at r.t. were published 2006 by Higashida et al..[102] Nevertheless phenanthrene was converted to 9,10-phenanthrenequinone which react then to cumarine. Furthermore functionalized TiO_2 photocatalyzed reaction is known. Recently Liu et al. published a thio-functionalized TiO_2 photocatalytic degradation of phenanthrene.[103] They succeeded the formation of 9,10-phenanthrene and other degradation products in heterogeneous photocatalytic process.

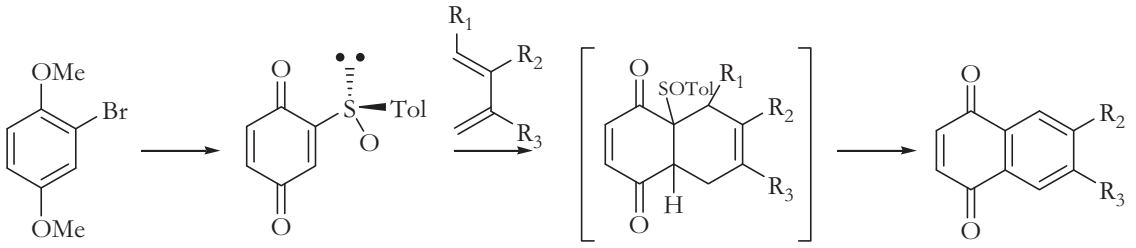
1.7 Naphthoquinone

Naphthoquinone forms the central chemical structure of several natural compounds, for example the series of Vitamin K are naturally occurring 1,4-naphthoquinone derivatives (*vide* infra). Furthermore juglone, lawsone, plumbagin and atovaquone are well known 1,4-napthoquinone derivates (*vide* supra). However the reactions of 1,4-naphthoquinone are versatile. Major reactions are nucleophilic addition, radical addition, acylation, reaction of quinone carbonyl, photo-chemical reaction, substitutions to aromatic ring and Diels-Alder reaction. After these reactions new 1,4-naphthoquinone derivates were developed, for

example anthraquinone. 1,4-Naphthoquinone and diene react to anthraquinone *via* Diels-Alder reaction. That's why naphthoquinone is an intermediate for the pulp and dye manufacture. Among them, 1,4-Naphthoquinone is industrially used as a raw material for pharmaceuticals, agrochemicals and other functional chemicals.

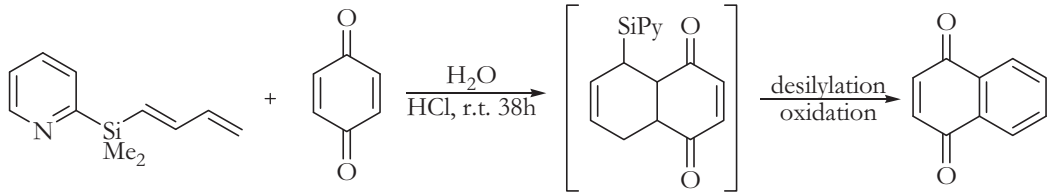
1.7.1 State-of-the-art Synthesis

The use of quinones as dienophiles has allowed the synthesis of some important natural products. This procedure was published in 1989.[104] Carreño and co-workers developed a general method to obtain chiral 2-sulfinylquinones in high chemical and optical yield. After this synthesis the new compound react with acyclic dienes to naphthoquinone, resulting from intermediate by pyrolysis of the sulfonyl group and further aromatization (Scheme 44). The isolation of the product is unsuccessful.



Scheme 44: Reaction of a chiral quinone to the 1,4-naphthoquinone.

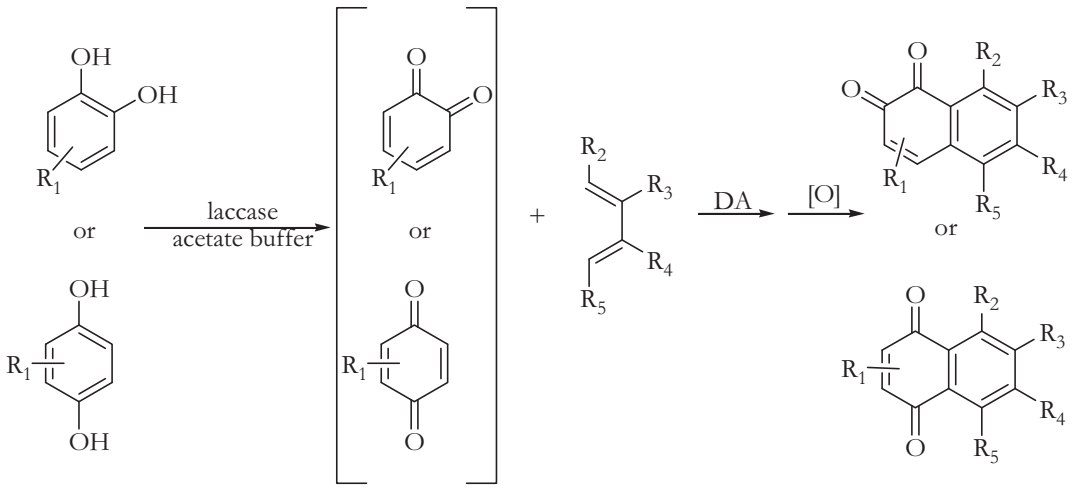
Further investigations on Diels-Alder reactions with quinones were published by Itami et al..[105] They developed a Diels-Alder reaction with 2-PyMe_2Si-1,3-diene with *p*-benzoquinone in water (containing 1 eq. of HCl) with simultaneous desilylation and oxidation to afford naphthoquinone quantitatively (Scheme 45).



Scheme 45: Diels-Alder reaction with 2-PyMe_2Si-1,3-diene.

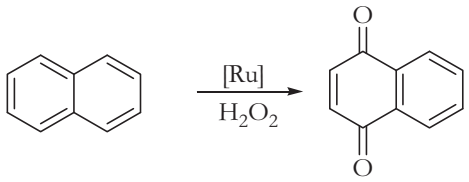
In the literature the synthesis of naphthoquinones *via* Diels-Alder by using an enzymes is also known.[106] Laccases are copper-containing glycoprotein oxidoreductase enzymes found in plants and fungi.[107] Witayakran et al. reported the use of laccase for the synthesis of substituted naphthoquinones. The reaction started by using catechol or hydroquinone with the enzyme which reacts to the corresponding quinone. Next the

compound reacts with a diene to the 1,2- or 1,4-naphthoquinone and its derivates. This reaction system can yield naphthoquinones up to 80% depending on the exact structure of the starting hydroquinone and diene (Scheme 46).



Scheme 46: Laccase catalyzed reaction to 1,2- or 1,4-naphthoquinone.

However for the synthesis of naphthoquinone quite more reactions are known. First it is possible to obtain naphthoquinone from naphthalene by catalytic gas phase oxidation.[108] Second the oxidation of 1,4-aminonaphthol, 1,4-diaminonaphthalene or 4-amino-1-naphthalenesulfonic acid to 1,4-napthoquinone are common procedures. The catalytic oxidation of naphthalene is the most used and published method to receive the corresponding quinone. 2007 and 2010 our group reported a ruthenium catalyzed oxidations of naphthalene (*vide* supra) (Scheme 47).[80] At first we published the ruthenium catalyzed in a two phase system with different phase transfer catalysts (PTC). 1,4-Naphthoquinone were obtained in 39% to 59% yield, depending on the PTC. Next we published a Ru(tpy)(pydic) catalyzed one phase system and we increased the yield of the quinone up to 63%. In both systems we used H_2O_2 (30%) as oxidant.

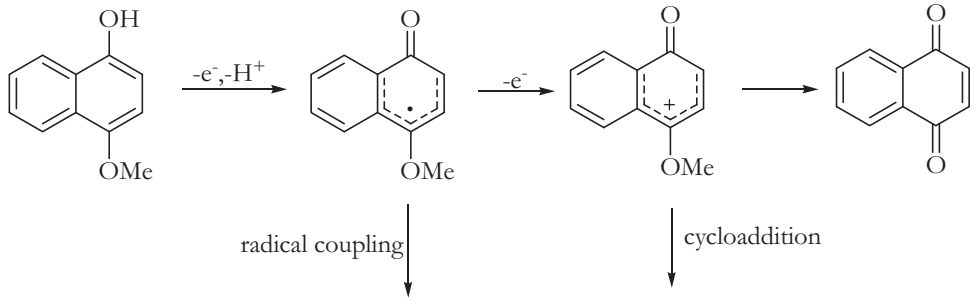


naphthalene 1,4-naphthoquinone

Scheme 47: Ruthenium catalyzed oxidation reaction.

In the literature transition metal oxidants such as chromium(VI), manganese(III), cobalt(III) and cerium(IV) are realized. The electrochemical recycle of these oxidants is also published. 1989 Kreh et al. mentioned the oxidation of naphthalene with cerium(IV) in methansulfonic acid to the corresponding quinone in 92% conversion and 98%

selectivity. Additionally, after separating the product and catalyst, they regenerate Ce(III) *via* electrochemical oxidation. This oxidation procedure with electrochemical oxidation subsequently was patented and published in the last years.[109] Moreover electrochemical oxidations have been reported whereas the reaction to naphthoquinone takes place on electrodes.[110] The paper describes the oxidation of naphthol, which was electrolyzed in the presence nBu$_4$NBF$_4$ as supporting salts and alkenic nucleophiles using a glassy carbon beaker as an anode. The cathode, a platinum wire and anode are divided cell through glass filters. Oxidation of 4-methoxy-1-naphthol afforded two kinds of the oxidized forms, the anodic oxidation occurred with the one-electron oxidation of 4-methoxynaphth-1-ol to give the radical 4-methoxynaphthalen-1-one, followed by the second diversion of an electron to the cation (Scheme 48).



Scheme 48: Electrochemical oxidation to 1,4-naphthoquinone.

Both active species might be stabilized, while the radical underwent a homogeneous coupling and the cation reacted with nucleophiles through the [3+2] cycloaddition reaction. Nevertheless this reaction system can yield 1,4-naphthoquinone up to 68% depending on the nucleophiles.

1.8 Vitamin K

The family of vitamin K includes the two naturally vitamins K_1 (phylloquinone or phytomenadione) and K_2 (menaquinone), and one synthetically produced vitamin K_3 (menadione or 2-methyl-1,4-naphthoquinone) (Figure 10).[111]

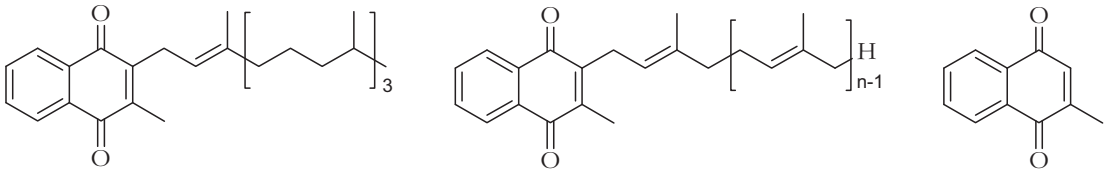


Figure 10: Vitamin K family.

All these compounds are 1,4-naphthoquinones. The methyl group at position 2 is responsible for the specific biological activity of vitamin K. All members of the vitamin K group vary in the length of the aliphatic side chain attached at the 3-postion, which influences the solubility and other properties. Vitamin K_1 is found in plant foods, for example, in soybeans, milk and milk products, flesh, tomatoes, rose hips, green vegetables and potatoes. In contrast to that, vitamin K_2 is synthesized by intestinal bacteria. Vitamin K_1 can only reabsorb with the help of bile acid, because of the fat solubility of the vitamin K. Therefore, the reabsorb increase by concurrent intake of fats. In the body, vitamin K is in the blood plasma and is saved in liver and kidney. The hydroxylated vitamin K_1 is the biologically active form. It acts as a cofactor for γ-glutamyl carboxylase and plays a crucial role for the γ -carboxylation of coagulation proteins. Furthermore it is also involved in the biosynthesis of proteins in bone, kidney and plasma. Menadione (vitamin K_3) is used as a vitamin K_1 and K_2 precursor and is important as food additive.[112] It shows a lower antihemorrhagic effect than vitamin K_1 and K_2. K-vitamins are able to inhibit the growth of many tumor cells. The mechanism of the inhibitory effect of vitamin K_1 and K_2 has not been clarified until now. Menadione shows inhibitory effects caused by alkylation of cellular nucleophiles damaging the cells, and by redox cycle. For this reason menadione is a model substrate for the application and state of the art follows.

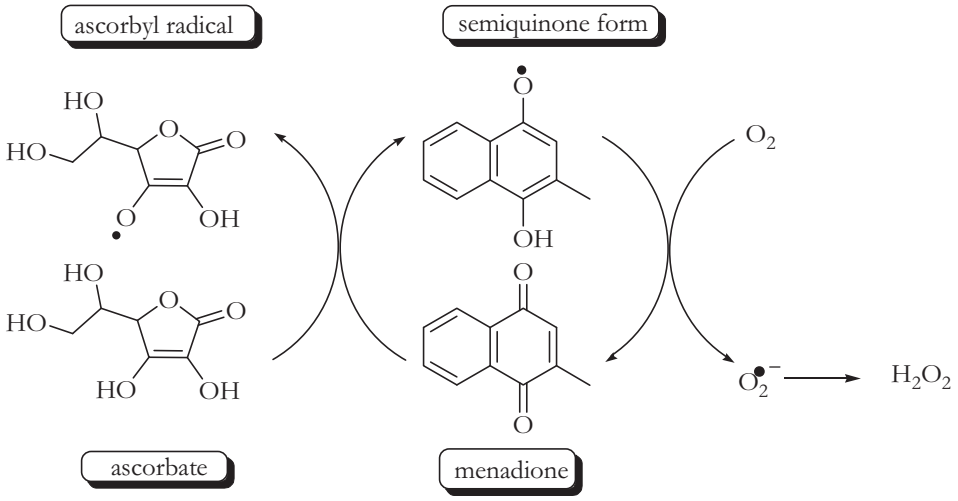
1.8.1 Application

1.8.1.1 Antitumor effect

Menadione inhibits the growth of tumor cells in vitro.[113] In the presence of reducing agents it runs a redox cycle. Menadione has a strong antitumor effect in rodent and human tumors, but it is also highly toxic to cells and causes side effects such as cardiotoxicity and anemia.[114] Cancer cells usually exhibit a poor antioxidant status,[115] thus raising the possibility to kill cancer cells through oxidative stress. The excessive production of reactive oxygen species (ROS) generates oxidative stress by quinones.

To do that, a synergistic association of ascorbate (vitamin C) and menadione was used, it reacts like a one electron redox cycle (*vide* supra).[116] As shown in the Scheme 49, menadione is reduced by ascorbate to form the dehydroascorbate and the semiquinone free radicals.

The semiquinone radical is rapidly reoxidized to its quinone form by molecular oxygen thus generating ROS. Among them hydrogen peroxide is likely the major oxidizing agent involved in the cytolytic process.[117] The molecular mechanisms of cell killing by ascorbate/menadione observed in several cell lines[118] are not totally clarified until now.

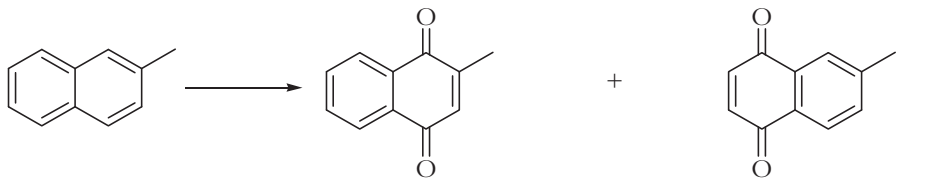


Scheme 49: Redox cycle of ascorbate and menadione.

Nevertheless, menadione is not justifiable in the human medicine, because of its side effect. Also the use in the food industry is not allowed according to Federal Ministry of Health. Menadione is known to be mutagenic and has toxic effects in particular for liver cells. The application of menadione causes skin and mucous membrane irritation, allergic reactions, and an accumulation for eczema. High doses show symptom of poisonings with vomiting and albuminuria.

1.8.2 State-of-the-art Synthesis

The industrial manufacture of menadione is similarly based on the selective oxidation of an arene. Here, 2-methylnaphthalene is selectively oxidized to menadione (Scheme 50).

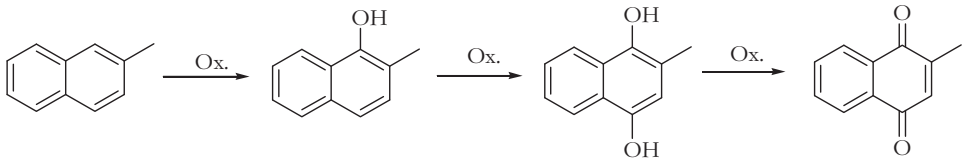


2-methylnaphthalene — 2-methyl-1,4-naphthoquinone, vitamin K_3, menadione — 6-methyl-1,4-naphthoquinone

Scheme 50: Oxidation of 2-methylnaphthalene to the corresponding quinones.

Unfortunately, the latter oxidation is still performed by using stoichiometric amounts of chromium trioxide in sulphuric acid. Depending on the reaction conditions product yields between 38–60% have been reported.[119] Due to the large amount of chromium-containing waste, e.g. 18 kg of waste per kg of product,[119] significant research efforts have been made to replace this process by more environmentally benign routes.

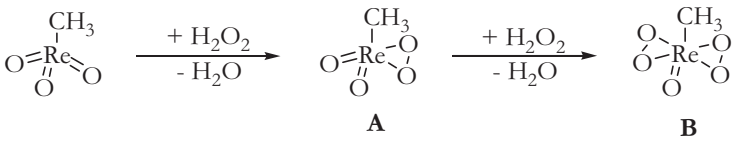
As early as 1940 Arnold et al. reported the synthesis of vitamin K_3 in about 30% yield by using hydrogen peroxide (30%) in acetic acid at 80 °C.[120] 30 years later the Mitsubishi Gas Chemical Co. patented an improved method for vitamin K_3 synthesis using 12 eq. HCl and 4 eq. H_2O_2 (60%) in MeOH.[121] In 1985, Yamaguchi et al. reported the first metal-catalyzed synthesis.[122] Here, the oxidation of 2-methylnaphthalene was carried out in acetic acid with aq. 60% H_2O_2 in the presence of Pd(II)-polystyrene sulfonic acid resin. At 50 °C after 8h the conversion was 93% and 2-methyl-1,4-naphthoquinone was obtained in yields between 50 and 60%. The catalyst recovered by filtration was reusable. However, the regioselectivity of the process was not discussed in this study. Mechanistic investigations by the Yamaguchi group suggested a hydroxylated naphthalene intermediate before the quinone is formed.[123] As shown in Scheme 51, 2-methylnaphthalene is oxidized to 2-methylnaphth-1-ol, before 2-methylnaphth-1,4-diol is formed and finally the oxidation to the corresponding 2-methyl-1,4-naphthoquinone takes place.



Scheme 51: Proposed pathway for the Pd-catalyzed oxidation of 2-methylnaphthalene.

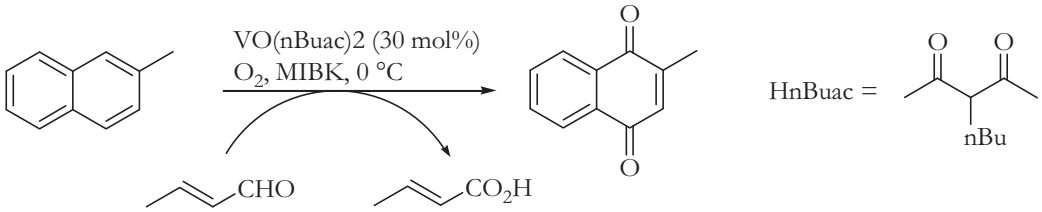
An interesting catalytic oxidation of 2-methylnaphthalene using hydrogen peroxide was described by Herrmann et al. in the beginning of the 1990s.[124] This reaction is catalyzed by methyltrioxorhenium (MTO), which is also active for several other transformations such as olefine metathesis or aldehyde olefination.[125]

Applying acetic acid/acetic anhydride as solvent in the presence of catalytic amounts of CH_3ReO_3 (1 mol%), 2-methylnaphthalene is preferentially oxidized by hydrogen peroxide (85% in water) to the 1,4-quinone (menadione). At 40 °C and after 4 h the conversion amounts to 89% (quinone yield 52%). The high regioselectivity is particularly remarkable, favouring the isomeric 2-methylnaphthoquinones (Scheme 50), which are formed in a 7: 1 ratio (46 % yield of menadione). From a mechanistic point of view MTO reacts with hydrogen peroxide to form two η^2-peroxorhenium complexes, the mono-peroxorhenium and the di-peroxorhenium species (**A** and **B** in Scheme 52).[126] Complex **B** represents the most active catalyst for the oxidation of the substrate. To prevent MTO deactivation by water hydrolysis, a mixture of acetic acid and acetic anhydride with H_2O_2 (85% in water) is employed minimizing the amount of water.[127]



Scheme 52: Formation of the active catalyst species from MTO.

In 1994, Takai and co-workers published the first catalytic system with molecular oxygen as oxidant.[128] By using an oxovanadium(IV)-1,3-diketone complex as a catalyst in the presence of molecular oxygen and crotonaldehyde, 2-methylnaphthalene was smoothly oxidized to the corresponding 1,4-naphthoquinone (Scheme 53). Under similar conditions menadione was obtained in a yield of 55%. The disadvantage of this system is the necessity of an auxiliary reducing agent and two equivalents of oxygen are used per oxidation taking place. Unfortunately, more than stoichiometric amounts of toxic crotonaldehyde have to be added successively.

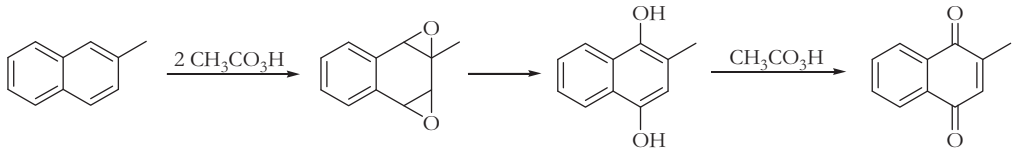


Scheme 53: Oxidation of 2-methylnaphthalene with O_2 and oxovanadium catalyst.

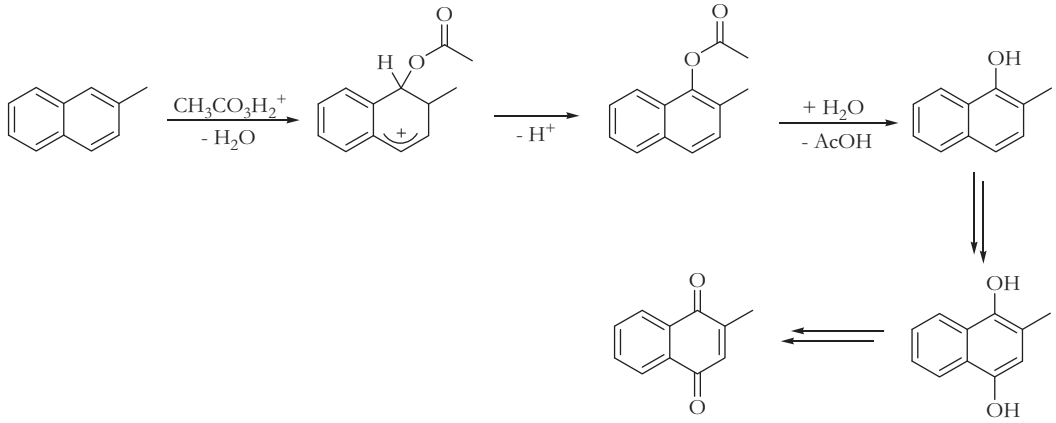
The current state-of-art oxidation system for arenes to quinones was developed by W. Thiel and co-workers in 2006. Here, yields up to 71% of menadione are obtained.[129] Their reported method utilized 50% hydrogen peroxide (aq.) in a mixture of glacial acetic acid and acetic anhydride without any metal catalyst! Instead a strong Brønstedt acid is used to catalyze the reaction. Different acids such as perchloric acid, phosphorus acid or sulfuric acid have been applied as catalysts. The observed ratio of regioisomers is approximately 8:1. From a mechanistic perspective two possible reaction paths were considered (Scheme 54).

On the one hand, initial epoxidation and subsequent rearrangement leads to the target molecules (**I**). On the other hand, protonation and acylation of the arene gives the mono-hydroxylated derivative (**II**). Notably, the hydroxylated intermediate was detected by gas chromatography.

I: Epoxidation pathway

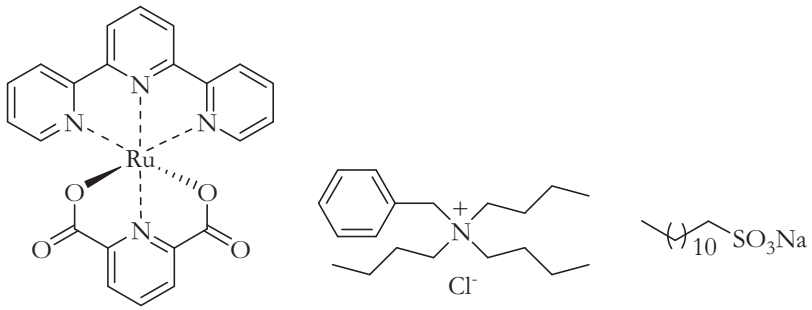


II: Electrophilic aromatic substitution pathway



Scheme 54: Possible reaction pathways towards vitamin K_3 according to Thiel and co-workers.

In our previous investigations a practical ruthenium phase-transfer catalyst (Ru-PTC) system for the oxidation of 2-methylnaphthalene has been developed.[80a),b)] We used a ruthenium catalyst in water without the addition of any organic solvent and acid and different phase transfer catalysts (Scheme 55). Yields of 64% and a combined selectivity towards the 1,4-quinone products of 73% were reported. The main drawback of this method remains the low product ratio of 3:1 between 2-methyl-1,4-naphthoquinone and 6-methyl-1,4-naphthoquinone, and the incomplete conversion of the starting material.

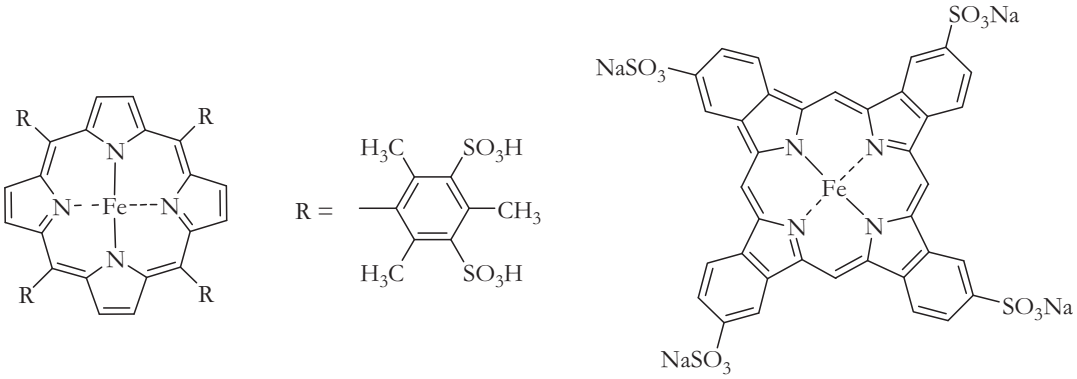


Scheme 55: Ru(tpy)(pydic)-catalyst and phase transfer catalysts employed for vitamin-K_3 synthesis.

To solve this problem we performed a solvent screening and were able to develop a one phase system with methanol as solvent. However, we published an environmentally benign method for the oxidation of 2-methylnaphthalene to vitamin K_3 in a one-phase system with a maximum yield of 62% and a ratio between the two regioisomers of 5:1. Only 3.2 equivalents H_2O_2 and a low catalyst loading of 1 mol% are required.

By applying the optimized conditions the feed additive menadione (vitamin K_3) is obtained from 2-methylnaphthalene with 64% yield and 73% selectivity.

Due to their interesting redox chemistry and easy availability also iron-based catalysts have been applied for the synthesis of quinones from arenes. The first example was published in 1997 by Meunier and co-workers, who described an iron-porphyrin catalyzed oxidation of 2-methylnaphthalene. The reported system makes use of a sulfonated porphyrin, allowing the catalyst to be water-soluble (Figure 11).[130] Unfortunately, potassium peroxomonosulfate had to be used as oxidant and vitamin K_3 is obtained only in moderate 44% yield due to the low regioselectivity of the oxidation. A different iron catalyst system utilized tetrasulfonic phthalocyanine (FePcS) immobilized on silica (Figure 11).[131] Sorokin et al. reported that the FePcS's are bound together to form an active dimer. The reaction was run in acetonitrile using 4 mol% of the catalyst and *t*-BuOOH as oxidant providing quinones and vitamin K_3 in yields of 65% and 45%, respectively.



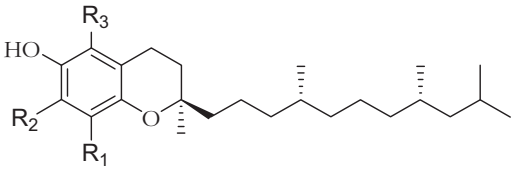
Porphyrincomplex Phthalocyanincomplex

Figure 11: Iron-porphyrin- and phthalocyanin complexes for arene oxidations.

Most recently, we described an efficient oxidation of 2-methylnaphthalen using easily available iron complexes.[132] We applied a simple and green *in situ* system $FeCl_3 \cdot 6H_2O$, pyridine-2,6-dicarboxylic acid (H_2Pydic) and benzylamine ligands with hydrogen peroxide (30%). Applying an acetonitrile/water mixture the desired quinone (menadione) is obtained in 44% yield. However, the ratio between the two regioisomers (Scheme 50) is 3:1.

1.9. Vitamin E

Vitamin E is the collective name / denotation of all tocopherols and tocopherol derivatives having the biological activity of RRR-α-tocopherol (the only stereoisomere occurred in nature). There are four different tocopherols (Figure 12) that differ in the number and position of methyl groups on the chromanol head.



α-tocopherol: $R_1=R_2=R_3=CH_3$
β-tocopherol: $R_1=R_3=CH_3$; $R_2=H$
γ-tocopherol: $R_1=R_2=CH_3$; $R_3=H$
δ-tocopherol: $R_1=CH_3$; $R_2=R_3=H$

vitamin E

Figure 12: Tocopherol derivates.

However the isoprenic side chain is the same.[133] Vitamin E is a fat soluble vitamin present in many foods, especially certain fats and oil. Due to their high antioxidant activity,[134] tocopherols have been used in medications, health-care and cosmetic formulations and as stabilizers in plastic packing.[135, 136] They help to protect the body against the formation of free radicals, effects of pollution and other toxins, it helps premature aging, cancer and other chronic, degenerative diseases. Vitamin E even protects other nutrients from damage. The immune system is dependent upon this vitamin for strength and stability. Adequate vitamin E is needed to heal injured tissues and prevent scarring.

1.9.1. Application

1.9.1.1 Antioxidants

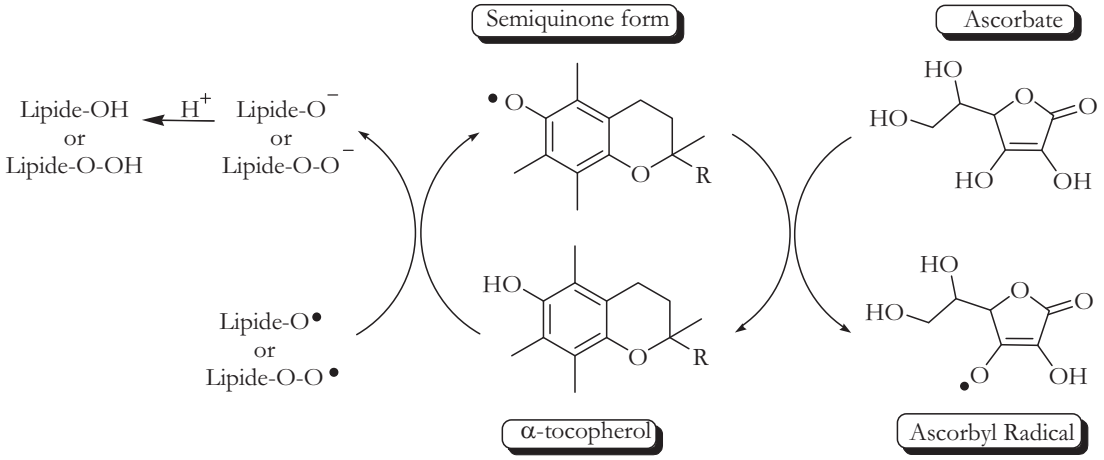
Oxygen is responsible for the destroying of biomolecules. The result of the reaction cascade is the biochemical reduction of O_2 to water. During this reaction four electrons and four protons were absorbed (Scheme 56)

$$O_2 + 4H^+ + 4e^- \longrightarrow 2H_2O$$

Scheme 56: Reduction of O_2 to water.

Some compounds were synthesized during this reaction, for example the superoxide O_2^- and the hydroxyl radical $OH^{\cdot}$. These compounds are responsible for the reaction of the chain growth. It is suspected, that processes like these are involved into the development of emphysema, arterioscleroses, several chronically inflammation, cancer und aging processes. A huge number of natural antioxidants inhibit this oxidative permutation and

protect the lipid molecule of the cell membrane. The tocopherol-anion is an electron donor and can stop the reaction cascade of the lipid oxidation by reduction to a radical product. After that the lipid radical was protonated and the vitamin E oxidized to a radical, followed be the recycling of vitamin E on the membrane surface with water soluble vitamin C (Scheme 57).

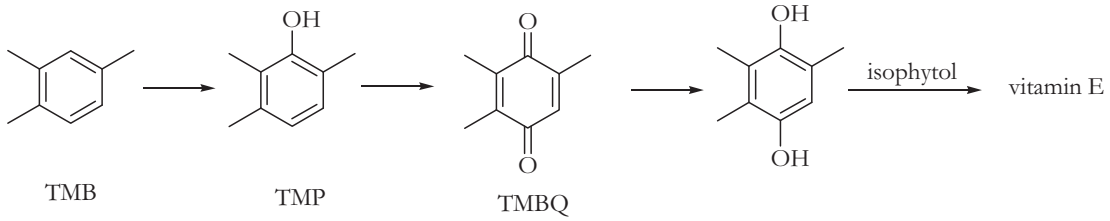


Scheme 57: Redox cycle of α-tocopherol and ascorbate.

Vitamin E possesses some anticoagulant activity to prevent the formation of blood clots. The natural form of vitamin E *D*-alpha tocopherol is highly superior to the synthetic form known as *DL*-α tocopherol. Only the natural *D*-α tocopherol is used in Vitamin E cream, which will be absorbed through the skin cells into the bloodstream, nourishing the skin inside and outside.[137]

1.9.2. State-of-the-art Synthesis

The well known reaction of α-tocopherol is shown in Scheme 58. The main key of this synthesis is the production of trimethylbenzoquinone (TMBQ). Thereby we focus on the synthesis of this compound. Two starting material are possible to obtain TMBQ in high yield. One is 1,3,4-trimethylbenzene (TMB) and the second is 2,3,6-trimethylphenol (TMP) (Scheme 58 & 59).

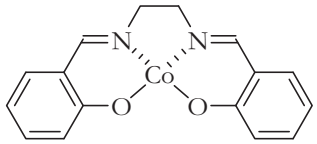


Scheme 58: Reaction of vitamin E.

To date several protocols have been established for the direct oxidation of TMP to TMBQ,[138] however only few of them are of industrial relevance.

In the technical process of TMP a $CuCl_2$-mediated oxidation with oxygen is used in the presence of lithium chloride. Applying a biphasic solvent of water and an aliphatic alcohol yields of up to 98% can be achieved.[139] Unfortunately, stoichiometric amounts of copper are applied under these conditions. This results in large amounts of copper waste and product contamination. Thus, the development of more environmentally friendly procedures for the oxidation of TMBQ is also of actual interest.

Regarding the direct oxidation of TMP to TMBQ the work of Schuster et al. is noteworthy. They reported that Salcomin (a salencobalt(II) complex) (Figure 13) catalyzed this oxidation under oxygen atmosphere to the corresponding quinone in 80–95% yield at 45 °C within 1h.[140]



Salcomin

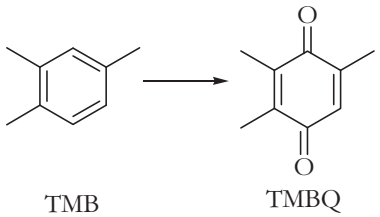
Figure 13: Salcomin catalyst for oxidation of TMP to TMBQ.

An industrial process developed by Shimizu et al. for this oxidation is performed in the presence of heteropolyacids. Apparently, the process is run in a two-phase solvent system of acetic acid and a non-polar solvent such as dichloromethane. As oxidizing agents both oxygen and hydrogen peroxide have been used. The yields for TMBQ achieved are in between 70% and 85%.[141] Another industrially applied method for the synthesis of TMBQ is based on the use of copper (II)-chloride. Attempts to reduce the stoichiometric amounts of copper salts, led to a catalyst system consisting of $CuCl_2$ (1.5 wt%) and hydroxylamine hydrochloride (2.8 wt%) as an additive. Reactions of TMP performed in acetic acid resulted in a yield of 80% of TMBQ. However, the disadvantage of this system is the use of *t*-BuOOH as a terminal oxidant. Conversion and yield of TMBQ using oxygen are low.[138d)] Already in 1983, the Ito group developed a Ru-catalyzed reaction of TMP in acetic acid as solvent.[138b)] In the presence of 1 mol% $RuCl_3$ and two equivalents H_2O_2 yields up to 90% of the desired quinine were achieved. Until to date this is still amongst the most effective catalytic processes; however there is no application in industry due to the high price of the catalyst. During the last years also a novel heterogeneous Ti(IV)/SiO_2-catalyst was developed by Kholdeeva et al.[138e)] Here, the oxidation of TMP with H_2O_2 in acetonitrile at 80 °C proceeded in yields up to 96%.[138f)]

In literature an iron catalyst system utilized tetrasulfonic phthalocyanine (FePcS) immobilized on silica (Figure 11) is also known for the synthesis of TMP to TMBQ.[142] Sorokin et al. reported that the FePcS's are bound together to form an active dimer. The reaction was run in acetonitrile using 4 mol% of the catalyst and *t*-BuOOH as oxidant providing quinones and TMBQ was obtained in yields up to 79%.

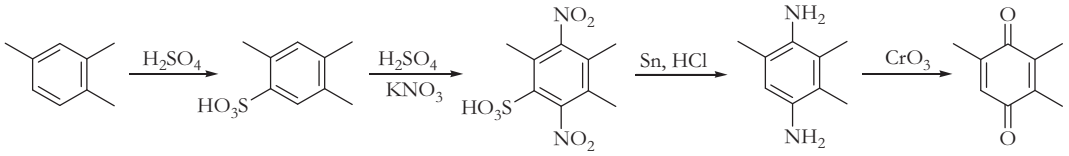
Most recently, we described an efficient oxidation of TMP using easily available iron complexes ($FeCl_3 \cdot 6H_2O/H_2Pydic/$*n*-butylbenzylamine) with hydrogen peroxide (30%) at 0 °C.[132] Applying an acetonitrile/water mixture the desired quinone is obtained in 89% yield. Closely related to the iron-catalyzed system an improved one phase system relying on a ruthenium(2,2',6':2''-terpyridine)(2,6-pyridinedicarboxylate) catalyst was developed.[80c)] With this catalyst system we obtained TMBQ in 83% yield after 1.5h.

An economically interesting alternative synthesis of TMBQ is based on the potential oxidation of 1,3,4-trimethylbenzene (TMB) (Scheme 59).



Scheme 59: Oxidation of TMB to TMBQ.

So far, this straightforward oxidation has been scarcely reported in the open literature. Although Scheme 60 a process for the conversion of TMB to TMBQ is shown that has been used even on industrial scale. Unfortunately, it needed several steps before the final quinone is generated (Scheme 60).



Scheme 60: Multistep synthesis of TMBQ from TMB.

Initially, TMB is sulfonated in the 5-position blocking it from the following nitration of the remaining aromatic positions. Subsequent reduction of the nitro groups and cleavage of the sulfonic acid are realized using stoichiometric amounts of tin in hydrochloric acid. Finally, oxidation by chromium (VI)-oxide gives the target compound resulting in an overall yield of 30%.[143] The disadvantages of this method is the four step linear synthesis as well as large amounts of waste including the highly toxic tin-and chromium compounds.

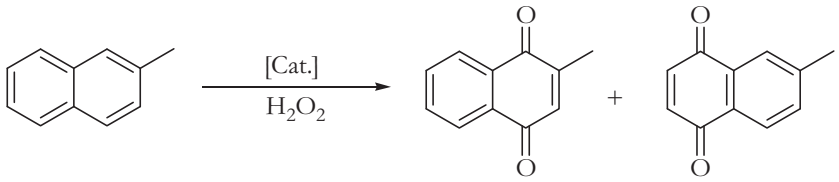
Obviously, the challenge for this substrate is the direct oxidation with benign oxidants. However, such processes have been described in literature only with moderate success, e.g. the oxidation of TMB by organic peracids in dichloromethane resulted in yields of up to 15%.[138a)] By-products in this reaction are 2,3,6-trimethylphenol and 2,4,5-trimethylphenol. Oxidation with H_2O_2 in formic acid was reported by Takehira et al. in 1989 and is more environmentally friendly; however the achieved yield is also low with 16%.[138c)] In general, these single-step procedures showed either low conversions and/or low selectivities to the desired product. Analogous to their MTO-catalyzed oxidation of 2-methylnaphthalene, Jacob et al. reported the reaction of TMB to TMBQ, too.[144] The reaction was run with 8 mol% MTO and a 20-fold excess of 30% H_2O_2. After 75% conversion a yield of 50% of TMBQ was obtained. In addition, the corresponding hydroquinone was generated with up to 25%.

Our group was also interested in this reaction. Thereby is possible to use the published iron system (*vide* supra) for the oxidation of TMP to TMBQ. We achieved the corresponding quinone in 69% conversion and 38% selectivity..

1.10 Conclusion

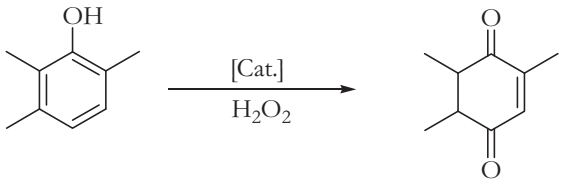
In summary, it has been demonstrated that quinones are versatile in occurs as well as applications. Therefore the development of isolation or rather syntheses of these compounds are important. Thereby the oxidation to vitamin K_3 and TMBQ a vitamin E precursor were our main focus in this dissertation (Scheme 61 and 62).

A drawback of most arene oxidations to quinones is the use of acidic solvents, *i.e.* acetic acid, or the necessity to add inorganic acid catalysts causing environmental pollution and carrying corrosion issues with it, especially on larger scale. In general, high concentrations of hydrogen peroxide (50-83%) are needed in order to achieve acceptable yields of menadione or TMBQ from its aromatic precursors.[127,145] Due to the explosive nature of highly concentrated hydrogen peroxide, especially in combination with metal salts, this may cause severe safety problems.[129] Thus, the development of more environmentally friendly procedures for the oxidation of these quinones is of actual interest.



Scheme 61: Oxidation of 2-methylnaphthalene to its corresponding quinones.

Recently it has been demonstrated that high activity and even excellent chemoselectivity can be achieved in Ru- and Fe-catalyzed oxidation of naphthalene derivatives and monohydroxylated arenes to the corresponding quinones with hydrogen peroxide.[80,132] The choice of catalyst was next to the oxidant the challenging goal for these oxidation reactions. Requirements for modern oxidation methods include cheap and selective catalysts, high atom efficiency, as well as environmentally friendly oxidants. On the basis of atom economy and environmental considerations, hydrogen peroxide and molecular oxygen, are the most desirable oxidants.



Scheme 62: Oxidation of TMP to TMBQ.

1.10 CONCLUSION

The ruthenium catalyzed process generated an environmentally benign method for the oxidation of 2-methylnaphthalene to vitamin K_3 in a one-phase system with a maximum yield of 62% and a ratio of 5:1 between the two regioisomers. Only 3.2 equivalents H_2O_2 and a low catalyst loading of 1 mol% are required. However the first iron-catalyzed oxidation of phenols and arenes to 1,4-quinones has been developed. Applying the inexpensive and practical catalyst system consisting of iron trichloride hexahydrate, pyridine-2,6-dicarboxylic acid, and benzylamine derivatives industrially important oxidations of TMP and 2-methylnaphthalene took place in 79% and 55% yield, respectively.

1.11 References

2. Objects of this work

3. Publication

3.1 A Novel Process for Selective Ruthenium-Catalyzed Oxidation of Naphthalenes and Phenols

3.2 An Environmentally Benign Synthesis of Quinones with an Iron Catalyst and Hydrogen Peroxide

3.3 Oxidation of 1,2,4-trimethylbenzene (TMB), 2,3,6-trimethylphenol (TMP) and 2-methylnaphthalene to 2,3,5-trimethylbenzoquinone (TMBQ) and menadione (vitamin K_3)

3.4 Selective Iron-catalyzed Oxidation of Benzylic and Allylic Alcohols

3.5 Pybox derived Schiff base adducts of MTO: asymmetric and symmetric reactions

3.6 2,6-Bis[(S)-4-benzyl-4,5-dihydro-1,3-oxazol-2-yl]pyridine

3.7 Enantioselective Zinc-catalyzed Hydrosilylation of Ketones using Pybox or Pybim Ligands

3.8 Zinc-Catalyzed Chemoselective Reduction of Esters to Alcohols

1.11 References

[1] K.P.C. Vollhardt, N.E. Schore *Organische Chemie* Ed. 4, Wiley-VCH, Weinheim, **2005**, 325-380.

[2] A. Wittcoff, B.G. Reuben, J.S. Plotkin *Industrial Organic Chemicals* Ed. 2, Wiley-Interscience, New Jersey **2004**.

[3] D.L. Miller *Biotechnology and bioengineering symposium* **1975** *5*, 345-352.

[4] a) H. Hock, S. Lang *Ber. Dtsch. Chem. Ges.* **1944**, B77, 257; b) W. Jordan, H. van Barneveld, O. Gerlich, M. K.-Boymann, J. Ullrich in *Ullmann's Encyclopedia of Industrial Organic Chemicals* Vol. A9, Wiley-VCH, Weinheim, **1985**, pp. 299-312.

[5] S. Mottram *Food Chemistry* **1998**, *62*, 4, 415-424.

[6] K.P.C. Vollhardt, N.E. Schore *Organische Chemie* Ed. 4, Wiley-VCH, Weinheim, **2005**, 857-914.

[7] a) N. Challand, X. Sava, M. Röper *WO/2008/116799* **2008**; b) H. Cheung, R. Tanke, G. P. Torrence in *Ullmann`s Encyclopedia of Industrial Chemistry*, Wiley-VCH, Weinheim **2005**, *1*, 24-25.

[8] R. Ditmar *Colloid & Polymer Science* **2008**, *3*, 2, 104.

[9] K.P.C. Vollhardt, N.E. Schore *Organische Chemie* Ed. 4, Wiley-VCH, Weinheim, **2005**, 967-1025.

[10] N.E. Leadbeater, R.J. Smith, T. M. Barnard, *Organic and Biomolecular Chem.* **2007**, *5*, 5, 822-825.

[11] a) M. Reid *J.Am. Chem. Soc.* **1931**, *53*, 1880-1881¸ b) R. Reid *J.Am. Chem. Soc.* **1937**, *59*, 402.

[12] H. Sies, L. Packer *Method Enzymol.* **2004**, 378, preface.

[13] H. Firouzabadi, N. Iranpoor, F. Kiaeezadeh,J. Toofan T*etrahedron* **1986**, *42,* 2, 719-726.

[14] L.F. Fieser *J.Am. Chem. Soc.* **1930**, *52*, 5204-5241.

[15] L.F. Fieser, M.A. Peters *J. Am. Chem. Soc.* **1931**, *53*, 793-805.

[16] L.F. Fieser, M.A. Peters *J. Am. Chem. Soc.* **1931**, *53*, 4080-4093.

[17] L.F. Fieser, M. Fieser *J. Am. Chem. Soc.* **1935**, *57*, 491-494.

[18] L.R. Philipps, J.E. Bartmess *Biomedical And Environmental Mass Spectrometry* **1989**, *18*, 878-883.

[19] P. Ballesteros, R.M. Claramunt, C. Escolbtico, M.D. Santa Maria *J. Org. Chem.* **1992**, *57*, 1873-1876.

[20] R. Ali, S.A. Sayeed *ACS Symposium Series* **1997**, *13*, 662, 223-244.

[21] G.R. von Kiparski, L.S. Lee, A.R. Gillespie *J. Environ. Qual.* **2007**, *36*, 709-717.

[22] W.U. Müller, E. Listner *Phytochemistry* **1976**, *15*, 407-410.

[23] S.A.R. Paiva, T.E. Sepe, S.L. Booth, M.E. Camilo, M.E. O'Brien, K.W. Davidson, J.A. Sadowski, R.M. Russell *Am J Clin Nutr* **1998**;*68,* 699-704.

[24] a) C.-Y Chang,. L.-J.Huang, J.-P. Wang, C.-M. Teng, S.-C. Chen, S.-C.Kuo *Chemical and Pharmaceutical Bulletin* **2000**, *48*, 7, 964-973 b) R. Eisler *Inflammation Research* **2003**, *52,* 12, 487-501; c) P.R. Dandawate, A.C. Vyas, S.B. Padhye, M.W. Singh, J.B. Baruah, *Mini reviews in medicinal chemistry* **2010**, *10*, 5, 436-454.

[25] Anon *Research and Development in Japan Awarded the Okochi Memorial Prize* **1982**, 89-92.

[26] T.S.S. Dikshith, Prakash V. Diwan *Industrial guide to chemical and drug safety*, Wiley-Interscience **2003**.

[27] D.E. Hofstra, J.S. Clayton *J. Aquat. Plant Manage.* **2001**, *39*, 20-24; b) S. Pekár *Anzeiger für Schadlingskunde* **2002**, *75*, 2, 51-55; c) X.-H. Su, M.-L. Zhang, W.-H. Zhan, C.-H. Huo, Q.-W. Shi, Y.-C. Gu, H. Kiyota Chemistry and Biodiversity **2009**, 6, 2, 146-161.

[28] M. Köhn, *Angewandte Chemie* **2006,** *39*, 1073–1074.

[29] H. Schildknecht *Angew. Chem* **1957**, *69*, 62-63.

[30] T. Eisner *J. Insect Physiol.* **1958***,2, 215-220.*

[31] T. Eisner, D.J. Aneshansley *Proc. Natl. Acad. Sci. USA* 96, **1999**, 9705–9709.

[32] R.H. Thomson *Naturally Occurring Quinones*, New York: Academic Press. **1971.**

[33] T. Eisner, D.J. Aneshansley, M. Eisner, A.B. Attygalle, D.W. Alsop, J. Meinwald *J. Exp. Biol.* **2000**, 203, 1265–1275.

[34] T. Eisner, T. Jones, D.J. Aneshansley, W. Tschinkel, R.E. Silberglied, J. Meinwald, *J. Insect. Physiol.* **1977**, 23, 1383-1386.

[35] H. Schildknecht, k. Holoubek *Angew. Chem* **1961,** *73*, 1-7.

[36] D.J. Aneshansley, T. Eisner, J.M. Widom, B. Widom *Science* **1969**, *165*, 61–63.

[37] a) H. Schildknecht, E. Maschwitz, U. Maschwitz *Naturforsch.* **1968**, *23b*, 1213–1218; b) Schildknecht, E. Maschwitz, U. Maschwitz *J. Insect Physiol.* **1970**, *16*, 749–789; c) J. Dean, D.J. Aneshansley, H.E. Edgerton,T. Eisner, *Science* **1990**, *248*, 1219–1221.

[38] T. Eisner, J. Dean *Proc. nat. Acad.* Sci. *U.S.A.* **1976**, 73, 1365-1367.

[39] Industrial routes: a) W.H. Shearon, L.G. Davy, H. von Bramer, *Ind. Eng. Chem.* **1952**, *44*, 1730; b) J. Varagnat, in *Kirk-Orhmer Encyclopedia of Chemical Technology*; Wiley: New York, **1981**; Vol. 13, p 39; c) H.H. Sunant *Organic Building Blocks of rhe Chemical Industry*; Wiley: New York, **1989**; Chapter 9.

[40] a) H.G. Franck, J.W. Stadelhofer, *Industrial Aromatic Chemistry*, Springer, New York, **1987**, pp. 146-183 b) J. Wallace in *Kirk-Othmer Encyclopedia of Chemical Technology*, Vol. 18 (Eds.: J. I. Kroschwitz, M. Howe-Grant), 4th ed., Wiley, New York, **1992**, pp. 592-602.

[41] O. Fukuda, S. Sakaguchi, Y. Ishii *Adv. Synth. Catal.* **2001**, *343*, 8, 809-813.

[42] M.O. Ratnikov, L.E. Farkas, E.C. McLaughlin, G. Chiou, H. Choi, S.H. El-Khalafy, M.P. Doyle *Journal of Organic Chemistry* **2001**, *76*, 8, 2585-2593.

[43] a) K.M. Draths, J.W. Frost *J. Am. Chem. Soc.* **1994**, *116*, 399-400; b) K.M. Draths, J.W. Frost *ACS Symp. Ser.* **1994**, *577*, 32-45; c) K.M. Draths, J.W. Frost *J. Am. Chem. Soc.* **1995**, *117*, 2395-2400; d) K. Li, J.W. Frost *J. Am. Chem. Soc.* **1998**, *120*, 10, 545-10546.

[44] J.M. Gibson, P.S. Thomas, J.D. Thomas, J.L. Barker, S.S. Chandran, M.K. Harrup, K.M. Draths, J.W. Frost *Angew. Chem. Int. Ed.* **2001**, *40*, 10, 1945-1948.

[45] A. Woskresensky *Justus Liebigs Ann. Chem.* **1838**, *27*, 257-270.

[46] K.M. Draths, T.L. Ward, J.W. Frost, *J. Am. Chem. Soc.* **1992**, *114*, 9726.

[47] N. Ran, D.R. Knop, K.M. Draths, J.W. Frost *J. Am. Chem. Soc.* **2001,** *123,* 10927-10934.

[48] C.A. Hansen, J.W. Frost *J. Am. Chem. Soc.* **2002**, 124, 5926-5927.

[49] a) R. Hill, F. Bendall, *Nature Lond.* **1960**, *186*, 136-137. b) A. Melis, *Phil. Trans. Soc. Lond. B* **1987**, *323*, 397-404.

[50] R.I. Cukier, D.G. Nocera *Annu. Rev. Phys. Chem.* **1998**. *49*, 337–369.

[51] V.P. Schinkarev, C.A. Wraight *Proc. Natl. Acad. Sci.* **1993**, *90*, 1834-1838.

[52] P. Adelroth, M.L. Paddock, L.B. Sagle, G. Feher, M.Y. Okamura *PNAS* **2000**, *97*, 24, 13086–13091.

[53] a) P. Mitchell, *J. Theor. Biol.* **1976**, *62*, 327-367; b) E.A. Berry, M. Guergova-Kuras, L.S. Huang, A.R. Crofts *Annu. Re*V. *Biochem.* **2000**, *69*, 1005-1075; c) A.R. Crofts, V.P. Shinkarev, D.R. Kolling, S. Hong *J. Biol. Chem.* **2003**, *278*, 36191-36201; d) D.L. Nelson, M.M. Cox, A.L. Lehninger, *Lehninger Principles of Biochemistry*, 4th ed.; W.H. Freeman: New York, **2005**; e) A.R. Crofts, J.T. Holland, D. Victoria, D.R. Kolling, S.A. Dikanov, R. Gilbreth, S. Lhee, R. Kuras, M.G. Kuras *Biochim. Biophys. Acta* **2008**, *1777*, 1001-1019;

[54] S. Hong, N. Ugulava, M. Guergova-Kuras, A.R. Crofts, *J. Biol. Chem.* **1999**, *274*, 33931-33944.

[55] C. Sasikala, C.V. Ramana *Appl. Microbiol.* **1995**, *41*, 173.

[56] Sigma Aldrich Mai 2011

[57] F.L. Crane, I. Hatefi, R.L. Lester, C. Widmer *Biochim. Biophys. Acta* **1957**, *25*, 220-221.

[58] K. Hamamura, I. Yamatsu, N. Miniami, Y. Yamagishi, Y. Inai, S. Kijima, T. Nakamura J Label *Radiopharm*. **2002**, *45*, 823-829.

[59] H. Fukawa, *Biomedical and Clinical Aspects of Coenzyme Q*, Eds. K. Folkers, Y. Yamaura, Elsevier, Amsterdam, **1984**, Vol. 4, p. 19.

[60] R. Rüegg, U. Gloor, R.N. Goel, G. Ryser, O. Wiss, O. Isler *Helv. Chim. Acta* **1959**, *42*, 2616-2621.

[61] H. Fukawa, M. Toyoda, H. Fukushima, T. Shimizu *US 3549668* **1970**.

[62] S. Kijima, I. Yamatu, K. Hamamura, N. Minami, Y. Yamagishi, Y. Inai *US3998858* **1976**.

[63] S. Kijima, I. Yamatsu, N. Minami, Y. Inai *US 4062879* **1977**.

[64] H. Eto, C. Eguchi *Chem. Lett.* **1988**, 1597-1600.

[65] F. Aquino, W. Bonrath, P. Bohrer, M. Hugentobler, T. Netscher, A. Radspieler *WO 2007/017168* **2007**.

[66] K. Sato, S. Inoue, R. Yamaguchi *J. Org. Chem.* **1972**, *37*, 12, 1889-1892.

[67] S. Inogue, R. Yamaguchi, K. Saito, K. Sato *Bull. Chem. Soc. Jpn.* **1974**, *47*, 3098.-8101.

[68] a)Y. Naruta *J. Org. Chem.* **1980**, *45*, 4097-4104; b)Y. Naruta, K. Maruyama *Chem. Lett.* **1979**, 885-888.

[69] E. Negishi, S.Y. Liou, C. Xu, S. Huo *Org. Lett.* **2002**, *4* (2), 261-264.

[70] B.H. Lipshutz, V. Berl, K. Schein, F. Wetterich *US 2005/0148675* **2005**.

[71] X.J. Yu, F.E. Chen, H.F. Dai, X.X. Chen, Y.Y. Kuang, B. Xie Helv. *Chim. Acta* **2005**, *88*, 2575-2581.

[72] Y. Fujita, T. Ohnishi, t. Nishida *US4270003* **1981**.

[73] A. Upare, N.Y. Pawar, G. Wagh, A. Chavan, M. Roy, H. Sivaramakrishnan *US 2008/0200732* **2008**.

[74] J.M. Campos-Martin, G. Blanco-Brieva, J.L.G. Fierro *Angew. Chem. Int. Ed.* **2006,** *45*, 6962-84.

[75] H.J. Riedl, G. Pfleiderer (I.G. Farbenindustrie AG.), *US2158525*, **1939** (*Chem. Abstr.* **1939**, *33*, 49337).

[76] G. Goor, W. Kunkel, O. Weiberg in *Ullmann´s Encyclopedia of Industrial Chemistry*. Vol. a13 (Eds. : B. Elvers, S. Hawkins, M. Ravenscroft, G. Schulz), VCH, Weinheim, **1989**, pp. 443-466.

[77] J.R. Kirchner in *Kirk-Othmer Encyclopedia of Chemical Technology*, Vol. 13 (Eds.: M. Grayson, D. Eckroth), 3rd ed., Wiley, New York, **1979**, pp. 12 -38.

[78] R. A. Sheldon, J.K. Kochi in *Metal-Catalyzed Oxidations of Organic Compounds*, Academic Press, New York, **1981**.

[79] H. Kotani, K. Ohkubo, S. Fukuzumi *J. Am. Chem. Soc.*, **2004**, *126*, 49, 15999-16006.

[80] a) F. Shi, M. K. Tse, M. Beller *Adv. Synth. Catal.* **2007**, *349*, 303-308; b) F. Shi, M. K. Tse, M. Beller *J. Mol. Catal. A: Chem.* **2007**, *270*, 68-75; c) G. Wienhöfer, K. Schröder, K. Möller, K. Junge, M. Beller Adv. Synth. Catal. **2010**, 352, 1615- 1620.

[81] W.A. Pryor, G.J. Gleicher, D.F. Church *J. Org. Chem.* **1983**, *48*, 4198-4202.

[82] T. Yamato, N. Shinoda, T. Kanakogi *J. Chem. Res.,Synopses* **2000**, *11*, 522-523.

[83] A.D. Claus *Chem. Ber.* **1877**, *10*, 926.

[84] S.G. Miller, M.A. Edward *US2496894* **1947**.

[85] H. Kaper, M. Antonietti, F. Goettmann *Tetrahedron Let.* **2008**, *49*, 29-30, 4546-4549.

[86] a) A.O. Brachmann, S. Forst, G.M. Furgani, A. Fodor, H.B. Bode, *J. Nat. Prod.* **2006**, *69*, 1830-1832; b) A.O. Brachmann, S.A. Joyce, H. Jenke-Kodama, G. Schwär, D.J. Clarke, H.B. Bode *Chem. Bio. Chem.* **2007**, *8*, 1721-1728.

[87] G. Bringmann, T.A.. Gulder, A. Hamm, M. Goodfellow H.P. Fiedler *Chem. Commun*. **2009**, 6810-6812.

[88] a) C. Hertweck *Angew. Chem. Int. Ed.* **2009**, *48*, 4688–4716.; b) J. Staunton, K.J. Weissman *Nat. Prod. Rep.* **2001**, *18*, 380–416.

[89] B.J. McConkey, C.L. Duxbury, D.G. Dixon, B.M. Greenberg. *Environ Toxicol Chem* **1997**, *16*, 892–899.

[90] W. Wang, J. Nykamp, X.-D. Huang, K. Gerhardt, D.G. Dixon, B.M. Greenberg *Environmental Toxicology and Chemistry* **2009**, *28*, 8, 1655-1662.

[91] a) A.J. Lin, L.A. Cosby, C.W. Shansky, A.C. Sartorelli *J Med Chem* **1972**, *15*, 1247-1252; b) R.J. Abdella, J. Fisher *Environ Health Prespec.* **1985**, *64*, 3-18; c)I. Wilson, P. Wardman, T.S. Lin, A.C. Sartorelli *J Med Chem* **1986**. *29*, 1381-1384.

[92] S. Sato, M. Iwaizumi, K. Handa, Y. Tamura *Gann* **1977**, *68*, 603-608; b) N.R. Bachur, S. L. Gordon, M.V. Gee *Cancer Res* **1978**, *38*, 1745-1750.

[93] S. Tani,, Y. Yonezawa, S. Morisawa, H. Nishioka *Mutation Research* **2007**, *628*, 123-128.

[94] P.L. Gutierrez *Frontiers in Bioscience* **2000**, *5*, 629-638.

[95] J.F. Hull, E.L.O. Sauer, G.W. Brudvig, R.H. Crabtree, D. Balcells, C. Raynaud, O. Eisenstein *J.Am. Chem. Soc.* **2010**, *132*, 22,7605-7616.

[96] F.B Mallory,C.W. Mallory, "Photocyclization of Stilbenes and Related Molecules" John Willey& Sons, NY,1984,1456. 10- Liu, L., Yang, B., Katz TJ., Poindexter, M.K., *1 Org.* Chem.**1991**,56,3769.

[97] J.B. de Vries, S.A. Hubbard *J. Am. Soc. Chem. Comun.* **1988**, 1172.

[98] D.M. Togashi, D.E. Nicodem, R. Marchiori, M.L.P. de F.C. Marchiori *Synthetic Communications* **1998**, 28, 6, 1051-1063.

[99] J. Kou, H. Zhang, Y. Yuan, Z. Li, Y. Wang, T. Yu, Z. Zou *J. Phys. Chem. C* **2008,** *112,* 4291-4296.

[100] J. Kou, H. Zhang, Y. Yuan, Z. Li, Y. Wang, T. Yu, Z. Zou *J. Phys. Chem. C* **2008**, *112*, 4291-4296.

[101] H.F. Lin, K.T. Valsaraj *J Hazardous Materials* **2003**, *99,* 203-219.

[102] S. Higashida, A. Harada, R. Kawakatsu, N. Fujiwaraa, M. Matsumura *Chem. Commun*, **2006**, 2804-2806.

[103] L. Liu, J.H. Kou, D.M. Guo, J. Yang, H.L. Liu, H.X. Yu, S. Chu, K.R. Jiang, Y. Wang, Z.G. Zou *Chinese Chem. Lett.* **2009**, *20*, 1366–1370.

[104] M.C. Carreño, J.L.G. Ruano, A. Urbano *Tetrahedron Letters* **1989**, *30*, 30, 4003-4006.

[105] K. Itami, T. Nokami, J. Yoshida *Adv. Synth. Catal.* **2002**, *344*, 3+4, 441-451.

[106] S. Witayakran, A. Zettilib, A. J. Ragauskas *Tetrahedron Letters* **2007**, *48*, 2983–2987.

[107] a) C.F. Thurston *Microbiology* **1994**, *140*, 19-26; b) A.I. Yaropolov, O.V. Skorobogat'ko, S.S. Vartanov, S.D. Varfolomeyev *Appl. Biochem. Biotechnol.* **1994**, *49*, 257-280.

[108] C.-Y. Song, L.-C. Wang, J.-H. Zhao, F.-A. Wang, *Xiandai Huagong/Modern Chemical Industry* **2007**, *27,* 11, 27-30.

[109] a) H.M. Becher *WO 92/06944* **1992**; b) S. Harrison *EP 0919533* **1999**; c) K. Deleersnyder, S. Schaltin, J. Fransaer, K. Binnemans, T.N. Parac-Vogt *Tetrahedron Letters* 2009, *50*, 4582-4586.

[110] a) H.R. El-Seedi, S. Yamamura, S. Nishiyama *Tetrahedron Letters* 2002, *43*, 3301-3304; b) H.R. El-Seedi, S. Yamamura, S. Nishiyama *Tetrahedron* 2002, *58*, 7485-7489.

[111] J.P. Eder *Integrated Pharmacology* (2nd). C. Page, M. Curtis, M. Sutter, M. Walker, B. Hoffmann, (eds.) Mosby, New York, **2002,** 163-187.

[112] a) J.W. Suttie in: *Handbook of Vitamins*, (Eds.: R.B. Rucker, J.W. Suttie, D.B. McCormick, L.J. Machlin), 3rd edn., M. Dekker, New York, **2001**, 115-164 b) D.W. Stafford, J. Thromb *Haemostasis* **2005**, *3*, 1873-1878.

[113] a) K.N. Prasad, J. Edwards-Prasad,.A. Sakamoto *Life Sci.* **1981**, *29*, 1387-1392; b) V. Noto, H.S. Taper, Y.H. Jiang, J. Janssens, J. Bonte, W. de Loecker *Cancer* **1989***, 63*, 901-906; c) R.T. Chlebowski,, J.B. Block, S. Akman, M. Dietrich *Cancer Treat. Rep.* **1985**, *69*, 527-532; d) L.M. Nutter, A.L. Cheng, H.L. Hing, R.K. Hsieh, E.O. Ngo, T.W. Liu *Biochem. Pharmacol.* **1991**, *41*, 1283-1292; e) F.Y. Wu, H.M. Chang, W.C. Liao, *LifeSci* **1993**,. *52*, 1797-1804; f) Y. Nishikawa, B.I. Carr, M. Wang, S. Kar, F. Finn, P. Dowd, Z.B. Zheng, J. Kerns, S. Naganathan, S. *J. Biol. Chem.* **1995**, *270*, 28304-28310; g) W.C. Liao, F.Y. Wu, C.W. Wu *Int. J. Oncol.* **2000**, *17*, 323-328; h) H. Okayasu, M. Ishihara, K. Satoh, H. Sakagami *Anticancer Res.* **2001**, *21, 2387-*2392;. i) S. Osada, S. Saji, K. Osada *Cancer* **2001**, *91*, 1156-1165.

[114] a) W.F. Tzeng, T.J. Chiou, J.Y. Huang, Y.H. Chen *Proc. Natl. Sci. Counc. Repub. China* **1992**, *16*,: 84-90; b) B.I. Carr, Z. Wang, S. Kar *J. Cell Physiol* **2002**., *193*, 263-27.

[115] a) Y. Sun, L.W. Oberley, J.H. Elwell, E. Sierra-Rivera *Int. J. Cancer* **1989**, *44*,1028-1033; b) T.D. Oberley, L.W. Oberley *Histol. Histopathol* **1997**, *12*, 525–535; c) J. Yang, E.W. Lam, H.M. Hammad, T.D. Oberley, L.W. Oberley *J. Oral Pathol. Med.*. **2002**, *31*, 71-77.

[116] B. Tareen, J.L. Summers, J.M. Jamison, D.R. Neal, K.McGuire, L. Gerson, A. Diokno *Int. J. Med. Sci.* **2008**, *5*, 62-67.

[117] a) J. Verrax, J. Cadrobbi, M. Delvaux, J.M. Jamison, J. Gilloteaux , J.L. Summers *Eur. J. Med. Chem.* **2003**, *38*, 451–457; b) J. Verrax, M. Delvaux, N. Beghein, H. Taper, B. Gallez, P. Buc Calderon *Free Rad. Res.* **2005**, *39*, 649–657.

[118] a) V. Noto, H.S. Taper, Y.H. Jiang, J. Janssens, J. Bonte, D. Loecker *Cancer* **1989**, *63*, 901–906; b) M. Venugopal, J.M. Jamison, J. Gilloteaux, J.A. Koch, M. Summers, D. Giammar *Life Sci.* **1996**, *59*, 1389-1400; c) P. Buc Calderon, J. Cadrobbi, C. Marques, N. Hong-Ngoc, J.M. Jamison, J. Gilloteaux *Curr. Med. Chem.* **2002**, *9*, 2271-2285.

[119] R.A. Sheldon *Top. Curr. Chem.* **1993**, *164*, 21-43.

[120] R.T. Arnold, R. Larson *J. Org. Chem.* **1940**, *5*, 250-252.

[121] J. Sugano, Y. Kuriyama, Y. Ishiuchi, Y. Minamikawa, M. Yokkaichi *DE 2341468* **1973**.

[122] a) S. Yamaguchi, M. Inoue, S. Enomoto *Chem. Lett.* **1985**, *14*, 827-828; b) S. Yamaguchi, M. Inoue, S. Enomoto *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2881-2884.

[123] S. Yamaguchi, H. Shinoda, M. Inoue, S. Enomoto, *Chem. Pharm. Bull.* **1986** *34*, 376, 4467-4473.

[124] a) W. Adam, W.A. Herrmann, J. Lin, C.R. Saha-Möller, R.W. Fischer, J.D.G. Correira *Angew. Chem.* **1994**, *106*, 2545-2546; b) W.A. Herrmann, R.W. Fischer, W. Adam, J. Lin, C.R. Saha-Möller, M. Shimizu *Eur. Pat. 0665209* **1995**.

[125] F.E. Kühn, A. Scherbaum, W.A. Herrmann *J. Organomet. Chem.* **2004**, *689*, 4149-4164.

[126] S. Yamazaki *Bull. Chem. Soc. Jpn.* **1997**, *70*, 877-883.

[127] W.A. Herrmann, J.J. Haider, R.W. Fischer *J. Mol. Cat. A: Chem.* **1999**, *138*, 115-121.

[128] T. Takai, E. Hata, T. Mukaiyama *Chem. Lett.* **1994**, *23*, 885-888.

[129] a) W. Thiel, Y. Sun, A. Schubert, A. Bohle *WO 123644* **2005**; b) A. Bohle, A. Schubert, Y. Sun, W.R. Thiel *Adv. Synth. Catal.* **2006**, *348*, 1011-1015.

[130] R. Song, A. Sorokin, J. Bernadou, B. Meunier *J. Org. Chem.* **1997**, *62*, 673-678.

[131] A.B. Sorokin, S. Mangematin, C. Pergrale *J. Mol.Cat.* **2002**, *182-183*, 267-281.

[132] K. Möller, G. Wienhöfer, K. Schröder, B. Join, K. Junge, M. Beller *Chem Eur. J.* **2010**, *16*, 10300-10303.

[133] a) W.H. Sebrell, R.S. Harris, (Eds.), *The vitamins*, 2nd edn., Academic Press, New York, **1972**, Vol. 5, Chapter 16, pp 166-317; a) G. Burton, K.U. Ingold, *Acc. Chem. Res.* **1986**, *19*, 194-201.

[134] For some reports on the antioxidant activity of Tocopherols see: a) G.W. Burton, K.U. Ingold *J. Am. Chem. Soc.* **1981**, *103*, 6472-6477; b) R. Reinton, A. Rogstad *J. Food Science* **1981**, *46*, 970-971, 973; c) M. Baldioli, M. Servili, G. Perretti, G.F. Montedoro *J. Am. Oil Chem. Soc.* **1996**, *73*, 1589-1593; d) X. Zhimin; N. Hua, S.J. Godber, J. Agric. *Food Chem.* **2001**, *49*, 2077-2081; e) J.M. Zingg, A. Azzi *NATO Science Series, Series I: Life and Behavioural Sciences* **2005**, *367* (Free Radicals and Diseases: Gene Expression, Cellular Metabolism and Pathophysiology), 113-136.

[135] a) B. Kupczyk, M. Gogolewski *Food Science Techn.* **2001**, *5*, 21-29; b) J.M Zingg, A. Azzi, *Current Medicinal Chemistry* **2004**, *11*, 1113-1133; c) M.C. Morris, A.D. Evans, C.C. Tangney, J.L. Bienias, R.S. Wilson, N.T. Aggarwal, P.A. Scherr *Am. J. Clinical Nutrition* **2005**, *81*, 508-514; d) B. Zhou, Z.L. Zhong-Li *Pure and Applied Chem.* **2005**, *77*, 1887-1903; e) H. Mahamongkol, R.A. Bellantone, G. Stagni, F.M. Plakogiannis *J. Cosmetic Science* **2005**, *56*, 91-103.

[136] a) C.K. Chow in *Handbook of Vitamins*, 3rd ed. (Eds.: R.B. Rucker, J.W. Suttie, D.B. McCormick, L.J. Machlin), M. Dekker, New York, **2001**, pp. 165 -198; for recent syntheses, see: b) L.F. Tietze, K.M. Sommer, J. Zinngrebe, F. Stecker *Angew. Chem.* **2004**, *116*, 262-264; *Angew. Chem. Int. Ed.* **2005**, *44*, 257-259; c) G. Malais, W. Bonrath, M. Breuninger, T. Netscher *Helv. Chim. Acta* **2006**, *89*, 797-812; d) S. Bell, B.W. Stenberg, S. Kaiser, F. Menges, T. Netscher, A. Pfaltz *Science* **2006**, *311*, 642-644; e) T. Netscher, G. Malais, W. Bonrath, M. Breuninger *Catal. Today* **2007**, *121*, 71-75; f) G. Hernandez-Torres, A. Urbano, M. Carmen Carreo, F. Colobert *Org. Lett.* **2009**, *11*, 4930-4933.

[137] R. Saladino, V. Neri, A. Farina, C. Crestini, L. Nencioni, A.T. Palamara *Adv. Synth. Catal.*. **2008**, *350*, 321-331.

[138] a) R.D. Chambers, P. Goggin, W.K.R. Musgrave *J. Chem. Soc.* **1959**, 1804-1807; b) S. Ito, K. Aihara, M. Matsumoto *Tetrahedron Lett.* **1983**, *24*, 5249-5252; c) H. Orita, M. Zu, T. Hayakawa, K. Takehira *Bull. Chem. Soc. Jpn.* **1989**, *62*, 1652-1657; d) Z. Bodnar, T. Mallat, A. Braiker *J. Mol. Catal. A* **1996,** *110*, 55-63; e) O.A. Kholdeeva, N.N. Trukhan, M.P. Vanina, V.N. Romannikov, V.N. Parmon, J. Mrowiec-Białon´, A.B. Jarzebski *Catal. Today* **2002,** *75*, 203-209; f) O.A. Kholdeeva, I.D. Ivanchikova, M. Guidotti, N. Ravasio *Green Chem.* **2007**, *9*, 731-733.

[139] a) T. Isshiki, T. Yui, H. Uno, M. Abe *Eur. Pat. 0127888* **1984**; b) R. Maasen, S. Krill, K. Huthmacher *Eur. Pat. 1132367* **2001**.

[140] L. Schuster, H. Pommer *DE 1793183* **1968**.

[141] a) M. Shimizu, K. Takehira, T. Hayakawa, H. Orita, *US 5245059* **1993**; b) M. Vandewalle *WO 18746* **1998**.

[142] A.B. Sorokin, S. Mangematin, C. Pergrale *J. Mol.Cat.* **2002**, *182-183*, 267-281.

[143] A. Pongratz, K.L. Zirm *Monatsheft Chemie* **1952**, *83,* 13-17.

[144] J. Jacob, J.H. Espenson *Inorg. Chim. Acta* **1998**, *270*, 55-59.

[145] W. Adam, W.A. Herrmann, J. Lin, C.R. Sahamöller, R.W. Fischer, J.D.G. Correia, Angew. Chem. Int. Ed. Eng. 33 (1994) 2475-2477.

Object of this work

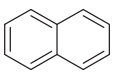
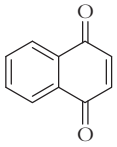
2. Objects of this work

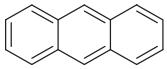
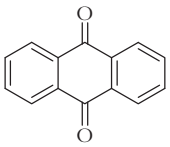
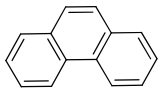
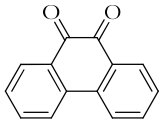
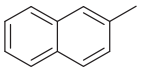
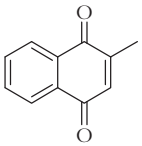
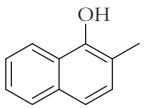
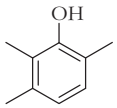
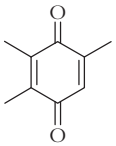
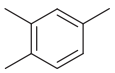
There is a continuing interest in the development of improved methods for the synthesis of quinones, owing to their importance in nature, agriculture, medicine and industry. Therefore the development of novel and improved methods for their synthesis is important. Our group has a significant experience on the use of homogenous catalysts for various oxidation reactions, which provided the basis for the present work.

The starting point of this thesis constituted the use of the known ruthenium (2,2',6':2''-terpyridine)(2,6-pyridinedicarboxylate) catalyst (chapter 3.1, publication *Adv. Synth.Catal.* **2010**) in the oxidation of naphthalene derivatives and monohydroxylated arenes to give the corresponding quinones. Herein, we developed an environmentally benign method for the oxidation of arenes to the corresponding quinones, e.g. 2-methylnaphthalene to vitamin K_3 or TMP to TMBQ, in a one-phase system. Based on former experiments,[80a)-b)] it was possible to improve yields and regioselectivity by using only 3.2 equivalents H_2O_2 and a low catalyst loading of 1 mol%.

Based on these promising results and our experience in iron-catalyzed oxidations, we were intrigued if an iron catalyst is also feasible for this transformation. Obviously, such iron-catalysts are desirable due to their lower toxicity and common availability. Indeed, we succeeded in the first iron-catalyzed oxidation of phenols and arenes to 1,4-quinones under mild conditions (chapter 3.2, publication *Chem. Eur. J.* **2010**). Our studies showed that an in situ generated iron complex ($FeCl_3 \cdot 6H_2O/H_2Pydic$/benzylamine) is a viable catalyst to perform this reaction efficiently using hydrogen peroxide as a terminal oxidant. The newly developed catalyst is able to fully convert naphthalene derivatives and monohydroxylated arenes to the desired products in high yields and selectivities. Table 3 gives an overview of selected oxidation results applying either the ruthenium or the iron catalyst system.

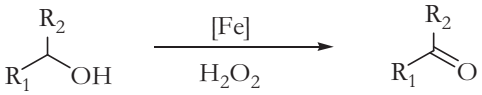
Table 3: Selected results in arene hydroxylation from our group.

Substrate	Product	Ru-system	Fe-system
		>99% conv. 63% select.	-

Substrate	Product	Ru-system	Fe-system
		>99% conv. 39% select.	-
		>99% conv. 34% select.	-
		>99% conv. 62% select.	>99% conv. 55% select.
		>99% conv. 78% select.	>99% conv. 55% select
		>99% conv. 83% select.	>99% conv. 79% select
		-	>99% conv. 38% select

Most recently, we published a detailed study and an overview of recent quinone synthesis, including the synthesis of vitamin K_3 and TMBQ, which is shown in chapter 3.3, publication *Catal. Today* **2011**. Thereby we focused on the use of environmental friendly oxidants like molecular oxygen or hydrogen peroxide.

Based on our iron catalyzed oxidation to quinones we developed also the oxidation of alcohols to aldehydes as well as ketones in the presence of iron complexes (chapter 3.4, publication *Adv. Synth. Catal.* **2011**) (Scheme 63). Based on our experience in iron catalyzed oxidations of arenes[132] and epoxidation we were asked ourselves if these systems would be feasible for alcohol oxidations, too.



Scheme 63: Oxidation of an alcohol to the corresponding aldehyde or ketone.

While for arene oxidations H_2Pydic turned out to be a suitable ligand, for epoxidation imidazole ligands were useful. For the first time we combined the two ligand systems and created a novel iron-catalyst ($FeCl_2$/L/Na_2CO_3) (Figure 14).

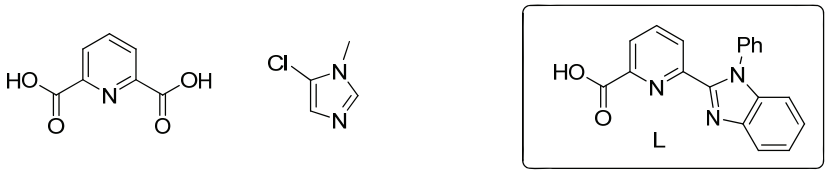
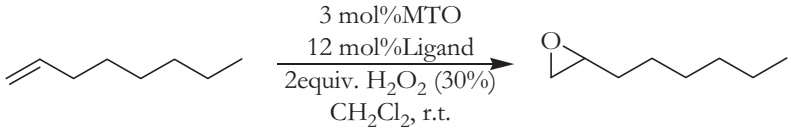


Figure 14: Ligands for arene oxidation, epoxidation and alcohol oxidation.

More specifically, we reported a novel iron-catalyzed oxidation of benzylic and allylic alcohols using hydrogen peroxide as oxidant under air and mild conditions. The developed method is applicable to a broad range of substrates. Good to excellent chemoselectivity for the oxo-product is demonstrated using substituted benzyl alcohols as well as sensitive substrates like terpenoidal alcohols. The various products have been synthesised in 48-95% yields and 58-99% selectivity. Mechanistic investigations (X-Ray analysis and ESI-MS measurements) have also been performed.

Next, we were also interested in non-chiral and and asymmetric epoxidations. In this respect, we developed a methyltrioxorhenium (MTO)-catalyzed epoxidation of olefins with hydrogen peroxide as the oxidant in the presence of non-chiral or chiral ligands (chapter 3.5, publication *J. Organom. Catal.* **2011**). Initially, we studied the epoxidation of 1-octene with chiral (oxazoline and pybox) and non-chiral ligands, which proceeded with excellent chemoselectivities (>90%) (Scheme 64).

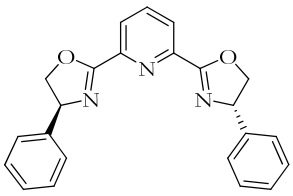
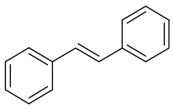
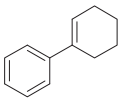
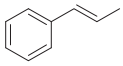
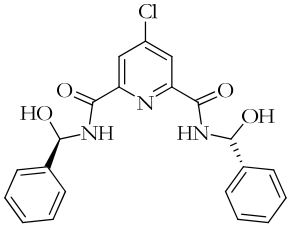
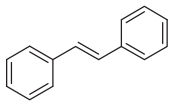
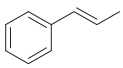


Scheme 64: Oxidation of 1-octene.

Depending on the ligand the activity of the catalyst was not influenced or inhibited or at best increased. By NMR measurements the reactivity of different oxazoline and pybox ligands could be explained. For example, electronic properties of the ligands determine the activity in the MTO-catalyzed epoxidation of olefins while steric factors have a negligible influence. In addition, the asymmetric oxidation of olefins with MTO and chiral ligands was investigated. This problem constitutes a long standing goal in asymmetric oxidations.

We achieved excellent chemoselectivities and up to 19% *ee* with several pybox ligands or its precursor (Table 4).

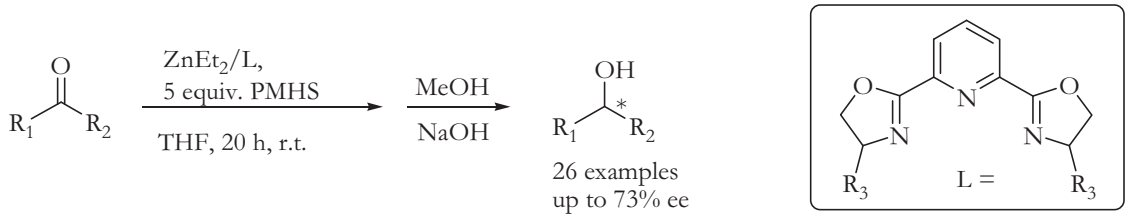
Table 4: Selected results in olefin oxidation with chiral ligands.

Ligand	Olefin	Conv. [%]	Select [%]	*ee* [%]
		86	100	18
		53	100	11
		81	92	11
		100	100	18
		100	88	11

Furthermore we succeeded in a novel X-Ray structure of one of the pybox ligands (chapter 3.6, publication *Acta. Cryst. E* **2011**) illustrating the spatial arrangement of this compound.

Parallel to the work on catalytic oxidations, also catalytic reduction reactions like hydrosilylation of carbonyl compounds in the presence of zinc catalysts were studied. Due to its abundant availability, low toxicity and biomimetic nature zinc proves to be a highly attractive candidate for catalysis. On one side we were interested in the asymmetric transformation of ketones to secondary alcohols by using pybox ligands (chapter 3.7, publication *Chem. Asien J.* **2011**) and on the other side on the chemoselective reduction of esters to alcohols (*Chem Eur. J.* **2011**).

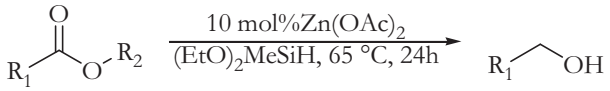
The asymmetric reaction of ketones to secondary alcohols represents an efficient approach for the preparation of chiral alcohols which are used as versatile building blocks for pharmaceuticals, agrochemicals, flavours and fragrances. We developed a simple in situ catalyst composed of $ZnEt_2$, commercially available pybox ligands and inexpensive polymethylhydrosiloxane (PMHS) as reductant (Scheme 65).



Scheme 65: Reduction of ketones to second chiral alcohols.

Enantioselective zinc-catalysed asymmetric hydrosilylations of carbonyl compounds were achieved under mild conditions with high yields and good enantioselectivities for a broad range of aryl alkyl, cyclic, heterocyclic and aliphatic ketones. In addition ESI measurements have been performed to characterize the active catalyst.

Furthermore, a general and chemoselective catalytic reduction of esters to alcohols using inexpensive zinc acetate and $(EtO)_2MeSiH$ has been developed. A variety of esters, including aromatic, aliphatic, heteroaromatic, and heterocyclic esters were reduced smoothly to the corresponding alcohols (Scheme 66).



R_1=Aryl, R_2= Alkyl

Scheme 66: Reduction of ester to alcohol.

After demonstrating the general applicability, we were interested in the functional group tolerance of our catalytic system. Hence, we studied the reactivity of more challenging substrates that might undergo additional reductive transformations. Such chemoselective reductions of esters are particularly interesting for the organic synthesis of multifunctional molecules. The operational simplicity and the high functional group tolerance, without the need for protecting and deprotecting steps, make this procedure particularly attractive for organic synthesis

.

Publication

3. Publication

3.1 A Novel Process for Selective Ruthenium-Catalyzed Oxidation of Naphthalenes and Phenols

Gerrit Wienhöfer, Kristin Schröder, Konstanze Möller, Kathrin Junge,
and Matthias Beller

Adv. Synth. Catal. **2010**, *352*, 1615-1620.

In this paper, I contributed to a significant amount of the argumentation and discussions to the design of several experiments and to the preparation of the manuscript. I was involved in the characterization of the active ruthenium H_2pydic terpyridine catalyst and performed all reproducibility experiments. My contribution as co-author of this paper is approximately 20%.

3.2 An Environmentally Benign Synthesis of Quinones with an Iron Catalyst and Hydrogen Peroxide

Konstanze Möller, Gerrit Wienhöfer, Kristin Schröder, Benoît Join, Kathrin Junge and Matthias Beller

Chem. Eur. J. **2010**, *16*, 10300-10303.

(VIP, cover picture)

In this paper, I contributed to a significant amount of the argumentation and the synthetic work. I developed and performed most of the catalytic reactions and wrote the manuscript. I also designed the cover picture. My contribution as co-author of this paper is approximately 80%.

3.3 Oxidation of 1,2,4-trimethylbenzene (TMB), 2,3,6-trimethylphenol (TMP) and 2-methylnaphthalene to 2,3,5-trimethylbenzoquinone (TMBQ) and menadione (vitamin K_3)

Konstanze Möller, Gerrit Wienhöfer, Felix Westerhaus, Kathrin Junge, Matthias Beller

Catalysis Today **2011**, *173*, 68-75.

This publication is based on my oral presentation during the *9th Congress on Catalysis Applied to Fine Chemicals*, Zaragoza (Spain), 13.-16. September 2010. In this paper, I did almost the literature research and I wrote the manuscript. My contribution as co-author of this paper is approximately 90%.

3.4 Selective Iron-catalyzed Oxidation of Benzylic and Allylic Alcohols

Benoît Join, Konstanze Möller, Carolin Ziebart, Kristin Schröder, Anke Spannenberg, Kathrin Junge and Matthias Beller

Adv. Synth. Catal. **2011**, *353*, 3023-3030.

In this paper, I contributed to a significant amount of the argumentation and the synthetic work. I performed all experiments including catalytic and mechanistic experiments, especially the X-Ray structure. My contribution as co-author of this paper is approximately 40%.

3.5 Pybox derived Schiff base adducts of MTO: asymmetric and symmetric reactions

Konstanze Möller, Yuehui Li, Kathrin Junge, Normen Szesni, Richard Fischer, Fritz E. Kühn and Matthias Beller

J. Organomet. Chem. **2011,** submitted.

In this paper, I performed all experiments and I wrote the manuscript draft. My contribution as co-author of this paper is approximately 85%.

3.6 2,6-Bis[(S)-4-benzyl-4,5-dihydro-1,3-oxazol-2-yl]pyridine

Konstanze Möller, Kathrin Junge, Anke Spannenberg and Matthias Beller

Acta Cryst. **2011**,. *E67*, o1181.

In this paper, I performed all experiments and I wrote the manuscript draft. My contribution as co-author of this paper is approximately 90%.

3.7 Enantioselective Zinc-catalyzed Hydrosilylation of Ketones using Pybox or Pybim Ligands

Kathrin Junge, Konstanze Möller, Bianca Wendt, Shoubhik Das, Dirk Gördes, Kerstin Thurow, and Matthias Beller

Chem. Asien J. **2011,** accepted.

In this paper, I contributed to a significant amount of the argumentation and the synthetic work. I performed all mechanistic experiments. My contribution as co-author of this paper is approximately 50%.

3.8 Zinc-Catalyzed Chemoselective Reduction of Esters to Alcohols

Shoubhik Das, Konstanze Möller, Kathrin Junge, and Matthias Beller

Chem. Eur. J. **2011**, *17*, 7414-7417.

In this paper, I contributed to a significant amount of the argumentation and the synthetic work. My contribution as co-author of this paper is approximately 50%.

Eidesstattliche Erklärung

Ich versichere hiermit an Eides statt, dass ich die vorliegende Arbeit selbstständig angefertigt und ohne fremde Hilfe verfasst habe, keine außer den von mir angegebenen Hilfsmitteln und Quellen dazu verwendet habe und die den benutzten Werken inhaltlich und wörtlich entnommenen Stellen als solche kenntlich gemacht habe.

Rostock, den 2011

Konstanze Kiersch

Scientific Work

Publications

1) *"Selective Iron-catalyzed Oxidation of Phenols and Arenes with Hydrogen Peroxide: Synthesis of Vitamin E intermediates and Vitamin K_3 "*
K. Möller, G. Wienhöfer, K. Schröder, B. Join, K. Junge and M. Beller, *Chem Eur. J.* **2010**, *16*, 10300-10303.

selected as Very Important Paper
selected as Cover Picture

2) *"A Novel Process for Selective Ruthenium-catalyzed Oxidation of Naphthalenes and Phenols"*
G. Wienhöfer, K. Schröder, K. Möller, K. Junge and M. Beller, *Adv. Synth. Catal.* **2010**, *352*, 1615-1620.

3) *"Zinc-Catalyzed Chemoselective Reduction of Esters to Alcohols"*
S. Das, K. Möller, K. Junge and M. Beller *Chem. Eur. J.* **2011**, *17*, 7414-7417.

4) *"2,6-Bis[(S)-4-benzyl-4,5-dihydro-1,3-oxazol-2-yl]pyridine"*
K. Möller, K. Junge, A. Spannenberg and M. Beller *Acta Cryst.* **2011**,. *E67*, o1181.

5) *" Oxidation of 1,2,4-trimethylbenzene (TMB), 2,3,6-trimethylphenol (TMP) and 2-methylnaphthalene to 2,3,5-trimethylbenzoquinone (TMBQ) and menadione (vitamin K_3)"*
K. Möller, G. Wienhöfer, F. Westerhaus, K. Junge and M. Beller, *Catal. Today* **2011**, in press.

6) *"Selective Iron-catalyzed Oxidation of Benzylic and Allylic Alcohols"*
B. Join, K. Möller, C. Ziebert, K. Schröder, D. Gördes, K. Thurow, A. Spannenberg, K. Junge and M. Beller, *Adv. Synth. Catal.* **2011,** accepted.

7) " Pybox *derived Schiff base adducts of MTO: asymmetric and symmetric reactions"*
K. Möller, Y. Li, K. Junge, N. Szesni, R. Fischer, F. E. Kühn and M. Beller, *J. Organomet. Chem.* **2011**, submitted.

8) *"Enantioselective Zinc-catalyzed Hydrosilylation of Ketones using Pybox or Pybim Ligands"*
K. Junge, K. Möller, B. Wendt, S. Das, D. Gördes, K. Thurow and M. Beller *Chem. Asien J.* **2011,** submitted.

9) "Zwei auf einen Streich"
K. Möller*, Leibniz Nordost* Journal der Leibniz-Institute MV, **11-2010**, 12-13.

Poster contributions

1) "*Iridium-catalyzed asymmetric hydrogenations with novel monodentate Phosphoramidites"*
G. Erre, S. Enthaler, K. Möller, D. Addis, K. Junge, M. Beller *42. Jahrestreffen Deutscher Katalytiker,* Weimar (Germany), 11.-13.03.**2009**.

2) *"An Environmentally Benign Synthesis of Quinones with an Iron Catalyst and Hydrogen Peroxide "*
G. Wienhöfer, K. Möller, K. Junge, M. Beller *43. Jahrestreffen Deutscher Katalytiker*, Weimar (Germany) 10.-12.03.**2010**.

3) *"An Environmentally Benign Synthesis of Quinones with an Iron Catalyst and Hydrogen Peroxide."*
K. Möller, G. Wienhöfer, K. Schröder, B. Join, K. Junge, M. Beller *3rd EuCheMS Chemistry Congress*, Nürnberg (Germany), 29.08 -02.09.**2011**.

4) *"Selective Iron-catalyzed Oxidation of Benzylic and Allylic Alcohols"*
K. Möller. B. Join, C. Ziebart, K. Schröder, A. Spannenberg, K. Junge, M. Beller *EuCOMC XIX EuCheMS Conference on Organometallic Chemistry*, Toulouse (France) 03.-08.07.**2011**.

Oral Presentations

1) "An Environmentally Benign Synthesis of Quinones with an Iron Catalyst and Hydrogen Peroxide."
K. Möller *CAFC9 (9th Congress on Catalysis Applied to Fine Chemicals,* Zaragoza (Spain), 13.-17.09.**2010**.