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Application of green techniques to cyclohexene and cyclohexane oxidation, catalyzed by [HC(pz)$_3$]-iron complexes and molybdenum-based complexes

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Abstract

This project, developed at Centro de Quimica Estrutural, Instituto Superior Tecnico, in Lisboa, concerns the use of iron scorpionate (namely $FeCl_2[HC(pz)_3]$) and Mo(II) carbonile complexes as catalytic compounds for oxidation of cyclohexene and cyclohexane, and the application of green techniques in these reactions.

The ligand tris(pyrazolyl)methane ($[HC(pz)_3]$ or Tpm) knew a recent development in alkane and alkene oxidation, thanks to the improvement done on its synthesis and its metal coordination. The importance of oxidation reactions in the chemical industry, as well as the tendency to find greener solutions to assure a sustainable growth, have brought the scientific community into this field of research.

Beside the reaction conditions usually investigated, i.e. reaction time, temperature and chemical quantities, the application of green techniques has also been studied. These include mainly the employment of hydrogen peroxide as oxidant, organic solvent replacement (investigating solvent-free system, water and ionic liquids) and the use of microwave irradiation as alternative energy source.

The Thesis is structured in five chapters and three appendices.

Chapter 1 gives information about the applied catalysts, and the state of art and synthesis procedure of $FeCl2[HC(pz)_3]$ (the most studied one).

Chapter 2 regards the industrial process involving cyclohexane oxidation, to underline the importance of this reaction but also its downsides. The industrial use of cyclohexene and its derivatives is also reported.

Chapter 3 exposes the principles of green chemistry and describes advantages and disadvantages of the green techniques used in this project. The synthesis procedure of [bmim][Cl] is also described.

Chapter 4 and Chapter 5 present the experimental work on cyclohexene and on cyclohexane oxidation, respectively.

Appendices A, B and C concern respectively the yield calculation method from GC data, the list of all performed reactions with relative parameters and the list of used materials and devices.

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Riassunto

I processi di ossidazione sono fondamentali nel panorama dell'industria chimica, in quanto permettono di ottenere intermedi chimici per numerose applicazioni, partendo da sostanze chimiche di base derivanti dal petrolio. Per questo motivo vi è un interesse scientifico sempre più ampio nei confronti delle problematiche che questo tipo di processo incontra industrialmente, ovvero, l'impiego di catalizzatori a base di metalli pesanti pericolosi per l'ambiente e l'utilizzo di agenti ossidanti che, dando come sottoprodotti sostanze pericolose, rendono necessario il trattamento degli off-gas.
Accanto a ragioni di tipo ambientale, vi è anche la tendenza allo sviluppo di processi a temperature e pressioni inferiori, che porterebbero vantaggi economici ed energetici. Pertanto, lo sviluppo di nuovi catalizzatori adatti ad essere impiegati in concomitanza ad agenti ossidanti benigni e a condizioni blande di reazione è uno dei punti fondamentali della chimica verde, la quale si presta, con i suoi 12 principi, ad essere un riferimento di innovazione per l'industria e la ricerca scientifica.
In questa sede si vuole studiare in particolare l'applicazione di un catalizzatore costituito da un ligando, il polipirazolilcarbonato, e da uno ione metallico, il ferro, su reazioni di ossidazione catalitica di cicloesene e di cicloesano. Il polipirazolilcarbonato appartiene alla famiglia dei cosiddetti "ligandi scorpionati", molecole costituite da anelli di pirazolo il cui principale vantaggio è rappresentato dalla possibilità di avere diversi gruppi funzionali, i quali determinano la reattività dello ione metallico con cui andranno a costituire il complesso catalitico. Vengono inoltre studiati, nell'ossidazione di cicloesano e cicloesene, alcuni complessi carbonilici di molibdeno (II), recentemente sintetizzati nel laboratorio dove la tesi è stata svolta.
Nel lavoro sperimentale, accanto ai parametri di reazione tradizionali, come il tempo di reazione, temperatura, quantità di reagenti e catalizzatori, sono state studiate condizioni che possano permettere lo sviluppo di un processo più *green*: l'utilizzo delle microonde come fonte di energia alternativa, la scelta del perossido di idrogeno quale agente ossidante, che dà acqua come unico sottoprodotto e la sostituzione di solventi organici con liquidi ionici, essendo questi ultimi meno volatili e perciò più stabili.
La Tesi è articolata in cinque capitoli e tre appendici.
Nel Capitolo 1 vengono descritti i polipirazolilborati, i primi ligandi azotati ad essere scoperti da Trofimenko, e i polipirazolilcarbonati, formalmente ricavati dalla sostituzione dell'atomo di boro con l'atomo di carbonio. Oggetto dello studio condotto sulle reazioni di ossidazione sopra descritte è il trispirazolilcarbonato ($HC(pz)_3$), del quale viene illustrata la sintesi e lo stato dell'arte nel campo della catalisi; viene inoltre descritta la procedura di preparazione del catalizzatore $FeCl_2[HC(pz)_3]$, usato nelle reazioni. Vengono inoltre elencati i complessi catalitici di molibdeno, oggetto successivo di studio.
Il Capitolo 2 riguarda i processi industriali di produzione di Nylon 6 e Nylon 66, che coinvolgono l'ossidazione catalitica del cicloesano, studiata in questa sede, per sottolineare l'importanza di questa

reazione nella produzione di beni di largo consumo e per evidenziare gli aspetti negativi di tali processi. Viene anche brevemente riportato l'uso industriale del cicloesene e dei suoi derivati.

Il Capitolo 3 illustra i 12 principi della *green chemistry* e le sue applicazioni in questo studio. Ogni applicazione è descritta in modo da evidenziare gli aspetti positivi e da non tralasciare gli eventuali aspetti negativi.

Infine, il Capitolo 4 e il Capitolo 5 riguardano rispettivamente il lavoro sperimentale sull'ossidazione di cicloesene e di cicloesano, che è stato svolto nel laboratorio del gruppo V del Centro di Chimica Strutturale dell'Instituto Superior Tecnico, con sede a Lisbona (Portogallo).

Le Appendici contengono il metodo utilizzato per calcolare resa e selettività dai dati ricavati dalla gas cromatografia (Appendice A), i parametri sperimentali utilizzati nelle reazioni studiate (Appendice B) e un elenco dei materiali e dei dispositivi utilizzati (Appendice C).

Introduction

Catalytic oxidation reactions are one of the most problematic processes in chemical industry, but also one of the most important for the production of useful chemical compounds, starting from petroleum-based materials.

Most of these reactions use heavy metal-based catalysts, which are quite expensive and produce hazardous, environmentally toxic waste, whereas transition metal complexes are gaining more and more importance as alternative catalysts in organic compound oxidation.

The other major problem of these reactions is the production of unwanted and dangerous by-product, due to the employment of certain oxidant agents; for example, nitric acid is the most exploited oxidant in industry because of its cheap price, but it is responsible for nitrogen oxide emissions.

Hence, one of the green chemistry goal is providing efficient, selective, eco-friendly and economic catalytic oxidation processes, through the development of proper catalytic complexes and the employment of benign oxidant agent.

This project focuses on the application of catalytic complexes, namely iron scorpionate and molybdenum (II) carbonile as catalysts, in cyclohexane and cyclohexene oxidation. In order to obtain a greener process, microwaves, hydrogen peroxide, mild conditions and ionic liquids have also been studied.

Regarding the catalytic complexes, $FeCl_2[HC(pz)_3]$ was the most employed in this study; tris(pyrazolyl)borate, $HB(pz)_3$, has been the most useful azotate ligand, since its discovery by Trofimenko[36], while tris(pyrazolyl)methane, $HC(pz)_3$, has been scarcely employed. Only recently, the improvement obtained on its synthesis extends the researchers' interest on this ligand, so that several catalytic complexes of this type have been tested in alkanes and alkenes oxidation, and Baeyer-Villiger reactions[26]. $FeCl_2[HC(pz)_3]$ has been already applied by Silva *et al.*[45] in the cyclohexane oxidation with hydrogen peroxide, instead for cyclohexene, $FeCl_2[HC(pz)_3]$ has never been tried. The main advantage of scorpionate-metal complexes is the versatility, due to the variation of steric and electronic effects, obtained by changing nature and position of the substituents in the pyrazole rings of the ligand. This affects the reactivity of the metal center that can therefore be fine-tuned.

Molybdenum complexes were also studied for both substrates: while in cyclohexane oxidation molybdenum is still understudied, it is very versatile in olefin oxidation. Mo(II) complexes were widely studied in coordination chemistry, but they have not been tested in alkane and alkene oxidations yet.

Nowadays researchers are giving more relevance to hydrophilic substituents that can perform reactions in aqueous media, promoting a sustainable and greener chemical route.

Although this project focuses only on homogeneous system, another important key factor is the possibility of supporting the catalyst, with zeolites, carbon materials, silica materials or polymeric membrane. The immobilization of the catalyst in an inert support can improve the catalytic activity and furthermore it can allow an easier final separation. In this work, another approach has been used: SILP (Supported Ionic Liquid Phase), a technology that has been established very recently as an innovative method to immobilize homogeneous transition metal complexes in catalysis. In recent years, the SILP technology has seen applications in hydroformylation, hydrogenation, carbonylation and fine chemical synthesis. The application to oxidation reactions is still at early stages[9][39].

Concerning the oxidant agent, one of the most promising for liquid-phase reactions is aqueous hydrogen peroxide. Sato, Aoki and Noyori[30] have already proven its efficiency in oxidize alcohols, olefins and sulfides, when combined with a quaternary salt as phase-transfer catalyst, and a tungstate complex.

The main benefit of hydrogen peroxide application is that the only obtained by-product is water. The employment of H_2O_2 as waste-avoiding oxidant is ideal only when the reaction is organic solvent-free and halide-free, therefore, an efficient catalyst and proper reaction conditions become the key factors.

The cost of hydrogen peroxide with respect to common employed oxidants is still too high to allow the production of chemical compounds in industrial scale quantities. The decrease of H_2O_2 cost, linked with stricter environmental legislation, can lead to significant changes in this field.

The task of finding green alternatives for well-established or new processes is always challenging. The need of efficiency and productivity, and on the other hand, the want of a sustainable growth made of an eco-friendly way of thinking are two goals that sometimes obstruct each other. The aim of this work is to combine new and greener strategies to oxidation reactions, namely hydrocarbons, and in this way contribute to provide alternatives for the actual industrial procedure.

Chapter 1

Coordination compounds for catalysis

Many of the green benefits of homogeneous catalysis arise from 'designed' catalysts made from transition metals and appropriate ligands. It is the partially filled d orbital that makes transition metals be attractive catalysts; this orbital has relatively high energy, enabling electrons to be readily transferred in or out. Ligands are coordination compounds that bond with transition metals via these partially filled d-orbitals and constitute the structure of the catalyst.

Phosphines are one of the most employed ligands, mainly for two reasons: they are good electron donors, forming stable bonds with transition metals; furthermore, a wide variety of phosphine can be synthetized, enabling to obtain compounds with very different properties.

Another important ligand is carbon monoxide, which is largely used in coordination chemistry. CO is a dative, L-type ligand that does not affect the oxidation state of the metal center upon binding, but does increase the total electron count by two units. It has been recently seen that there are really two bonding interactions at play in the carbonyl ligand: a ligand-to-metal $n \rightarrow d\sigma$ interaction and a metal-to-ligand $d\pi \rightarrow \pi^*$ interaction. The latter interaction is called backbonding, because the metal donates electron density back to the ligand[42].

In this project, the work is focused on scorpionate ligands and in particular on tris(pyrazolyl)methane.

1.1 Scorpionate ligands

One of the most popular ligand is poly(pyrazolyl)borate (generally abbreviated as Tp^x), a complex discovered in the mid 60s by Trofimenko[36]. It is constituted by pyrazole rings, connected to a central boron atom, through the nitrogen atoms of the rings.

This type of coordination compounds is called scorpionate, because of the manner in which it forms a catalytic complex with the metal. Like the pincers of a scorpion, this ligand binds the metal with the nitrogen heteroatoms of the two pyrazole rings, while the third group bonded to boron (it can be a pyrazole ring or another group) rotates forward to “sting” the metal[36] (Fig. 1.1).

According to the nature of the third group (the pseudoaxial group), two type of scorpionates can be distiguished: homoscorpionates (Fig 1.2), when the third group is a pyrazole ring (pz^x) identical to the other two bridging pyrazole rings, and heteroscorpionates, when the third group is anything else but pz^x [36].

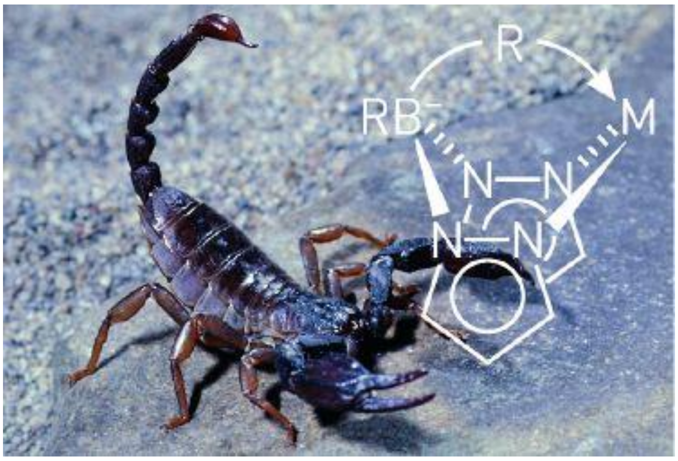


Figure 1. 1 *Bonding in a polypyrazolylborate–metal complex.* [32]

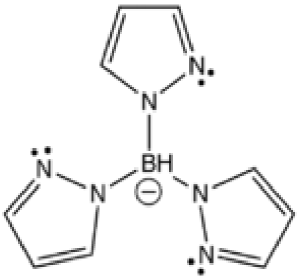


Figure 1. 2 *Homoscorpionate tris(pyrazolyl)borate*

The tris(pyrazolyl)borate (HB(pz)$_3$) (Fig. 1.2) is widely used as catalyst, especially for polyolefin polymerization: yttrium complexes of Tp^x can catalyze ethylene polymerization to give linear ethylene (Long and Bianconi)[36]. The main advantage of this type of catalyst is the versatility: by changing nature and position of the substituents in the pyrazole rings, different steric and electronic effects result. The ease of modify this ligand is the main advantage over metallocene based catalytic system. Even Tp^{x}TiCl$_3$ and Tp^{x}TiCl$_2$OR produce successfully linear polyethylene (Murtuza *et al.*)[36], while rhodium complexes are employed in the homopolymerization of phenylacetylene derivatives (Hatayama *et al.*)[36], in the regioselective homogeneous hydrogenation of quinoline (Alvarado *et al.*)[36] and in the dimerization of terminal alkynes (Trujillo)[36]. Copper complexes catalyze under mild condition the reaction of ethyldiazoacetate with alkenes to form cyclopropane (Diaz-Requeio *et al.*)[36] and are employed in the functionalization of aliphatic C-H bonds. The application of ruthenium complexes in the dimerization and polymerization of acetylenes and the hydrogenation of ketones has been also reported (Slugovc *et al.*)[36].

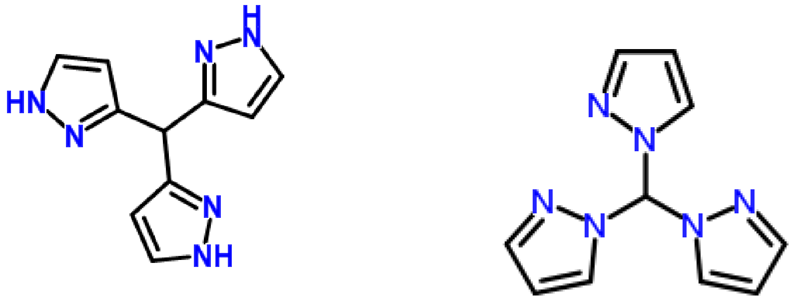


Figure 1. 3 *Tris(pyrazolyl)methane (left) and tris(1-pyrazolyl)methane (right)*

Formally replacing the boron atom with a carbon atom, tris(pyrazolyl)methane (generally abbreviated as Tpm) can be obtained (Fig. 1.3).

This isoelectronic and neutral ligand had been less developed, because of the more difficult synthesis compared to borate compounds, but recent breakthroughs in this field offer the opportunity to further investigate these promising ligands. By replacing the hydrogen atom bonded to the central carbon atom (the procedure is called functionalization), several derivatives can be made: changes in the ligand backbone influence the catalytic complex properties and extends the variety of possible applications.

The C-scorpionate ligands can assist proton-transfer steps that are believed to be involved in key processes (such as the metal-promoted generation of the hydroxyl radical from H_2O_2).

Reger elaborated some procedures for the synthesis of tris(pyrazolyl)methanes and also reported a summary of their coordination chemistry towards copper(I), silver(I), lead(II), strontium and thallium[37].

Two patents by Nakazawa *et al.* report the synthesis of Tpm[TiCl$_3$] and Tpm[TiOCl$_2$] as catalysts for the polymerization of ethylene using methylaluminoxane, at 313K for 60 minutes[37].

A patent by Uhlenbrock and Vaarstra has recently described the use of tris(pyrazolyl)methane ligands for the formation of group IIA metal-containing films on a substrate. The prepared compounds are suitable for the preparation of semiconductor structures[37].

Reaction between $HC(pz)_3$ and $LiBH_4$ leads to a lithium complex, that could be a potential hydrogen source for proton exchange membrane fuel cells (Aiello *et al.*) [37].

The first iron, cobalt, nickel, chromium, molybdenum, manganese and tungsten complexes have been synthetized by Trofimenko[37], while other complexes have been reported by Mani (vanadium) [37], by Otero and Fernandez-Baeza (niobium) [32][37] and by Gioia Lobbia (zinc, mercury, cadmium) [37].

An interesting application of tris(pyrazolyl)methane is the possibility to obtain ligands that are soluble in polar-solvent (therefore also in water). This is due to the acidic nature of its methine proton, that can therefore be easily removed by butyllithium, leaving a carbon readily attainable by electrophiles[37]. Using sulfurtrioxide–trimethylamine, Kläui *et al.*[37] were able to synthesize two water-soluble ligands, tris(pyrazolyl)- and tris(3-*tert*-butylpyrazol)-methanesulfonic acids.

So far, tris(pyrazolyl)methane has been successfully employed as metal complex of V(III, IV or V), Fe(II), Cu(II), Re(III, VII) and Au(III) in peroxidative oxidation of cycloalkane, alkene epoxidation and Baeyer-Villiger oxidation[26].

1.2 Synthesis of tris(pyrazolyl)methane

The synthesis of the homoscorpionate tris(pyrazolyl)methane has been done, following the experimental procedure of Reger *et al.*[38].

The preparation of this ligand involves four steps:

- Synthesis: join 5 g of pyrazole with 1.175 g of tetra-n-butylammonium bromide in 73.5 mL of distillated water, stir the mixture and then add 46.75 g of sodium carbonate, pouring it in small amounts so that it dissolves. After the dissolution of the carbonate, let the mixture cool down at room temperature and then add 36.75 mL of chloroform. Put the mixture under the reflux, at 70 °C for 72 hours.
- Isolation: filter to remove sodium carbonate in excess. Add 125 mL of ethyl ether and 75 mL of distillated water to the filtered mixture, as to create two phases. Split the two phases and do three extractions to the aqueous phase using 50 mL of ethyl ether each time, in order to recover the product remained in the aqueous phase. Join the three extractions to the organic phase. Add now 50 mL of a saturated solution of sodium chloride to the organic phase: this helps extracting more water, eventually trapped in the organic phase. Throw the aqueous phase and keep the organic one, in which add 1 g of active carbon; filter it after 5 minutes. Filter now the mixture through sodium sulfate that will remove water molecules still present. Proceed with the solvent evaporation.
- Crystallization: after the evaporation, add some hexane in the mixture, sufficiently to cover the solid. The remaining ethyl ether will evaporate, and the product, insoluble in hexane, will precipitate and form crystals. Then, after some hours, put the sample under vacuum, to evaporate the remaining solvent.
- Purification: sometimes the product needs to be purified through a re-crystallization. Dissolve completely the solid product into a small amount of hot ethyl ether and put the liquid mixture in a covered Erlenmeyer. While the mixture is cooling down at room temperature, crystals should form. If not, the mixture needs to be cool down in ice, to reach lower temperature and allow crystal formation. Analysis made on the ligand before the purification may be useful to see whether the re-crystallization is needed or not. Usually, the impurity is the unreacted pyrazole.

Infrared analysis and nuclear magnetic resonance spectroscopy have been done on the fresh ligand before purification, while NMR spectroscopy has been done on the residue obtained after re-crystallization, to identify the impurity. In Figure 1.4 and Figure 1.5 the IR and NMR spectra of $HC(pz)_3$ are reported, respectively.

The IR spectrum exhibits a band at 3145 – 3127 cm^{-1}, corresponding to the stretching of the methine proton of the ligand and a smaller band at 1620 – 1517 cm^{-1}, assigned to the double bonds C=C and C=N of the pyrazole rings.

The NMR spectrum of the residue (Fig 1.6) was confronted with the pyrazole spectrum[1]: since the signal of the NH bond is missing it can be assumed that the residue is not unreacted pyrazole.

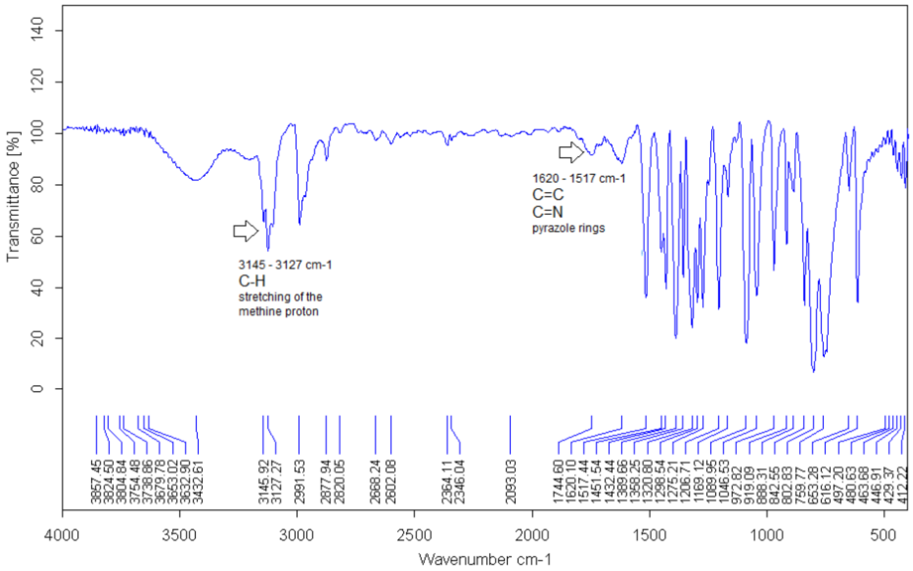


Figure 1. 4 *IR spectrum of HC(pz)$_3$*

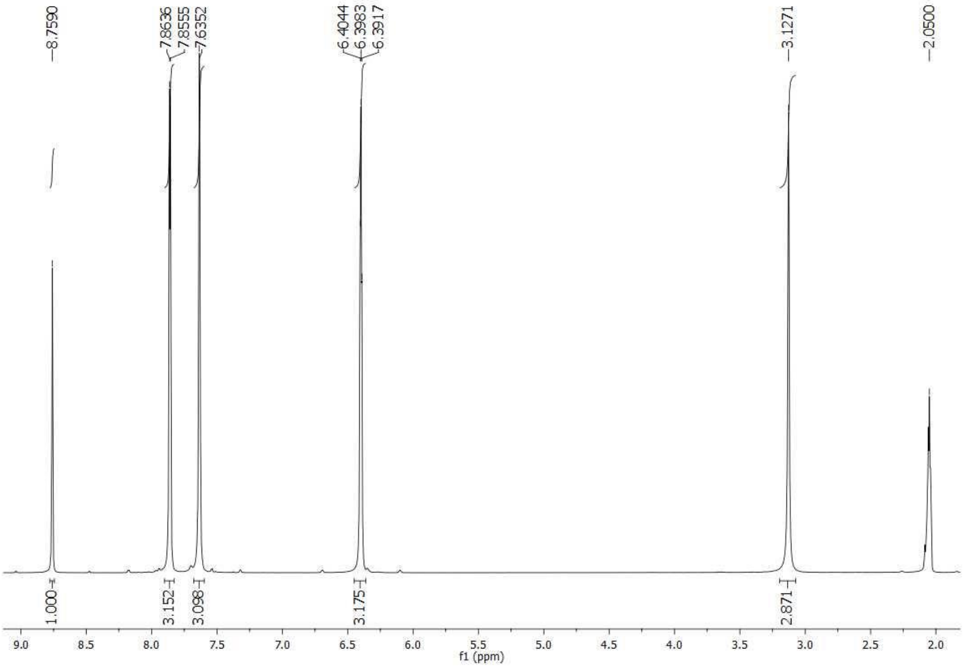


Figure 1. 5 *^{1}H-NMR spectrum of HC(pz)$_3$*

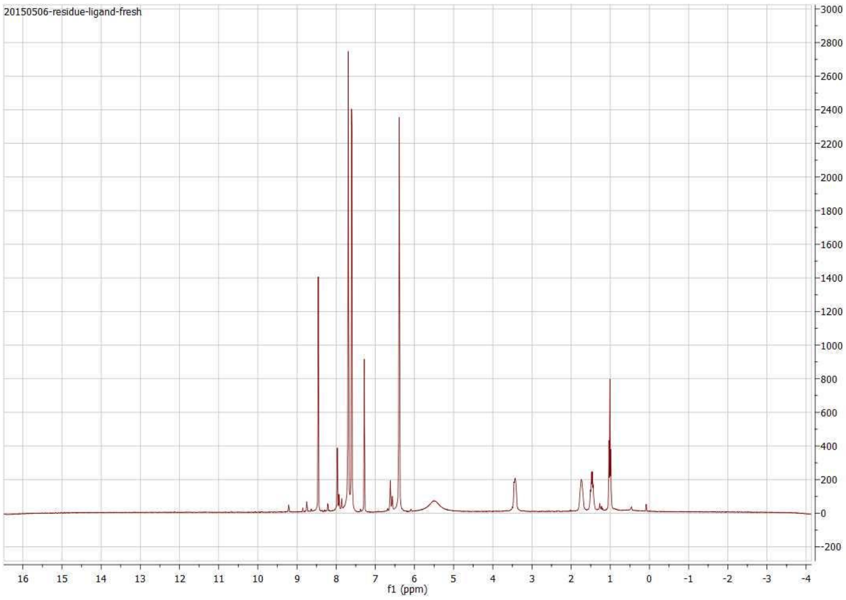


Figure 1. 6 *^{1}H-NMR spectrum of the residue after re-crystallization of tris(pyrazolyl)methane*

1.3 Iron chloride tris(pyrazolyl)methane $FeCl_2[HC(pz)_3]$

Starting from the synthesized ligand, the iron catalyst (Fig 1.7) has been prepared using iron chloride $FeCl_2$, joining the compounds in the molar ratio 1:1. The procedure is the following: weight 500 mg of tris(pyrazolyl)methane and 379 mg of $FeCl_2$ and put them in a Schlenk, as the reaction has to be carried under nitrogen, as to have an inert atmosphere. Add to the solid mixture a solvent, i.e. ethanol, and let the mixture stir under nitrogen for several hours[45].

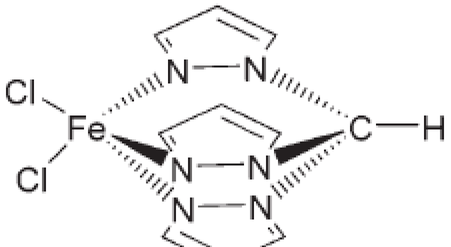


Figure 1. 7 *Structure of $FeCl_2[HC(pz)_3]$* [25]

At first, the mixture presents a purple color, but after a while, a pink powder starts to precipitate letting an uncolored solution. The solid is then filtered, washed with methanol and dried under vacuum. When the solvent is all evaporated, a yellowish-brown powder remains (Fig. 1.8)

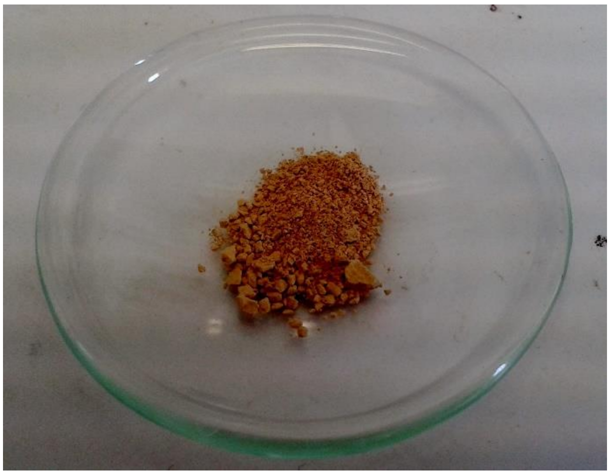


Figure 1. 8 *FeCl2[HC(pz)$_3$]*

Characterization of the catalyst has been done with NMR spectroscopy and the spectrum is reported in Fig. 1.9.

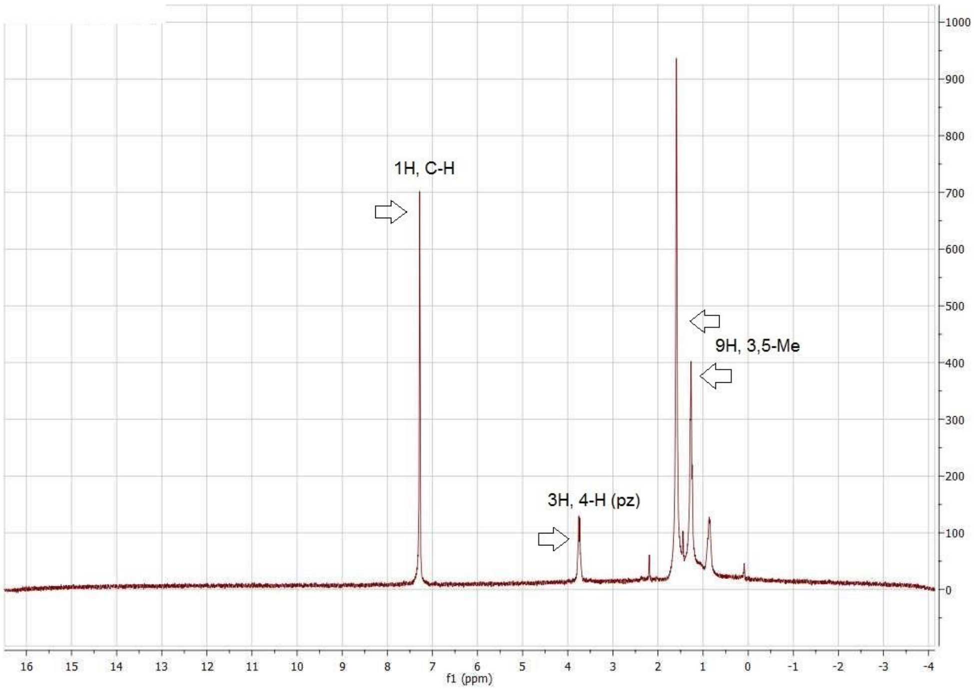


Figure 1. 9 *^{1}H-NMR spectrum of iron chloride tris(pyrazolyl)methane*

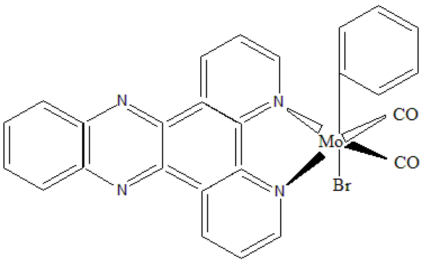
1.4 η-Allyldicarbonylmolybdenum catalytic complexes

Catalytic reaction are very important, particularly in the chemical and pharmaceutical industries where 80% of the compounds produced requires a catalytically step. Consequently, the pursuit for better, more active and selective catalysts that can allow more affordable and benign conditions for the environment has been a huge focal point in many research papers. The family of η-allyldicarbonyl complexes of Mo(II) has been widely studied in coordination chemistry and catalysis, since they couple an easy synthetic procedure to the possibility of introducing a variety of ligands. The complex [MoX(η3-C3H5)(CO)2(CH3CN)2] (X=halide), in particular, is a very useful precursor, as both the nitriles and X can be substituted by neutral or anionic ligands, to yield complexes displaying catalytic activity in a large range of reactions. Immine aziridination, oxidation of triphenylphosphine with molecular oxygen, allylic alkylations or epoxidation of olefins are examples of such reactivity. Mo(VI) complexes are known for their industrial applications in homogeneous olefin epoxidation, such as the ARCO-Halcon process, where TBHP is the source of oxygen[42]. Although it is well known that Mo(VI) species are the active species in oxidation catalysis, several Mo(II) systems, such as [MoX(η3-C3H5)(CO)2(L)] of (X=halide; L=bidentate ligands), suffer oxidative decarbonylation in the presence of oxidants (hydrogen peroxide, tert-butyl hydroperoxide and cumene hydroperoxide) to give epoxidation. The carbonyl complexes can be used directly, as the formation of the active species is not rate determining in the whole catalytic process. The use of these complexes as the catalysts is preferable to the Mo(VI) complexes due to their higher stability and are more easily stored for long periods of time. Recently, the priority in chemistry is in the development of catalysts that combine the high activity, selectivity of the homogeneous catalysts with the advantages of the heterogenous catalysts, such as easy recovery of products and recycling of the catalyst. Many of the efforts made in this sense involve the immobilization of the catalysts in different supports such as mesoporous materials, lamellar materials, nanoparticles carbon nanotubes, and more recently ionic liquids (SILP)[12][41].

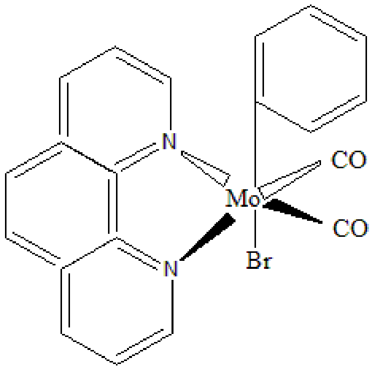
The Mo-based complexes tested in this project, as catalysts in cyclohexane and cyclohexene oxidation are:

- MS11 ($MoBrO_2N_4C_{23}H_{15}$), (Fig 1.10); molecular weight: 555.23 g/mol;
- MS14 ($MoBrO_2N_2C_{17}H_{13}$), (Fig. 1.11); molecular weight: 757.55 g/mol.
- MS104 ($MoBrO_2N_2C_{23}H_{29}$, (Fig.1.12) molecular weight: 541.33 g/mol;
- MS155 ($MoPF_6N_3O_4C_{31}H_{38}$), (Fig. 1.13); molecular weight: 669.39 g/mol;
- MS154 ($MoPF_6N_3O_4C_{25}H_{22}$), (Fig. 1.14); molecular weight: 453,14 g/mol;

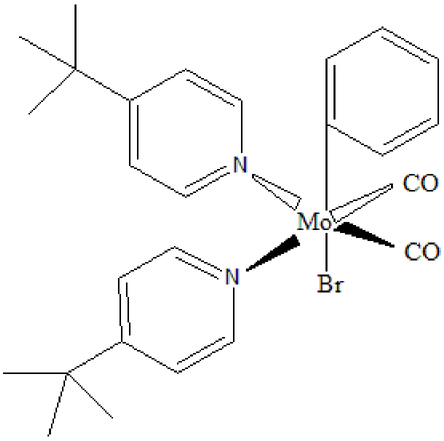
These compounds have been synthesized in the laboratory of the Group V, at Centro de Quimica Estrutural of Instituto Superior Tecnico.



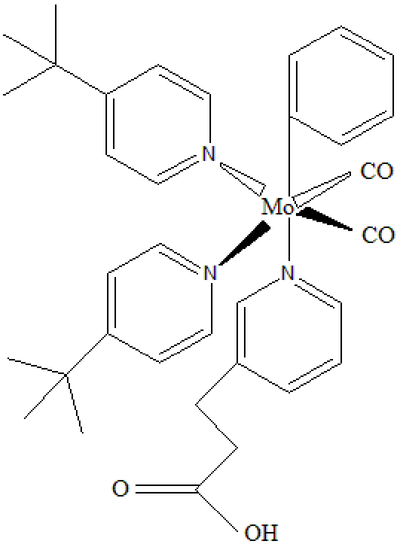
Figures 1. 10 *Structure of MS11*



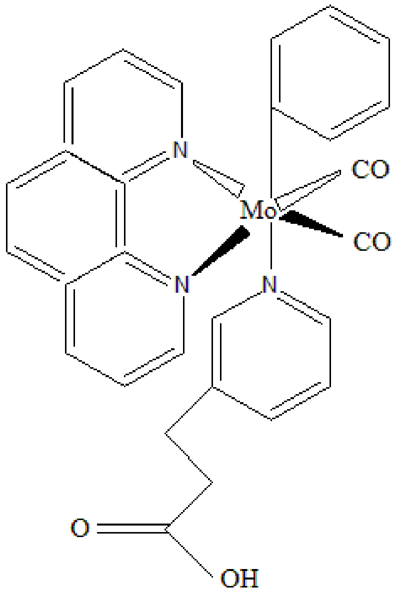
***Figures* 1. 11** *Structure of MS14*



***Figures* 1. 12** *Structure of MS104*



***Figures* 1. 13** *Structure of MS155*



Figures 1. 14 *Structure of MS154*

Chapter 2

Industrial oxidation processes

The increasing demand for more environmental-friendly atom- and energy- transformations is a challenge for modern chemistry[19]. Metal-catalyzed oxidations can lead to high value oxygenated intermediates for pharmaceutical, perfume, flavouring and agrochemical industries[20]. The use of some complexes, inspired in the active centers of metalloenzymes (e.g. based on Fe and Cu) resulted in significant achievements in hydrocarbon functionalizations, but truly efficient and selective catalysts, operating under eco-benign conditions, have not been found[11].

Many important chemicals are highly oxidized compounds, obtained from industrial catalytic oxidation processes. These chemicals constitute the raw materials for many products, used by people in everyday life. The reactions studied in this project are cyclohexane oxidation, which is a step for Nylon 6 and Nylon 66 production, and cyclohexene oxidation, which has been the subject of extensive studies, as cyclohexene derivatives are important synthetic intermediates for the production of fine chemicals. The following paragraphs present Nylon 6 and Nylon 66 production processes, and briefly the industrial application of cyclohexene and its derivatives.

2.1 Nylon 66 production

Nylon 66 was the first synthetic fiber appeared on the market in 1940. This polyamide is the product of the polycondensation of adipic acid and hexamethylendiamine.

World adipic adic productivity is around 2 million tons/year; the 93% of this capacity comes from the oxidation of cyclohexane, whose products are cyclohexanol and cyclohexanone (a mixture called *KA oil*), further oxidized to obtain adipic acid. Other routes are the production of the KA oil from phenol oxidation, which accounts for 3% of the total production and the hydration of cyclohexene to cyclohexanol, which accounts for 4% (Fig 2.1). All these routes start from benzene hydrogenation[23].

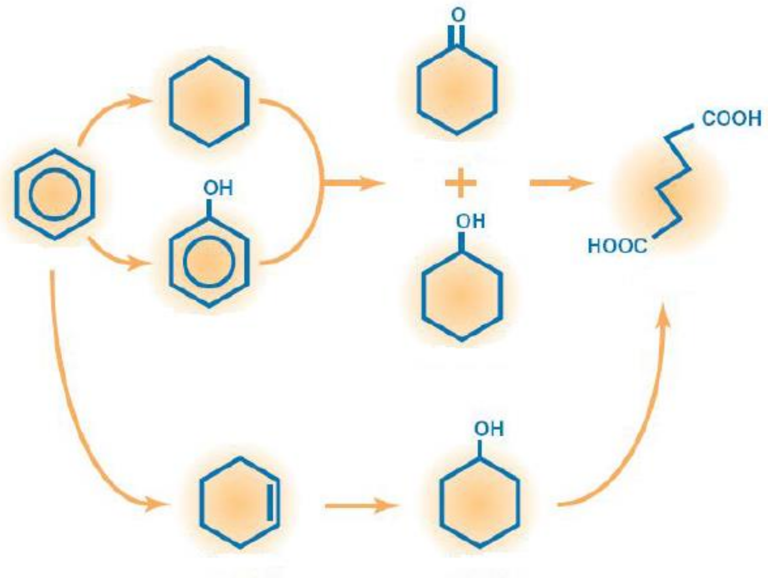


Figure 2. 1 *Chemical routes for adipic acid production*

Hexamethylendiamine is produced via adiponitrile hydrogenation; adiponitrile can be obtained through different chemical routes (Fig 2.2)[23]:

- adipic acid ammoniation;
- butadiene hydrocynation;
- acrylonitrile dimerization.

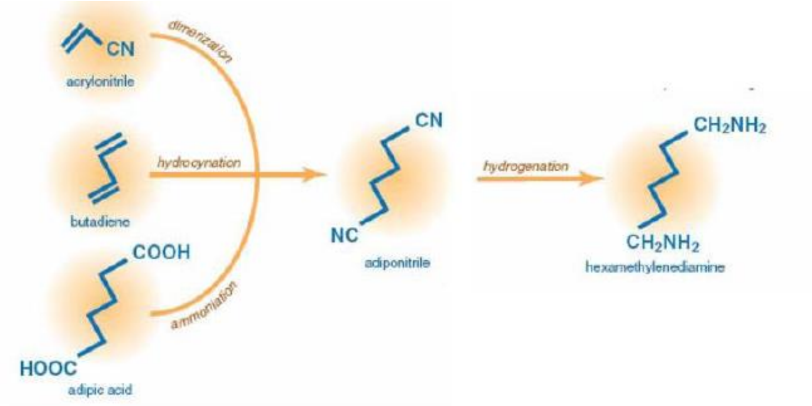


Figure 2. 2 *Chemical routes for hexamethylamine production*

Although the technology for this process is fully developed, efforts in innovation are underway, especially for discovering even more selective and effective catalysts, in order to reduce production costs and to prevent waste and by-products formation.

The following paragraphs present in details the oxidation processes involved in the adipic acid production, through the major route, and briefly, how cyclohexane is obtained from benzene.

2.1.1 Benzene hydrogenation to cyclohexane

Cyclohexane is produced by catalytic hydrogenation of benzene, which is an exothermic reaction (51.7 kcal/mol), conducted in liquid or vapor phase. Due to the chemical equilibrium between cyclohexane and benzene, the temperature control has to be very strict: for temperature above 300 °C benzene formation is favorited. Moreover, temperature above 200 °C leads to methylcyclopenthane formation. This isomerization reaction takes place even at lower temperatures when in presence of acidity. Therefore, the choice of a proper catalyst is fundamental. Generally, for hydrogenation, the most interesting catalysts are platinum, nickel and palladium, in this order of activity. Because of the high cost of platinum, nickel is usually preferred: Ni-Raney is a porous metal with good mechanical properties that is often used in cyclohexane production.

The main use of cyclohexane in the whole world, as shown in the chart in Figure 2.3, is the production of adipic acid and caprolactam: for this reason, according to ASTM standard, cyclohexane has to undergo some quality requirements, which are 99.8% purity and sulfur content below 1 ppm. The stereochemistry of cyclohexane (chair or boat configurations) does not influence its use as raw material for adipic acid[48].

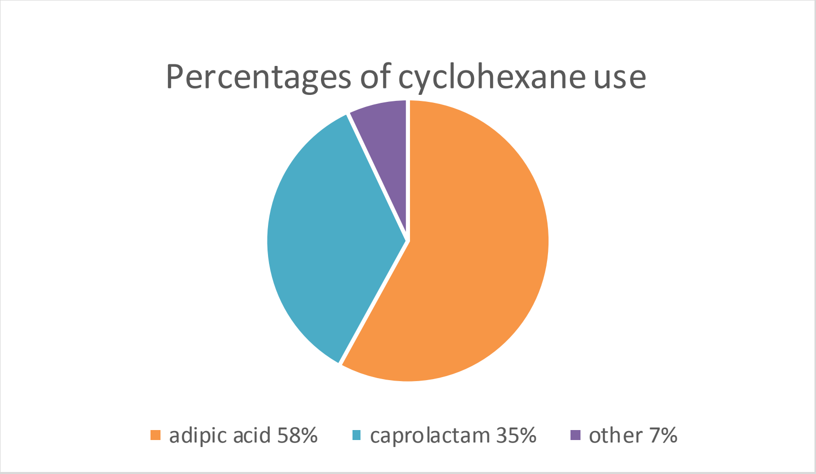


Figure 2. 3 *Chart of cyclohexane world use*

2.1.2 Cyclohexane oxidation to KA oil

The industrial cyclohexane oxidation is usually a liquid phase reaction carried in a series of mixed reactors, with temperature between 140 and 180 °C, and pressure between 0.8 and 2 Mpa. Residence time can vary from 15 minutes to one hour: this is due to mass transfer, as oxygen from the air has to be solubilized in the organic phase, to make the reaction occur[48].

The most employed catalysts are cobalt naphthenates, soluble in the reaction mixture, but there are other methods that employ boric acid or vanadium-, molybdenum- and chromium-based catalysts. The nature of the catalyst and the reaction conditions may change significantly the ratio alcohol/ketone in the KA oil: cyclohexanol and cyclohexanone are not in stoichiometric quantity[48].

Another use of cyclohexanol is to synthesize the bicyclohexyl adipate and the bicyclohexyl phthalate, which are plasticisers for polymer additivation.

The reaction, as all oxidation reactions, is exothermic, with an enthalpy of -70 Kcal/mol, and it is composed by two steps: first, the formation of an intermediate, the hydroperoxide cycloexyl (2.1), then, the KA oil formation, with other by-products (carboxylic acids, esthers, aldehydes, oxidized compounds etc...). The catalyst is responsible for the peroxide decomposition (2.2) [48].

$$C_6 H_{12} + O_2 \rightarrow C_6 H_{11}OOH \tag{2.1}$$

$$3C_6 H_{11}OOH \rightarrow 2C_6 H_{11}OH + C_6 H_{10}O + H_2O + O_2 \tag{2.2}$$

In Figure 2.4, the DuPont process is shown. The first reactor is fed with fresh and recycled cyclohexane and air, while the following reactors receive the mixture from the previous reactor, and fresh air (a). The product exits from the last reactor and is washed with water (b), creating a biphasic system, left in a decantation vessel, from which the aqueous phase is removed (c). In this way, the water produced during the reaction is separated from the organic products. The organic phase is then washed with a caustic solution (d), creating again a biphasic system, from which the aqueous phase is removed (e), while the organic one feeds a recovery column (f). Cyclohexane is recovered from the top of this column and recycled to the first reactor. Instead, the bottom product feeds another column (g), from which the KA oil exits on the top.

The functions of NaOH treatment are two:

- the further decomposition of unreacted hydroperoxide cycloexyl, that will lead mainly to the formation of cyclohexanone, rather than cyclohexanol;
- the removal of acid by-products, such as glutaric acid, capronic acid etc...

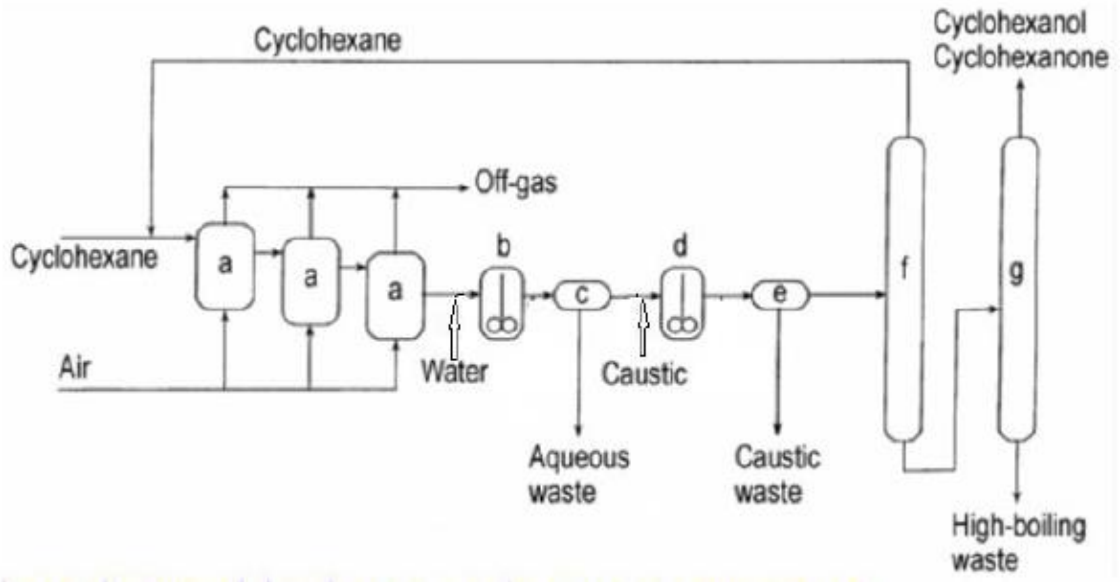


Figure 2. 4 *DuPont process scheme for cyclohexane oxidation to KA oil* [48]

As the intermediate peroxide and the KA oil are more easily oxidized than cyclohexane, the cyclohexane conversion in the reactors has to be kept low (usually around 6%) in order to maximize the selectivity. This means a huge amount of recycled cyclohexane[48].

2.2 Nylon 6 production

Cyclohexanone is an important intermediate for caprolactam production, which counts nowadays around 4.2 million tons per year. The caprolactam ring opening leads to one important polyamide, Nylon 6, which, with Nylon 66, covers 95% of the total manufacture of polyamides[48].
All routes for caprolactam production pass through cyclohexanone, which can derive from cyclohexane oxidation (73%) or from phenol hydrogenation (20%), both routes starting from benzene. Minor routes are the photonitrosation of cyclohexane, starting from benzene (4%), used exclusively by Toray industries and a route from toluene, via cyclohexane carboxylic acid (3%), developed by Snia Viscosa[48].
Nylon 6 is then obtained from caprolactam by anionic polymerization or by polycondensation[48].

2.2.1 KA oil dehydrogenation to cyclohexanone

Most of the KA oil produced by cyclohexane oxidation (§ 2.1.2) is destined to the adipic acid production, but part of it withstands a dehydrogenation process in order to transform the present cyclohexanol into cyclohexanone. The reaction is endothermic, with an enthalpy of 65 kJ/mol, and requires zinc oxide (or silver oxide) as catalyst, 400 °C and 1 bar[48].
Some problems of this process are[48]:

- the coke formation on the catalyst, which needs therefore to be often regenerated;
- the competitive cracking reaction that takes place, with respect to dehydrogenation;
- the difficulty of providing heat at such high temperature.

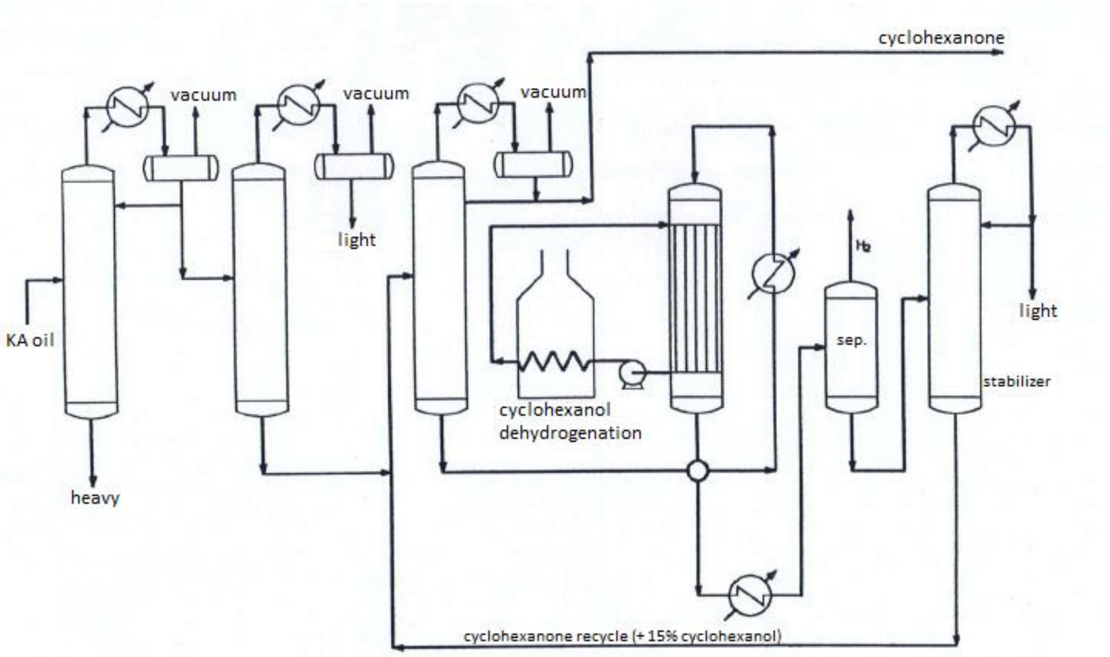


Figure 2. 5 *Process scheme of KA oil dehydrogenation to obtain cyclohexanone* [48]

As shown in the plant scheme in Figure 2.5, the KA oil enters the system and it is initially purified from heavy and light component, through two under vacuum columns. The fresh KA oil is then mixed with a recycled stream, containing cyclohexanone and around 15% of cyclohexanol, and enters the product column, from which cyclohexanone is taken from the top. The rest is sent to the dehydrogenation reactor, after a proper heating, exploiting also the heat from the product stream. The product stream is sent to a separator to remove the formed hydrogen, and then to a stabilizer, that removes light components and recovers the KA oil mix, that now contains less cyclohexanol. This mixture joins fresh KA oil in the product column to separate cyclohexanone[48].

2.3 Industrial use of cyclohexene and its derivatives

Cyclohexene is produced by partial dehydrogenation of benzene, although this process is not viable to produce only cyclohexene in a very large volume. The reason is that the ΔG°(298K) of benzene hydrogenation to cyclohexene is -22.8 KJ/mol, and the ΔG°(298K) to cyclohexane is - 97.9 KJ/mol, hence, the reaction will always lead preferably to cyclohexane. Several studies on this reaction discovered that a ruthenium catalyst could improve the production of cyclohexene, but the selectivity remains still less than 30%. The problem of a large production of cyclohexane is minimized by maintaining the conversion less than 60% while, the difficulty in the separation of the mixture benzene-cyclohexane-cyclohexene is overtaken by making the cyclohexene react selectively in this mixture, adopting proper catalysts[48]. This selective reaction is the transformation of cyclohexene to cyclohexanol, which is then dehydrogenated to cyclohexanone, precursor of caprolactam. With almost the same route, adipic acid can be obtained (see Fig. 2.1), although this process counts only for the 4% of the total adipic acid production[48].

Noyori *et al.*[30] have recently developed a green route for adipic acid by cyclohexene oxidation, which has not been applied in industry yet, because the cost of the whole process (especially because of hydrogen peroxide cost) is higher than the cost of nitrogen oxide treatment, necessary in the current industrial route.

Cyclohexene is also precursor for cyclohexene oxide, obtained by epoxidation reaction and used to produce poly(cyclohexene oxide) by cationic polymerization. Epoxides are very important intermediates for the production of fine chemicals but are easily obtained with direct oxidation employing molecular oxygen only with short alkenes (ethylene and butene mainly). Instead, for longer chain alkenes and cycloalkene, the direct oxidation is not employed: the process is a liquid phase reaction with peroxides as oxygen donors and catalysts that have transition metals, for example Mo(VI), that allow the transfer of oxygen from the peroxometallic complex to the olefinic double bond.

Among the interesting derivatives from cyclohexene, there is the corresponding ketone, cyclohexenone, which is actually obtained from anisole through the Birch reaction and an acid hydrolysis (Fig. 2.6): the reduction of anisole occurs in liquid ammonia with lithium (or sodium) and methanol.

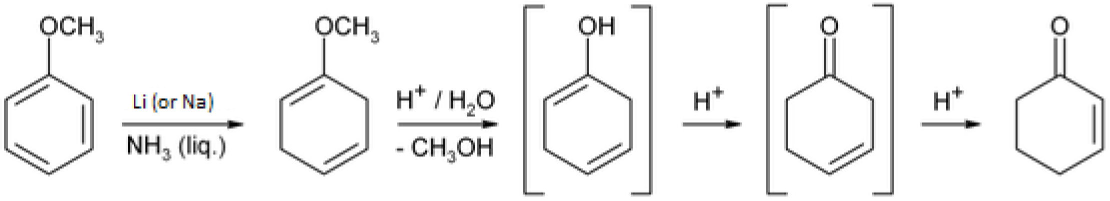


Figure 2. 6 *Chemical route to cyclohexenone, starting from anisole*

Cyclohexenone is used as intermediate in the synthesis of several fine chemicals such as pharmaceuticals and fragrances.

The cyclohexene corresponding alcohol, cyclohexenol, has biological application. It has been used as intermediate for the synthesis of pumiliotoxin C, a toxin that is naturally present is the skin of *Dendrobates pumilio,* a Panamiam native frog. In this work, cyclohexenol is enantiomerically pure and it is obtained from enantiomerically pure carboxylic acid, which is treated with iodine and potassium iodide[46].

In the published patent from Imazaki *et al.*[17], the possibility of synthetize cyclohexenyl-isoindole-dione starting from cyclohexenol is described. This compound is an inhibitor of rho kinase, a protein in mammals that is responsible for the shape and the movement of the cells.

Cyclohexenol can be found as impurity in cyclohexanol, from which the cyclohexanone for caprolactam is obtained. The presence of this impurity can lead to unsaturated lactam and therefore compromise the quality of the final Nylon.

A synthesis route for cyclohexenol from cyclohexene oxide has been reported. The process uses a chiral catalyst – cyclohexyl[(S)-1-ethylpyrrolidin-2-yl] methylamine, n-butyl lithium and hexamethylphosphoramide as an additive[51].

Chapter 3

Green routes for oxidation processes

The main aim of Green Chemistry is producing the chemicals and the materials we need, with a negative impact on the environment as minimum as possible, without losing in product performance. Hence, industrial research and chemistry knowledge are contributing with always more relevance in the development of new eco-friendly chemical technology, meeting at the same time product and process requirements and a sustainable development.

The World Commission on Environment and Development in 1987 defined the sustainability as "meeting the needs of the present without compromising the ability of future generation to meet their own needs", and it is therefore a balance among three main objectives: social, economic and environmental.

The Green Chemistry expresses itself through 12 principles, formulated by the chemist Paul Anastas, in 2000[3]:

1. waste minimization: it is better to prevent the waste, instead of treat it;
2. atom economy: synthesis methods should be design in order to maximize the number of atoms incorporated in the final product;
3. use of safer chemical routes and safer reactants and production of safer products;
4. design of safer chemicals: design chemicals, reducing their toxicity but maintaining their efficiency and function;
5. solvent replacement: use of solvent should be avoided whenever possible; when it is necessary, the solvent should be harmless;
6. energy efficiency: the use of energy should be minimize in order to reduce economic and environmental impact, room temperature and atmospheric pressure are preferable whenever possible;
7. use of renewable feedstock;
8. derivative reduction: secondary undesired products should be reduced, whenever possible;
9. catalysis promotion: catalysts should be selective and re-usable and their application should be preferable with respect to stoichiometric reactants;
10. end-of-life design: design should focus on the disposal of chemicals, in order to have harmless degradation products and to prevent long persistency in the environment;
11. pollution prevention analysis: real time process analytical methodology should be developed to have measurements before undesired substances can form, allowing pollution prevention;

12. process intensification: all the choices made on the process and the plant should be done in order to minimize the risk of chemical accident.

It is important to be aware that zero pollution does not exist, and that all the green alternatives have to be carefully analyzed, in order to understand what is their real benefit and if they can improve on traditional processes. For example, a renewable resource is not always preferable and completely green, if, in order to exploit it, the pollution would increase. The following paragraphs mostly present ionic liquids as green alternatives, concurrently with their advantages and disadvantaged.

So far, significant improvements on the catalytic performance, in terms of yield and selectivity, have been observed using ILs as solvents for the H_2O_2 oxidation reaction[34][39]. Actually, in many cases, ILs are active participant because the formation of radical species, the stabilization of the charged reactive intermediate and the immobilization of the actual catalyst can be strongly affected by the presence of an ionic environment. In comparison with traditional organic solvents, the use of ILs in catalytic oxidation has been regarded as a new mean for recycling the catalyst and enhancing the yield and selectivity of the product. Though a great number of catalytic oxidation have been performed in ILs, there are still rare examples that demonstrate how the ILs affect the reaction pathway and the reactivity.

According to the green chemistry, the use of solvents has to be avoided, whenever possible, and if it is not, solvents have to be harmless. In oxidation processes, solvents are used for several purposes: solubilizing reactants and catalysts when performing homogeneous reactions, favoring mass transfer, dispersing heat produced by the reaction, separating obtained products. The presence of a non-toxic solvent does not make necessarily a process green, in fact, many other variables must be considered: the energy needed to make the solvent reach the process temperature and to separate it at the end, the possibility of recycling it, the toxicity of potential by-products, process conditions such as solute solubility and product purification.

Current approaches to solvent replacement, when solvent-free systems are not possible, beside ILs, are the use of water, supercritical carbon dioxide, fluorinated hydrocarbons and solvents obtained from renewable resources (ex. lactate esters from corn). All of them have advantages and disadvantages that need to be considered when assessing the suitability for replacement.

3.1 Ionic liquids

Ionic liquids (ILs) are compounds comprised exclusively of ions, usually a bulky organic cation and an organic or inorganic anion (Fig. 3.1). Because of their entirely ionic nature, they commonly have a very large liquidus range and an extremely low vapor pressure. Since there are millions of possible anion/cation combinations, the properties of ionic liquids can be tailored, whereupon they are also referred to as ‘designer solvents’.

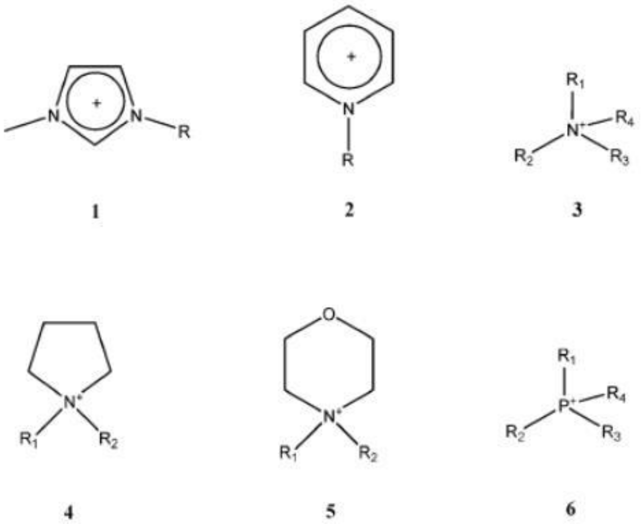


Figure 3. 1 *Examples of cations and anions commonly used in ionic liquids: (**1**) 1-alkyl-3-methylimidazolium; (**2**) 1-alkylpyridinium; (**3**) quaternaryammonium; (**4**) 1,1'-dialkylpyrrolidinium; (**5**) 1,1'-dialkylmorpholinium;(**6**) phosphonium*[18].

Ionic liquids have already been widely applied as electrolytes, due to their high ionic conductivity and a large electrochemical window, and as solvents and/or catalysts, owing to their capability to dissolve a range of solutes, especially catalytic complexes[9].

Especially the 1-alkyl-3-methylimidazolium ions are often used as the cationic part of ionic liquids. Catalytic reactions in ionic liquids (ILs) have seen an explosion in their use in the past decade, in a wide range of catalytic and stoichiometric reactions[14], and this has led to a greater than exponential growth in the number of papers published. Higher rates and better selectivity in selected ionic liquids than in classical solvents have been observed in the case of Friedel-Crafts reactions[14], Diels-Alder reactions[16], Heck reactions and radical polymerizations[14]. Beside their advantages with respect to environmental impact, a number of critical aspects of ILs make them an interesting medium in which studying chemical syntheses. Chiral ionic liquids (CILs) are very important due to their potential chiral discrimination capabilities. The first attempt at using of CILs in asymmetric synthesis (Diels-Alder reaction) was reported by Howarth *et al.*[16]. However, they were not successful in obtaining stereoselectivity. The first successful chiral induction by a CIL was reported in 2004 by Vo-Thanh and coworkers, who used a chiral ephedrinium ionic liquid as the reaction media in an asymmetric Baylis-Hillman reaction to obtain 44% enantiomeric excess in the product [35]. As then, the number and variety of CILs synthesized have increased tremendously, and new applications are being explored continuously. The synthesis and characterization of room temperature liquid salts of Mo(VI) have been recently published where they act as self-supported reactants for oxidation reactions under solvent-free and biphasic conditions. The preparation of room temperature liquid salts of Mo(II) that combine the properties of ionic liquids and Mo(II) complexes is still a new and appealing field, that is still quite unexplored in catalysis.

Limitations on ionic liquid application are due to several factors:

- their higher cost with respect to common solvents;
- their synthesis still implies VOC or chlorinated solvents, which means moving the solvent problem from a process stage to another. Product extraction and purification of recycled ionic liquid involve solvent use too. Moreover, for industrial use, chlorinated compounds are dangerous because of equipment corrosion and product contamination;
- possible toxicity, that for many ionic liquids has not been assessed yet;
- their ultimate disposal protocol has not been established yet.

On the other hand, the advantages that can come from the ILs use are important and straightforward:

- as previously said, their low vapor pressure and high boiling point; sometimes the difficult evaporation can be a drawback: if the reactants used to prepare the IL contain impurities, then it would be very hard to purify it. The required purity of the reactants is one of the main reason of their high final cost;
- the easy tunability of the properties, by varying the nature of the ions;
- they can act both as catalyst and solvent: a wide range of reactions has been already demonstrated in this medium, as also their solvent properties for organic, inorganic and polymeric compounds;
- many ionic liquids are stable at high temperature (> 300°C), allowing high temperature reactions that are limited by solvent evaporation;
- they can be used in conjunction with other alternative solvents like supercritical CO_2;
- ionic liquids that are not miscible in organic solvents or water may be employed in liquid-liquid extraction or in product separation;
- their use as solvent in homogeneous catalytic system brings the advantage of an heterogeneous system, since the catalyst stays in the ionic liquid and can be therefore reused, but maintaining the characteristic of an homogeneous system, which are less aggressive reaction conditions and higher selectivity.

Supported Ionic Liquid Phase (SILP) will be used as a protocol for the immobilization of transition metal catalysts since it may combine the advantages of ionic liquids with those of heterogeneous support materials[4]. In comparison to traditional liquid-liquid biphasic systems, higher catalytic activity and lower metal leaching can be achieved by appropriately tuning the experimental conditions[27]. These materials are prepared by the covalent attachment of IL to the support surface or by simply depositing the IL phases containing catalytically active species.

Another aspect within this research line is an acceleration of the chemical reactions by irradiation. Due to its direct and specific action towards certain chemical bonds, many irradiation-induced processes are more sustainable, consume less energy, generate less by-products or can be conducted using greener solvents than analogous conventional reactions[24]. On the other hand, sometimes the application of irradiation is crucial to perform a specific reaction, which cannot be conducted with a reasonable rate or would not occur at all, if the irradiation is not applied. In recent years, the use of a room-temperature ionic liquid (IL) in MW-assisted synthesis, as a (co-) solvent and/or (co-)catalyst, is becoming an increasingly exploited area since the ionic nature of ILs allows them to absorb MW energy very efficiently[34].

In oxidation processes with hydrogen peroxide, ionic liquids act like phase transfer catalysts (PTCs), which means that they help the transfer of ions between two phases (liquid/liquid or solid/liquid), in this case the transfer of the anion HOO^- to the organic phase that constitutes the reactant.

Phase transfer catalysis offers several potential green advantages:

- once anions are in the organic phase, they have very few associated water molecules: this reduces the activation energy, resulting in reactivity enhancement, which means a more rapid reaction, less energy requirement and higher productivity;
- since the activation energy is lower, lower temperature are sufficient: this limits by-product formation, allowing higher selectivity;
- ease in product separation;
- no solvent is required as the reactant constitutes the organic phase.

The disadvantage in the use of PTC is that the aqueous phase has to be treated, since organic substances contaminate it.

3.1.1 Ionic liquids employed in the experiments

Three ionic liquids have been applied as solvents in cyclohexane oxidation. These are:

- $[C_4mim][NTf_2]$ (Fig. 3.2): Butyl-methylimidazolium bis(trifluoromethanesulfonyl)imide, well studied in liquid-liquid extraction;

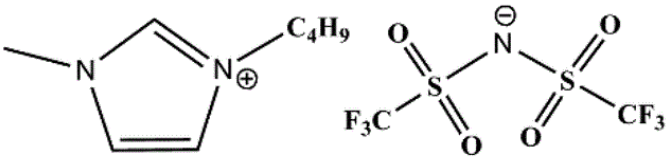


Figure 3. 2 *Butyl-methylimidazolium bis(trifluoromethanesulfonyl)imide*

- CYPHOS® 105 (Fig. 3.3): commercial name of trihexyl(tetradecyl)phosphonium dicyanamide; registered trademark of Cytec Industries Inc.

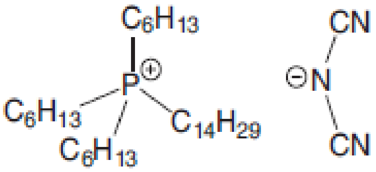


Figure 3. 3 *Trihexyl(tetradecyl)phosphonium dicyanamide*

- [C_8mim][NTf_2] (Fig. 3.4): Octyl-methylimidazolium bis(trifluoromethanesulfonyl)imide, well studied for gasoline desulfurization.

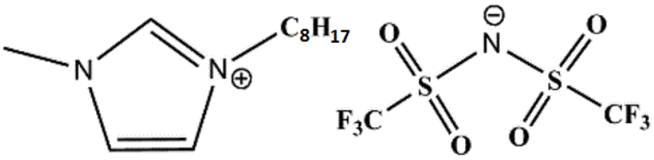


Figure 3. 4 *Octyl-methylimidazolium bis(trifluoromethanesulfonyl)imide*

In cyclohexene oxidation, CYPHOS 105® and other ionic liquids have been used:

- [C_6mim][NTf_2] (Fig. 3.5): Hexyl-methylimidazolium bis(trifluoromethanesulfonyl)imide;

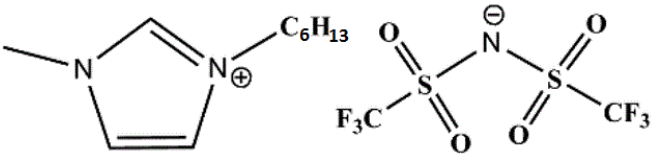


Figure 3. 5 *Hexyl-methylimidazolium bis(trifluoromethanesulfonyl)imide*

- Aliquat® 336 (Fig. 3.6): commercial name of a mixture composed by tricaprylylmethylammonium chloride and trioctylmethylammonium chloride with predominance of the C_8 chain compound. Registered trademark of BASF.

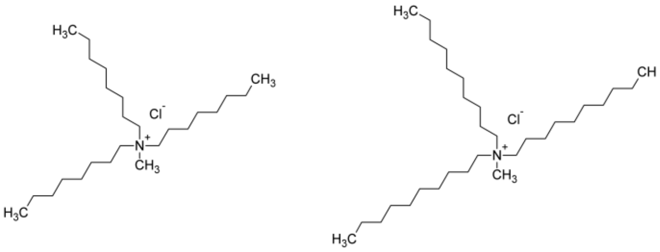


Figure 3. 6 *Tricaprylylmethylammonium chloride (right) and trioctylmethylammonium chloride (left)*

Up to now, 1,3-Dialkylimidazolium salts appear to be the most stable and conductive ionic liquids. There are almost 34 salts based on that type of cation. Usually anions are perfluorinated compounds, as strong delocalization of the negative charge weakens the hydrogen bonding with the cation and lowers the viscosity. However, better charge delocalization by lengthening the perfluoroalkyl chain results overcompensated by stronger van der Waals interactions, which leads to a viscosity increase.
One of the most used complexes is dialkyimidazolium bis(trifluoromethanesulfonyl)amides: easy to prepare, they conduct well and are thermally and electrochemically very resistant materials, they are hydrophobic (saturated by less than 2% of water) so, they are immiscible in water and in solvents of low polarity[8].

3.1.2 Synthesis of [bmim][A] ionic liquids

Among the ionic liquids applied in the experiments, some have been directly synthesized in the laboratory, others were used as supplied.

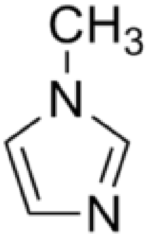


Figure 3. 7 *1-Methylimidazole*

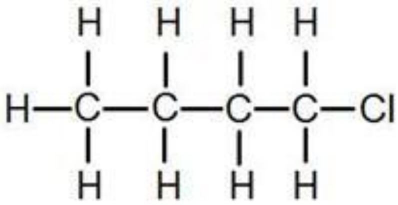


Figure 3. 8 *1-Chlorobutane*

The type of ionic liquids that have been prepared uses butyl-methylimidazolium (abbreviated bmim or C_4mim) as cation.
The precursor [bmim][Cl] was prepared as follows[8]: join an equimolar quantity of 1-methylimidazole (Fig. 3.7) and 1-chlorobutane (Fig. 3.8) and let the mixture under reflux at 60 °C for 48 hours; for 50 g of 1-methylimidazole, 56.47 g of 1-chlorobutane was added. The obtained product, [bmim][Cl] has to be washed with ethyl acetate (Fig. 3.9), to remove impurities. A biphasic system is formed: the upper layer is the ethyl acetate that has to be taken off, the lower layer is the ionic liquid. This still contains some solvent that has to be evaporated, so, a rotating evaporator is employed to put the flask at 60 °C and under vacuum for 2 hours.

Figure 3. 9 *Washing of [bmim] [Cl] with ethyl acetate. The system is biphasic, with the ethyl acetate on the top and the [bmim] [Cl] on the bottom.*

The butyl chain of the 1-chlorobutane attaches to the nitrogen atom of the methylimidazole, making it gain a positive charge, while the chloride atom becomes an anion.

With the same principle, C_6mim and C_8mim can be synthesized, using 1-chlorohexane and 1-chloroctane.

NMR analysis was performed to characterize the [bmim][Cl]. Proton and carbon NMR spectra are reported in Fig 3.10 and 3.11, respectively. The spectra have been confronted with those obtained by Dharaskar *et al.* [8].

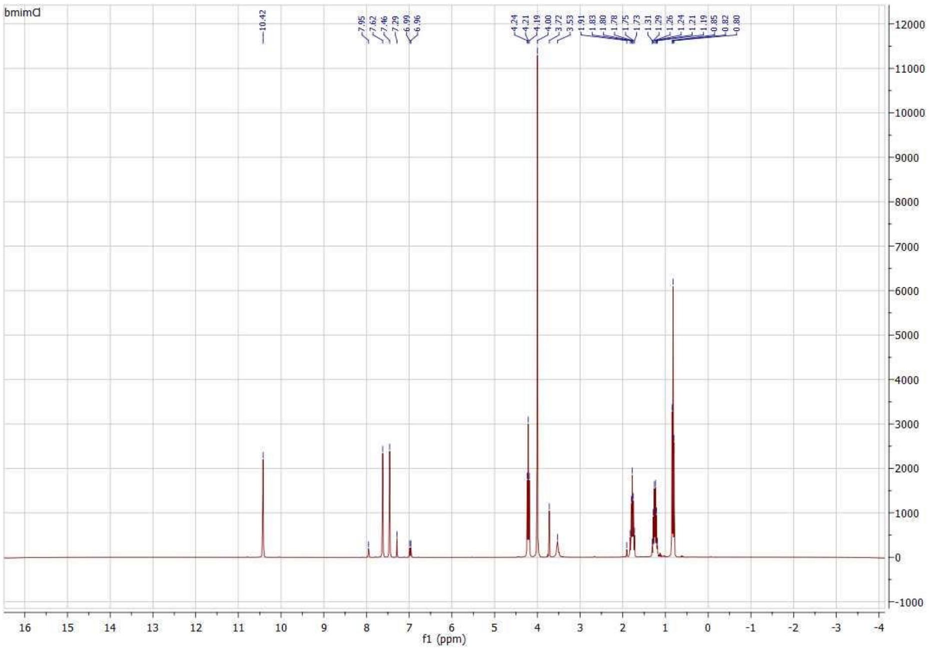


Figure 3. 10 *1H-NMR spectrum of [bmim] [Cl]*

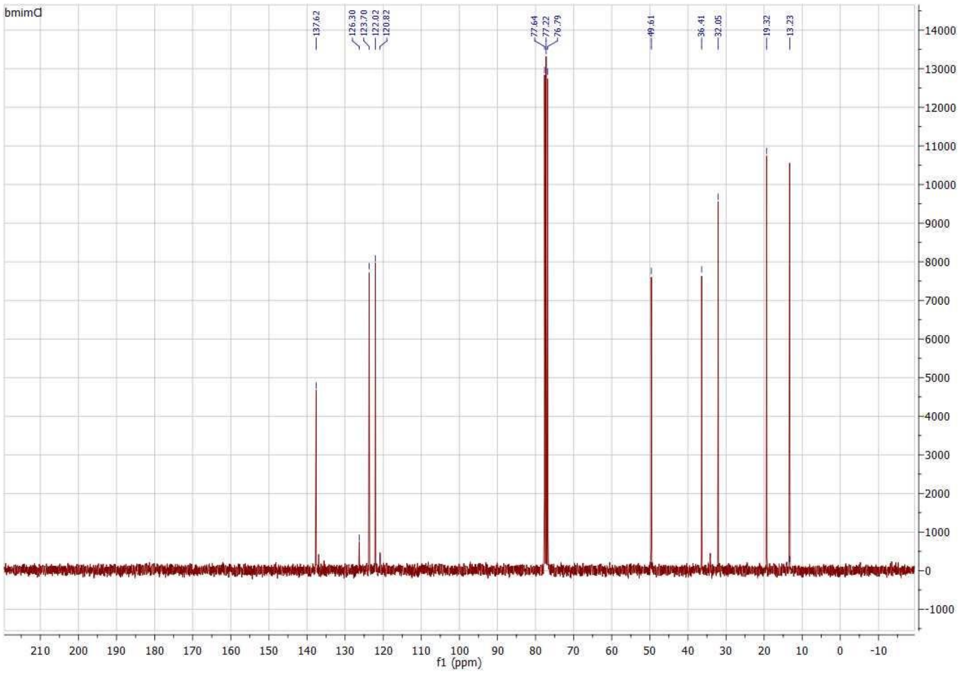


Figure 3. 11 *13C-NMR spectrum of [bmim][Cl]*

Several different ionic liquids can be now prepared by replacing the Cl^- with other anions, for example BF_4^- or PF_6^-. The replacement occurs when joining the [bmim][Cl] with a substance that contains the interested anion A^-, so the ion exchange will form [bmim][A] and a byproduct[10]:

- [bmim][PF_6]: hexafluorophosphoric acid (60% wt. water solution) was added to [bmim][Cl] in equimolar amount (10.05 g of [bmim][Cl] for 14 g of acid, corresponding to 0.057 moles). The mixture was stirred for two hours. At the end, a biphasic system is observed: the organic phase contains the IL, the other phase contains chloridric acid. The organic phase is separated and washed with 3x50 µL of distillated water and then dried under vacuum, in order to be purified. 100 mL of dicholoromethane and 35 g of magnesium sulfate are added to it: after one hour, the obtained suspension is filtered and put under vacuum to remove the remaining dichloromethane. The synthesized [bmim][PF_6] is a light yellow and viscous liquid.
- [bmim][BF_4]: sodium tetrafluoroborate, in 200 mL of distilled water, was added to [bmim][Cl] in equimolar amount (31,98 g of [bmim][Cl] for 20 g of powder, corresponding to 0.183 moles). The mixture was stirred for two hours and at the end, the heterogeneous system, composed by an organic part containing the IL and an aqueous phase containing the sodium chloride, is separated. Eventual water is removed from the organic phase at 80 °C, under vacuum. The remaining liquid withstood the same procedure with dichloromethane and magnesium sulfate, used for [bmim][PF_6]. The synthesized [bmim][BF_4] is a light yellow and viscous liquid.

3.1.3 Current applications of ionic liquids in chemistry

Chemistry application of ionic liquids are several and a list of them is reported in this paragraph, along with the advantages that they brought into the processes (beside yield and selectivity improvement and an easier catalyst separation)[39]:

- hydrogenation: the risk of hydrogen ignition is reduced thank to the solubilization into the ionic liquid;
- oxidation: in oxidation reactions, the ionic liquid is usually employed as additive solvent (therefore not replacing completely the organic solvent); this makes easier the industrial application since there is no need to change the whole equipment;
- Heck reaction;
- Diels-Alder reaction: the major advantage is the replacement of the organic solvent and the $AlCl_3$ catalyst;
- Wittig reaction;
- Suzuki-Miyaura coupling reaction;
- Stille reaction: the use of ionic liquid allow to have less byproducts and to reduce the reaction time;
- fluorination: with the application of ionic liquid the reaction time is sensibly lower, thus reducing the time of exposure of industrial equipment to the corrosive reaction system;
- hydroformilation; reaction in ionic liquid results in higher n/iso ratio of the products;
- Difasol process: industrial process in combination with Dimersol process, for alkenes dimerization (typically propene and butene to branched hexene and octane). In the Dimersol, the conversion is kept low and the outlet is transferred to the Difasol process, in which the ionic liquid solubilize the catalyst and the reactant but not the products: in this way the produced dimers cannot react and give higher chain alkenes (C_9 and C_{12}). This enhancement in selectivity leads to cheaper separation processes.
- Biocatalysis: the employment of ionic liquids leads to an enhancement in the enantioselectivity.

3.2 Hydrogen peroxide as green oxidant

Hydrogen peroxide is one of the strongest oxidant available on the market, thanks to the high reactivity given by the bond between two oxygen atoms, and it is not pollutant. It is a very attractive oxidant, according to the green chemistry, since it can oxidize compounds with an atom efficiency of 47 % with the only production of water as by-product.

For safety reason hydrogen peroxide is commercialized in aqueous solution, usually not over 50% of volume concentration and the concentration depends on the final use. Impurity in the solution may act like catalysts, accelerating its decomposition with the consequent production of gaseous oxygen. In addition, hydrogen peroxide is thermodynamically unstable: dismutation reactions may occur and produce water and oxygen, increasing the pressure inside storage vessels. The overall production of hydrogen peroxide in the world (expressed at 100% hydrogen peroxide) is about 3.8 million tons per year (source: *University of York website: www.essentialchemicalindustry.org*). It is largely used for bleaching in paper industry but also in textile industry; the applications in chemical industry include the production of iron sulfates, hydrazine, perborates, percarbonates, propylene oxide and its use as additive or initiator in polymerization. Minor percentages regard water treatment and mineral extraction and manufacturing; other uses are as rocket fuel and cosmetic and medical applications (Fig. 3.12).

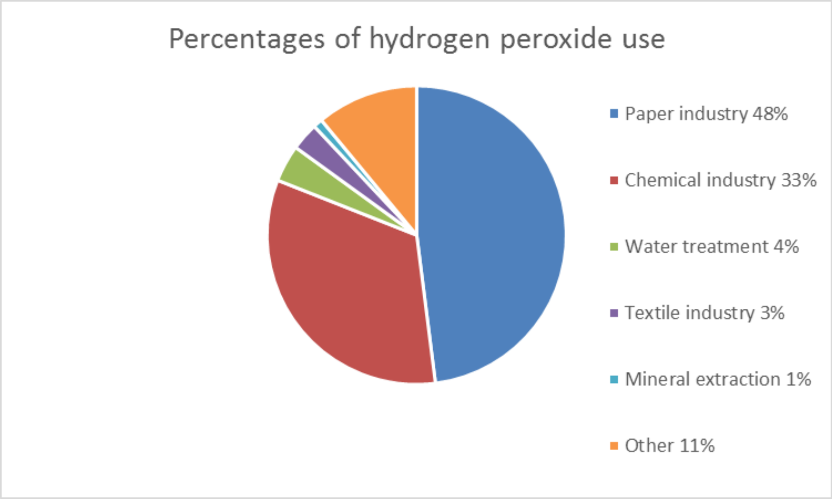


***Figure 3. 12** Chart of hydrogen peroxide world use*

Discovered in 1818 by the french chemist Louis Jacques Thenard, hydrogen peroxide was initially produced treating barium peroxide with nitric acid, a technique successively improved using hydrochloric acid and sulfuric acid to let the barium sulfate precipitate. From the mid of 20th century, hydrogen peroxide was industrially obtained by the hydrolysis of ammonium persulfate, while nowadays it is produced with a process developed by BASF that involves anthraquinone (Fig. 3.13). Anthraquinone is solubilized in a mixture containing organic C_6 - C_{11}, and a polar solvent (ex. Trioctyl phosphate); then the mixture is hydrogenated in a triphasic fixed bed reactor, with Nichel or Palladium catalyst, to obtain anthraquinol. The anthraquinol withstands autoxidation when in presence of oxygen, producing hydrogen peroxide and anthraquinone again[6].

The process presents two important positive factors: it avoids the potential danger of a direct contact between hydrogen and oxygen and it implies mild process conditions (5 bar and 80 °C)[6].

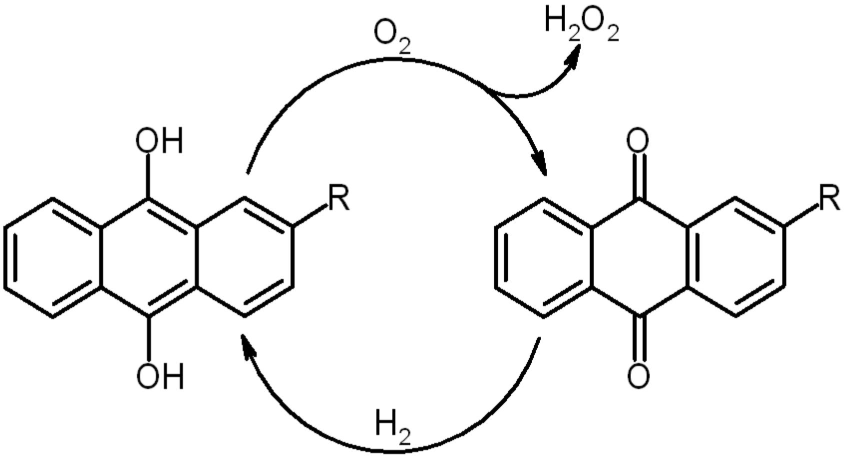


Figure 3. 13 *Hydrogen peroxide production process [6]*

Although hydrogen peroxide can be considered a green oxidant according to its characteristics, the process to produce it is quite expensive and has a consistent environmental impact. The major problems are the following[6]:

- a huge quantity of waste due to the selectivity that is not 100%;
- the limited solubility of anthraquinone in the solvent;
- the use of an hazardous organic compound as solvent;
- the low concentration of produced hydrogen peroxide (less than 1.5% w.);
- the conversion of hydrogen is kept under 70% to minimize secondary products;
- a high energy consumption due to purification of the hydrogen peroxide and to the recirculation of big flowrates (the substances needed are 50 times the quantity of the produced 50% hydrogen peroxide solution).

An interesting alternative for hydrogen peroxide production is the direct synthesis, which is under development. This method reduces consistently the process complexity, allowing *in situ* production, and therefore diminishing the risks connected to transportation and storage. It consists on the direct reaction between hydrogen and oxygen (3.1), which is complicated by other three competitive reactions: water synthesis (3.2), hydrogen peroxide hydrogenation (3.3) and hydrogen peroxide decomposition (3.4)[23].

$$H_2 + O_2 \rightarrow H_2O_2 \tag{3.1}$$

$$H_2 + \frac{1}{2}O_2 \rightarrow H_2O \tag{3.2}$$

$$H_2O_2 + H_2 \rightarrow 2H_2O \tag{3.3}$$

$$H_2O_2 \rightarrow H_2O + \frac{1}{2}O_2 \tag{3.4}$$

The peroxide decomposition influences limitedly the global reaction rate; on the contrary, the peroxide hydrogenation is a quite fast reaction that greatly reduces the hydrogen peroxide production. The synthesis has to be conducted at low temperature, between -10 °C and 5 °C, to minimize the secondary reactions, with brief reaction time and at high pressure to solubilize the reactants in the liquid medium (i.e. methanol)[23].

In this project, both hydrogen peroxide and tert-butyl hydroperoxide (TBHP) have been used as oxidant agents to test the catalysts, but it is clear that a successful application of hydrogen peroxide on oxidation reactions would lead to the replacement of TBHP (Fig. 3.14[b]), which is more instable, flammable, toxic and corrosive than the hydrogen peroxide (Fig. 3.14[a]). TBHP is widely used in lots of oxidation reactions and it is normally supplied in a solution at 70%. The transportation of solutions above 90% is prohibited by law.

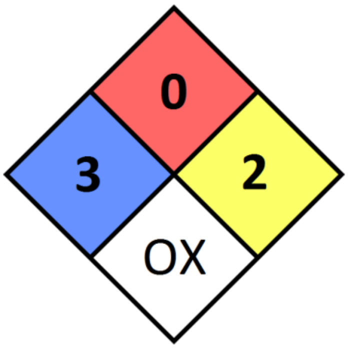


Figure 3. 14[a] *NFPA 704 of hydrogen peroxide*

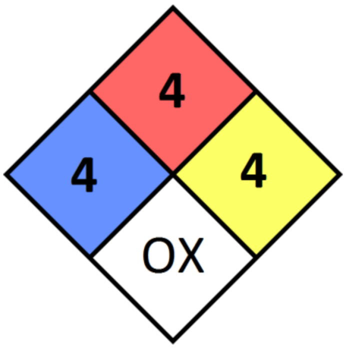


Figure 3. 14[b] *NFPA 704 of tert-butyl hydroperoxide*

The synthesis routes for TBHP are mainly three[40]:

- reaction between hydrogen peroxide and tert-butyl hydrogensulfate, which is obtained from tert-butyl alcohol or from isobutene;
- reaction between tert-butyl alcohol and persulfuric acid, that can lead however to explosive intermediates;
- autoxidation of isobutylene with oxygen.

3.3 Microwave irradiation

One of the green chemistry principles is the necessity of minimize the use of energy, in order to reduce the economic and environmental impact (6th principle). One step towards energy efficiency is represented by alternative energy sources, such as photochemistry, microwaves, sonochemistry, electrochemistry and fuel cells; although these technologies are not new, they are just recently emerging in manufacturing industry.

In this project microwave irradiation has been largely used.

Wavelength range of MW irradiation goes from 1mm to 1 m, which corresponds to a frequency range of 300 MHz – 300 GHz. However, only certain frequencies are allowed in domestic and industrial MW equipment, because of radar and telecommunication interference; these are 2.45 GHz, 5.8 GHz, 24.125 GHz, 434 MHz and 915 MHz. The most used is 2.45 GHz, which corresponds to 0.0016 eV (Table 3.1): this energy is not clearly sufficient to break molecular bonds; in fact, MW irradiation does not enhance chemical reaction by direct energy absorption, like UV and visible light do (higher frequencies). Therefore, other physical phenomena are behind microwave working principle[21].

Table 3. 1 *Radiation energy and atom bonds energy*

Radiation type	**Frequency [MHz]**	**Quantum energy [eV]**	**Bond type**	**Bond energy [eV]**
Gamma rays	3.0×10^{14}	1.24×10^{6}	CC single bond	3.61
X-rays	3.0×10^{13}	1.24×10^{5}	CC double bond	6.35
Ultraviolet	1.0×10^{9}	4.1	CO single bond	3.74
Visible light	6.0×10^{8}	2.5	CO double bond	7.71
Infrared light	3.0×10^{6}	0.012	CH bond	4.28
Microwaves	2450	0.0016	OH bond	4.80
Radiofrequencies	1	4×10^{-9}	Hydrogen bond	0.04 – 0.44

A process that can explain why microwaves can heat certain substances (and not others) is the termed dipolar polarization: when a molecule has a dipole moment and is exposed to electromagnetic irradiation, it tends to align in the electromagnetic field direction by rotation. In liquids, this rotation causes friction between adjacent molecules, therefore the temperature increases. The rotation rate influences the heating rate, so the heating rate is correlated to the radiation frequency. Potentially, all radiation frequencies have this effect, however, when the frequency is too high, the change in electromagnetic field direction is too rapid that the molecules do not have time to rotate, while when the frequency is too low, the thermal effect is negligible. On the contrary, microwave frequencies are appropriated to produce high rotation rates and so, a rapid temperature rise in dipolar substances. At the frequency of 2.45 GHz, the electric field oscillates 4.9×10^{9} times per second, leading to a heating rate of 10 °C per second[21].

Gases cannot benefit from MW irradiation, because the distance between molecules in a gas is too high to have friction between them, while non-polar substances can be heated by MW only when a dipolar substance is added, even in small amount[21].

Another mechanism, due to MW irradiation is the ionic polarization, for substances containing ions: under electromagnetic field, positive ions migrate towards the field direction, while negative ions migrate in the opposite direction. The frequent collision of the ions while migrating causes the heating effect[21].

It can happen that substances with the same polarity heat at different rates. This is explained by a third mechanism, called "dielectric loss". Every molecule has a dielectric constant ε' and a loss factor ε" that change with temperature and frequency: ε' is related to the molecule polarizability by electric field, while ε" is related to the efficiency of the molecule to convert absorbed energy into heat; the higher the ε", the faster the heating. The ratio between the loss factor and the dielectric constant gives the dissipation loss tangent (or dissipation factor), tanδ. A higher dissipation factor means therefore a more rapid heating[21].

The main advantage of MW irradiation is that the substances are heated selectively, because the energy is uniformly distributed and it targets directly the reaction medium. On the contrary, the conventional heating depends on convection currents and thermal conductivity of the materials that have to be penetrated, resulting in a temperature gradient where the vessel wall is hotter than the reaction mixture (Fig. 3.15). In addition, local overheating may occur in the reaction mixture due to the internal gradient, leading to sample decomposition[21].

Using microwaves, the temperature gradient is exactly the opposite, resulting in an efficient internal heating and no hot vessel surface[21].

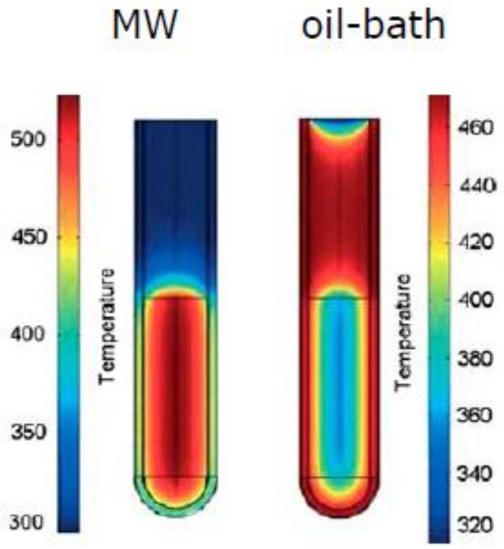


Figure 3. 15 *Temperature profiles in MW irradiated sample and conventional heated sample*[21]

Although the reasons why the microwaves enhance chemical transformations are not fully understood, there are three main explanations, on which the scientific community debates[21]:

- Thermal effect: reaction rate increases only because of thermal/kinetic effect, since high temperature can be rapidly obtained.
- Specific microwave effects: due to the microwave dielectric heating mechanism, they can lead to acceleration of chemical reactions that cannot be obtained with conventional heating. These effects are:

i. solvent superheating: there is the possibility to heat the solvent 40 °C above its boiling point, at atmospheric pressure. This allows reaching reaction rates that normally are possible only under pressure;
ii. the elimination of wall heating, which avoids the decomposition of the catalyst in case of contact with the wall, increasing the lifetime of the catalyst;
iii. mass heating: the fast and uniform heating of the whole reaction mixture allows having the same reaction rate in the whole system. In conventional heating, temperature and therefore reaction rate are higher at the wall: resulting products and by-products can form a layer on the wall that adds a new heat resistance;
iv. selective heating: in heterogeneous catalysis, solid/liquid system or gas/liquid system can be performed using a poor radiation absorber as solvent/reactant, and a high absorber as catalyst. The temperature on the catalyst surface will be much higher than the solvent bulk temperature, enhancing the reaction rate.

- Non-thermal microwave effects: those that do not belong to thermal or specific microwave effects but cause reaction rate acceleration as well. Many scientists agree that the orientation of dipolar molecules under electric field changes the pre-exponential factor A and the activation energy, in particular decreasing the latter.

Safety aspects and limitation on usable solvents imposed by MW technology lead to the development of three important reaction process for the green chemistry: reactions conducted in water, solvent-free reactions, reactions conducted in ionic liquids, which are perfect candidates for MW use, thanks to their polarity, non-volatility, and the possibility of applications over 200 °C [21].

Industrial applications of microwave technology are so far limited to rubber devulcanization, food drying, sterilization and cooking, polymer drying and a small-scale in-situ process for HCN production, from methane and ammonia. As reactant are gases, only the catalyst absorbs microwaves, the heating is rapid and the HCN is produced only when needed, reducing the risks correlated to its toxicity[21].

Chapter 4

Cyclohexene oxidation experimental section

So far, cyclohexene oxidation has been much less studied than cyclohexane oxidation; therefore, more attention was given to the former in this project.

The synthetized complex $FeCl_2[HC(pz)_3]$ (see §1.2) and molybdenum-based complexes have been applied in cyclohexene oxidation. Expected product are cyclohexenol, from the oxidation of the allylic C-H bond, cyclohexenone from further oxidation of cyclohexenol, cyclohexene oxide from carbon-carbon double bond break, and cyclohexandiol from further reaction of cyclohexene oxide[2].

4.1 Cyclohexene oxidation applying $FeCl_2[HC(pz)_3]$ as catalyst

The applications of iron catalysts to cyclohexene oxidation are few. In the nineties', Medina *et al.* [28] applied a complex made of iron and a macrocyclic ligand, tetramethyl-tetraazacyclotetradeca-tetraene, supported on Y-zeolite in cyclohexene oxidation with iodosylbenzene as oxidant, while Lei[22] used a catalytic complex of iron and bipyridine and molecular oxygen as oxidant. In 2004, Serwicka *et al.*[43] studied different porphyrin ligands with iron, manganese and cobalt, supported on aluminated mesoporous silica, on cyclohexene oxidation with iodosylbenzene. More recently, cyclohexene has been used by Oloo *et al.* as substrate for verifying the oxidizing nature of nonheme iron catalysts Fe(TPA)[31].

Hence, iron scorpionate has never been tried in cyclohexene oxidation with hydrogen peroxide.

Different conditions have been applied in the experiments, in order to understand the effect of microwave irradiation, additives, reaction time and temperature.

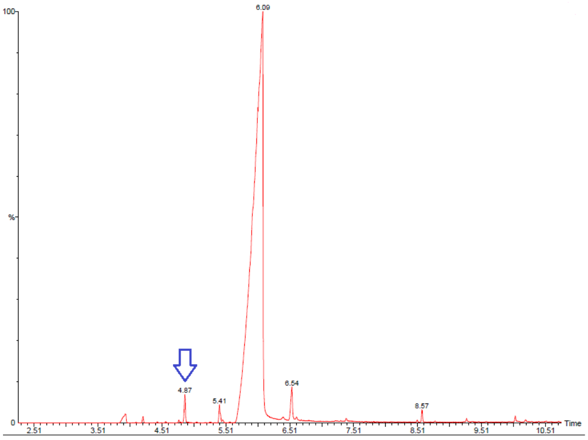
4.1.1 Cyclohexene oxidation with hydrogen peroxide and $Na_2WO_4 \cdot 2H_2O$ as additive: effect of microwave irradiation and reaction time

The reaction was initially performed in hot plate and later in microwaves, starting from the procedure of Noyori and Sato[30], but changing the following aspects with respect to their technique:

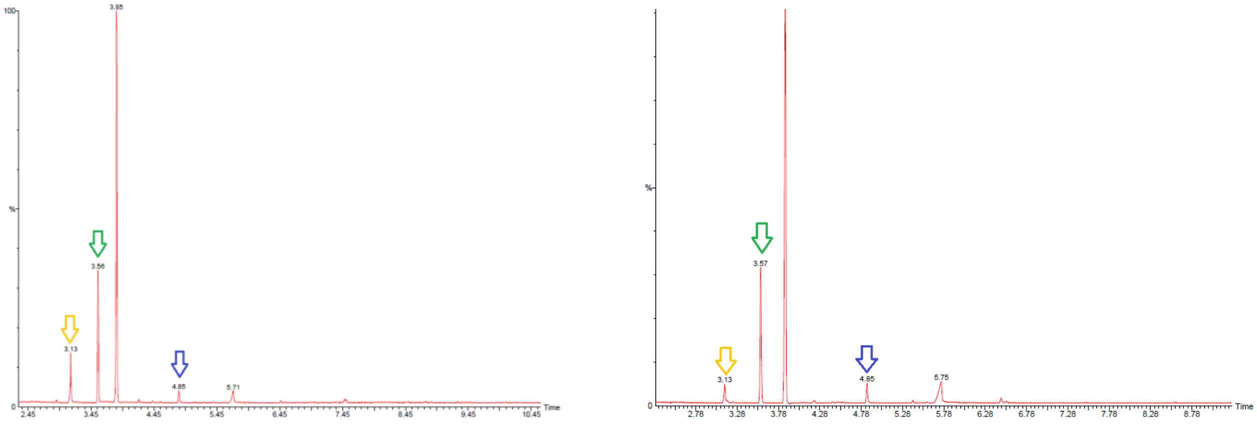
- The catalyst used is not a quaternary ammonium salt but it is iron scorpionate $FeCl_2[HC(pz)_3]$;
- the molar ratio [reactant : additive : catalyst = 100 : 1 : 1] was taken in mass basis and the amount of catalyst was halving;
- reaction time was also halving initially.

The procedures were the following (see Appendix B):

- cyclohexene oxidation with hydrogen peroxide and with additive (reaction #4).
  Add to 1 g of cyclohexene, 5 mg of catalyst and 0.01 g of $Na_2WO_4 \cdot 2H_2O$ and stir at 80 °C for 5 minutes. Add now the oxidant agent: 500 µL of hydrogen peroxide. Leave the mixture stirring at 80 °C for 4 hours in a hot plate.
- cyclohexene oxidation with hydrogen peroxide in microwaves (reaction #5).
  Add to 1 g of cyclohexene, 5 mg of catalyst and 0.01 g of $Na_2WO_4 \cdot 2H_2O$ and stir at 80 °C for 5 minutes. Add now the oxidant agent: 250 µL of hydrogen peroxide. The amount of oxidant has been decreased for safety reason of the microwave equipment use. Put the sample in the microwave oven at 80 °C for 4 hours.
- cyclohexene oxidation in microwaves, increasing reaction time (reaction #7).
  Add to 1 g of cyclohexene, 5 mg of catalyst and 0.01 g of $Na_2WO_4 \cdot 2H_2O$ and stir at 80 °C for 5 minutes. Add now 250 µL of hydrogen peroxide. Put the sample in the microwave oven at 80 °C for 8 hours.



a) reaction 4



b) reaction 5

c) reaction 7

Figure 4. 1 *Mass spectra of cyclohexene oxidation with hydrogen peroxide, $FeCl_2[HC(pz)_3]$ as catalyst and $Na_2WO_4 \cdot 2H_2O$ as additive, at 80 °C: reaction in hot plate for 4 hours (a), reaction in MW for 4 hours (b), reaction in MW for 8 hours (c). According to the qualitative analysis of the peaks, cyclohexenone, cyclohexenol and cyclohexanediol peaks are underlined with green, yellow and blue arrows, respectively.*

In all procedures, the products were extracted with ether and analyzed by mass spectroscopy, to observe product formation. Figures 4.1 report the mass spectra of the reacted mixtures.

The use of microwave irradiation seems to enhance the reaction efficiency, since in reaction 4, cyclohexanediol is the major product, while reaction 5 gives also cyclohexenone and cyclohexenol. What is also interesting is that comparing the reaction time, the mass spectra are very similar.

Hence, shorter reaction times have also been tried: 10 minutes, 30 minutes and one hour. Other parameters and conditions are kept the same (see Appendix B: reaction 75÷77).

Table 4. 1 *Experimental values for the cyclohexene oxidation*

Entry	Reaction number	Method	T [°C]	Reaction Time (min)	Yield %				TON	TOF(h^{-1})
					Cyclo-hexenol	Cyclo-hexenone	Cyclo-hexandiol	Cyclo-hexandione		
1	4	hot plate	80	240	<0.1	<0.1	2.5	2	358	89
2	5	MW	80	240	3.75	11.25	<0.1	<0.1	1192	298
3	7	MW	80	480	2.1	15.3	2.4	3.75	1872	234
4	75	MW	80	10	11.8	11.3	<0.1	<0.1	1836	11015
5	76	MW	80	30	14.06	14.13	0	0	2240	4481
6	77	MW	80	60	2.2	5	0	0	572	572

Reaction conditions, unless stated otherwise are presented in appendix B. TON = moles of product per mol of catalyst. TOF (h-1) = TON/reaction time. Additive: Na_2WO_4

Analysis in the gas chromatograph showed greater yields when the time is between 10 and 30 minutes. The best TON (turn over number) is at 30 minutes of reaction time (see Table 4.1).

4.1.2 Use of sodium tungstate dehydrate $Na_2WO_4(2H_2O)$ as oxidant.

In the reference of Noyori and Sato[30] considered so far, sodium tungstate dehydrate is used as an additive that helps oxidation of cyclohexene, and as additive it was tried.

Na_2WO_4 is a white solid, water soluble, usually employed in its hydrated form. It is obtained treating the tungsten minerals with a base: for example, the wolframite is treated with sodium hydroxide, the scheelite with sodium carbonate and the tungsten carbide with a mixture of sodium nitrate and sodium hydroxide[49]. In organic chemistry, the sodium tungstate is applied in the catalytic epoxidation of alkenes and oxidation of alcohols to give corresponding aldehydes and ketones.

In this experimental section, an attempt in using sodium tungstate as the only oxidant for cyclohexene (hence, not using hydrogen peroxide) was made.

The usual molar ratio[30] was using, always halving the amount of catalyst, therefore 500 mg of substrate reacted with 10 mg of catalyst and 20 mg of $Na_2WO_4(2H_2O)$. Three reaction times have been applied: 10, 30 and 60 minutes. No solvent was used at first.

The systems at the end of the reaction resulted liquid, with dispersed solid particles: the samples needed centrifugation in order to have a clear mixture. The resulting spectra are reported in Fig. 4.2 and yields in Table 4.2. What is particularly interesting is that, in this case, the product formation increases with the increasing of time, a behavior that was found to be exactly the opposite when using hydrogen peroxide.

However, it is again demonstrated that longer reaction time are not convenient because the reaction results to be less selective, since other products over cyclohexenol and cyclohexenone are detected. This is due probably to the fact that at longer reaction times other reactions may be involved, including catalyst decomposition.

Usually, in industry it is preferable to have low yield and high selectivity (less products but also less by-products), then reaching a high yield but with low selectivity, since the advantage of having a high output will be penalized by separation cost.

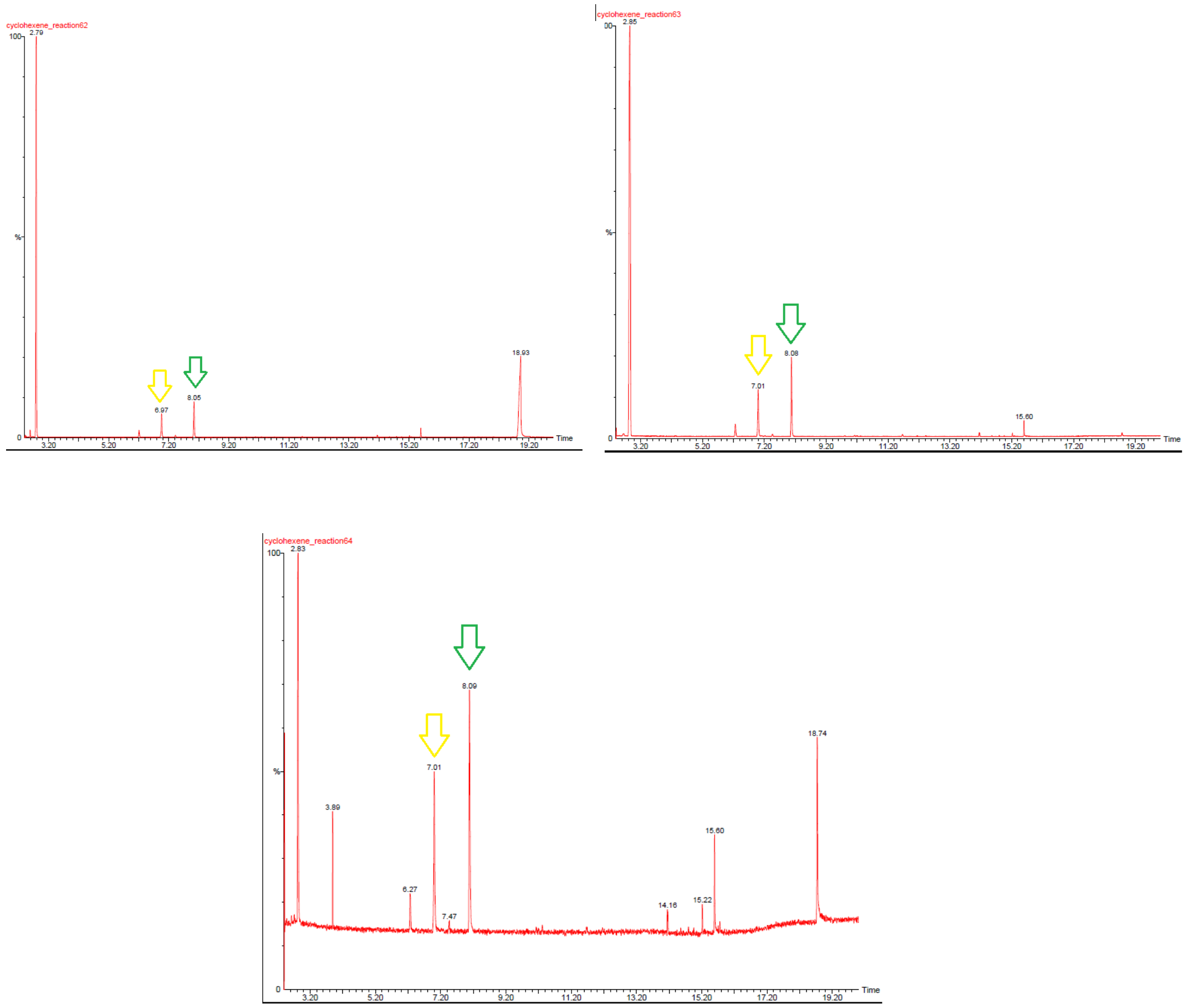


Figure 4. 2 *Mass spectra of cyclohexene oxidation in MW, with* $FeCl_2[HC(pz)_3]$ *as catalyst and* $Na_2WO_4{\cdot}2H_2O$ *as the only oxidant, at 50 °C, at different reaction times: 10 minutes (left), 30 minutes (right), 60 minutes (below). The green arrow underlines the cyclohexanone, the yellow one the cyclohexenol.*

***Table 4. 2** Experimental values for the cyclohexene oxidation*

Entry	Reaction number	Method	T [°C]	Reaction Time (min)	Yield % Cyclo-hexenol	Yield % Cyclo-hexenone	TON	TOF(h^{-1})
1	62	microwave	50	10	5.6	9.38	300	1798
2	63	microwave	50	30	2.8	14.54	347	694
3	64	microwave	50	60	5	28.4	668	668

Reaction conditions, unless stated otherwise are presented in appendix B. TON = moles of product per mol of catalyst. TOF (h-1) = TON/reaction time. Oxidant: Na_2WO_4.

4.1.3 Cyclohexene oxidation with hydrogen peroxide, no additive and reduced temperature: effect of reaction time

According to the results of the previous experiments, further reactions have been conducted with shorter time, and just one reaction has been put in microwaves overnight, to investigate a very long reaction time. Evaluated times were: 30 minutes, one hour, two hours, three hours, fifteen hours. The differences in reaction conditions with respect to the previous experiments were the following (see Appendix B, reactions 53÷57).

- The applied catalyst was the fresh-synthetized one (see §1.3); catalytic activity is expected to be higher when using fresh catalysts;
- No additive was used;
- The amount of oxidant was increased to 1 mL;
- The temperature was reduced to 50 °C.

The procedure was the following: add to 1 g of cyclohexene, 5 mg of catalyst and stir for 5 minutes at room temperature; add then 1 mL of hydrogen peroxide (30%). Put the sample in the microwave equipment at 50 °C for the desired time.

All the systems, at the end of the reaction, resulted to be biphasic, with one phase yellow pale colored, and the other brown-orange. This is due to the water formation from hydrogen peroxide that does not mix with the organic part.

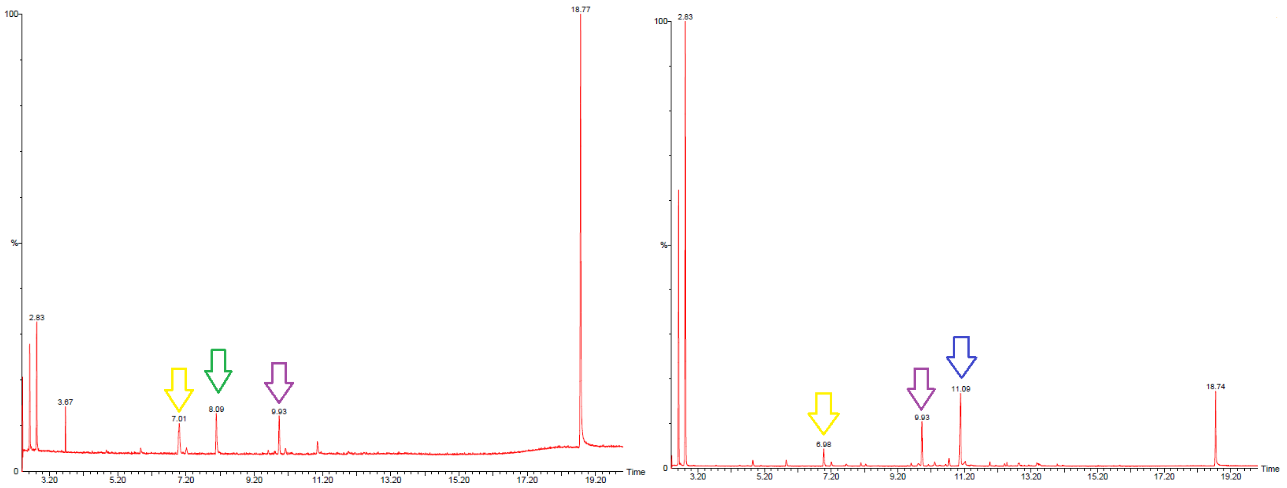
Both phases were separated and diluted with diethyl ether in order to perform the MS analysis.

The analysis showed that the products were mainly in the dark phase, while the light phase contains part of the reactant and cyclohexenone traces. The analysis also reports a decreasing in product formation with the increasing of reaction time as shown in Fig. 4.3 and Table 4.3. In fact, in the reaction with the longest time, cyclohexenone is not present. The figures represent the dark phases spectra of 30 minutes (a) and 15 hours reactions (b).

Table 4. 3 *Experimental values for the cyclohexene oxidation*

Entry	Reaction number	Method	T [°C]	Reaction Time (min)	Yield % Cyclo-hexenol	Yield % Cyclo-hexenone	Yield % Cyclo-hexandione	TON	TOF (h^{-1})
1	53	microwave	50	30	2.83	3.53	0	505	1011
2	54	microwave	50	60	1.77	2.85	0	367	367
3	55	microwave	50	120	0	1.6	1.94	281	141
4	56	microwave	50	180	0	1.24	1.6	226	75
5	57	microwave	50	900	1.63	0	7.07	691	46

Reaction conditions, unless stated otherwise are presented in appendix B. TON = moles of product per mol of catalyst. TOF (h-1) = TON/reaction time.



a) reaction 53 *b) reaction 57*

Figure 4. 3 *Comparison between mass spectra of the dark phases obtained from cyclohexene oxidation reaction, at 50 °C, without additive and with* $FeCl_2[HC(pz)_3]$*, at different reaction times: 30 minutes (a), 15 hours (b). The peak of cyclohexenone (underlined by the green arrow) is not present in the 15 hours reaction, which has instead the peak (blue) of cyclohexanediol. Yellow and purple arrows underline cyclohexenol and cyclohexandiol, respectively.*

Before proceeding with the study of cyclohexene oxidation, the reactant has been purified, in order to be sure that the peaks appearing in GC analysis come from the reaction and not from cyclohexene impurities, since cyclohexene is very easily compromised by light, heat and oxygen. To do that, at first, the thin layer chromatography method has been applied, to see if different spots except cyclohexene appear. Even if no spots was detected, cyclohexene was passed through a Pasteur pipette, in which a retention column was prepared with cotton and silica.

4.1.4 Use of HPCA as additive at low reaction times: comparison between hydrogen peroxide and TBHP

Since long reaction times seem to have no benefits on the reaction, and that an additive presence seems to enhance the product formation, according to previous experiments, the addition of HPCA has been tried at short reaction times (10 minutes and 30 minutes).

Reactant, additive and catalyst have been added still following the molar ratio used by Noyori and Sato for the cyclohexene oxidation to adipic acid[30], halving the amount of catalyst but basing the calculation on moles: this means that for 500 mg of cyclohexene, 11 mg of HPCA and 10 g of $FeCl_2[HC(pz)_3]$ are necessary. The amount of hydrogen peroxide was also halving with respect to the previous experiments (see Appendix B, reaction 58, 59).

The reacted systems still resulted biphasic: the layer on the top presented a light yellow colour, while the other phase was dark red (similar to blood); the former was diluted with diethyl ether, the latter with acetonitrile, since it revealed to be immiscible with diethyl ether.

After one night at low temperature, both phases changed their colors into transparent (the light one) and dark orange, similar to ice-tea (the dark one), both visible in Fig. 4.4.

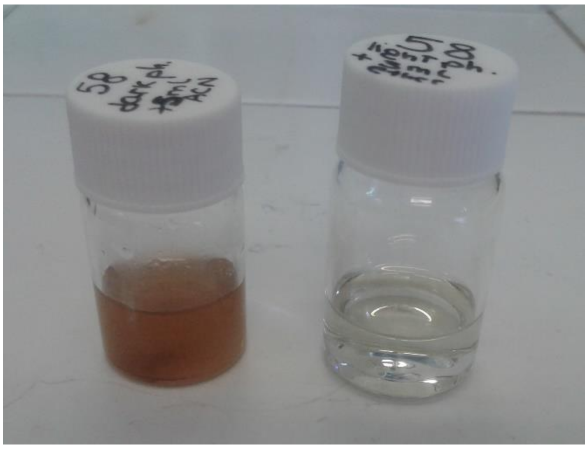


Figure 4. 4 *Dark phase and light phase, after one night at low temperature, of reaction #58: cyclohexene oxidation with hydrogen peroxide, HPCA and $FeCl_2[HC(pz)_3]$, reaction time: 10 minutes.*

A comparison between oxidants was tried, performing the same reactions with 500 µL of TBHP instead of hydrogen peroxide (reactions 60 and 61). Mass spectra of reactions 58 and 59 are reported in fig. 4.5, while reactions 60 and 61 in Fig. 4.6; results are reported in Table 4.4.

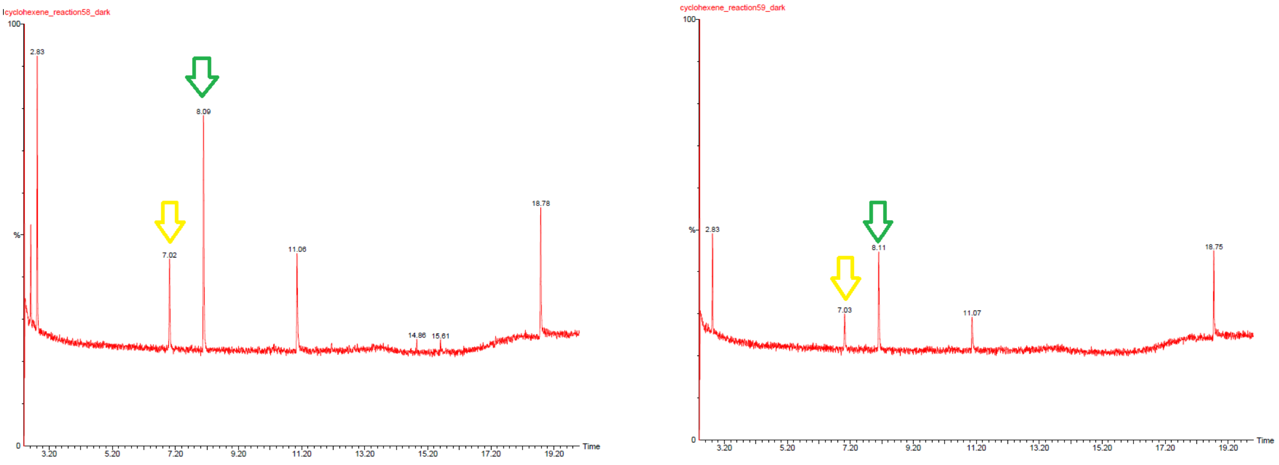
__Table 4. 4__ Experimental values for the cyclohexene oxidation (reactions 58÷61)

Entry	Reaction number	Oxidant	Method	T [°C]	Reaction Time (min)	Yield %			TON	TOF (h^{-1})
						Cyclo-hexenol	Cyclo-hexenone	Cyclo~ hexandiol		
1	58	H_2O_2	microwave	50	10	15.9	27.55	15.9	119	712
2	59	H_2O_2	microwave	50	30	2.83	8.12	3.53	29	58
3	60	TBHP	microwave	50	10	1.77	2.91	0	9	56
4	61	TBHP	microwave	50	30	1.8	3.62	0	11	22

Reaction conditions, unless stated otherwise are presented in appendix B. TON = moles of product per mol of catalyst. TOF (h-1) = TON/reaction time. Additive: HPCA.

The first noticed difference was the less developed dark phase, which was not a continuous phase but a dispersed one, letting assume that less products were produced. This would promote the reactions with hydrogen peroxide, since better developed phases means an easier phase separation.

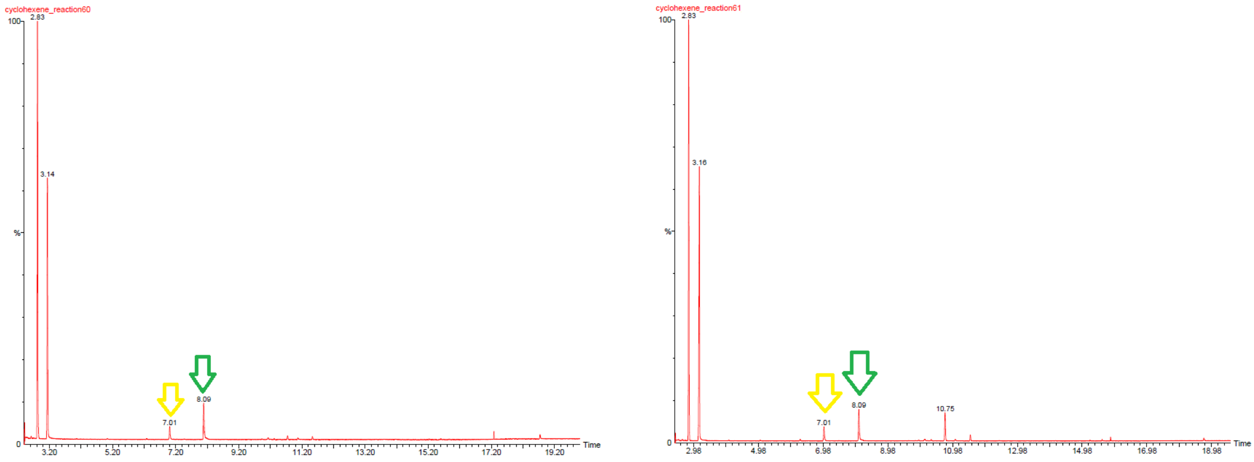
Another detail to underline is that the reaction at only 10 minutes has a similar chromatogram to the ones at 30 minutes.



a) reaction 58

b) reaction 59

__Figure 4. 5__ Mass spectra of cyclohexene oxidation with hydrogen peroxide, at 50 °C, with $FeCl_2[HC(pz)_3]$ and HPCA, at different reaction times: 10 minutes (a), 30 minutes (b). The peaks of cyclohexenone and cyclohexenol are underlined by the green and the yellow arrow, respectively.



a) reaction 60 *b) reaction 61*

Figure 2. 6 *Mass spectra of cyclohexene oxidation with TBHP, at 50 °C, with $FeCl_2[HC(pz)_3]$ and HPCA, at different reaction times: 10 minutes (a), 30 minutes (b). The peaks of cyclohexenone and cyclohexenol are underlined by the green and the yellow arrow, respectively.*

4.1.5 Cyclohexene oxidation with hydrogen peroxide using ionic liquids as solvents

One of the main aim when performing a catalytic reaction is the recovery and reuse of the catalyst, since it is often an expensive compound. One of the way to achieve this is running the reaction with ionic liquids. As explained in the paragraph 3.1, they allow having a biphasic system, in which the catalyst remains in the ionic liquid while the products stay in the organic phase: the catalyst is recovered by extracting the products and reusing the ionic liquid.

The two tested ionic liquids in this case are $[C_6mim][Ntf2]$ and [P66614][DCA].

10 mg of $FeCl_2[HC(pz)_3]$ has been added to 1.5 mL of each ionic liquid: a green mixture has been obtained. At the end of the reactions, the green color turned into orange, letting assume that the oxidation state of iron changed.

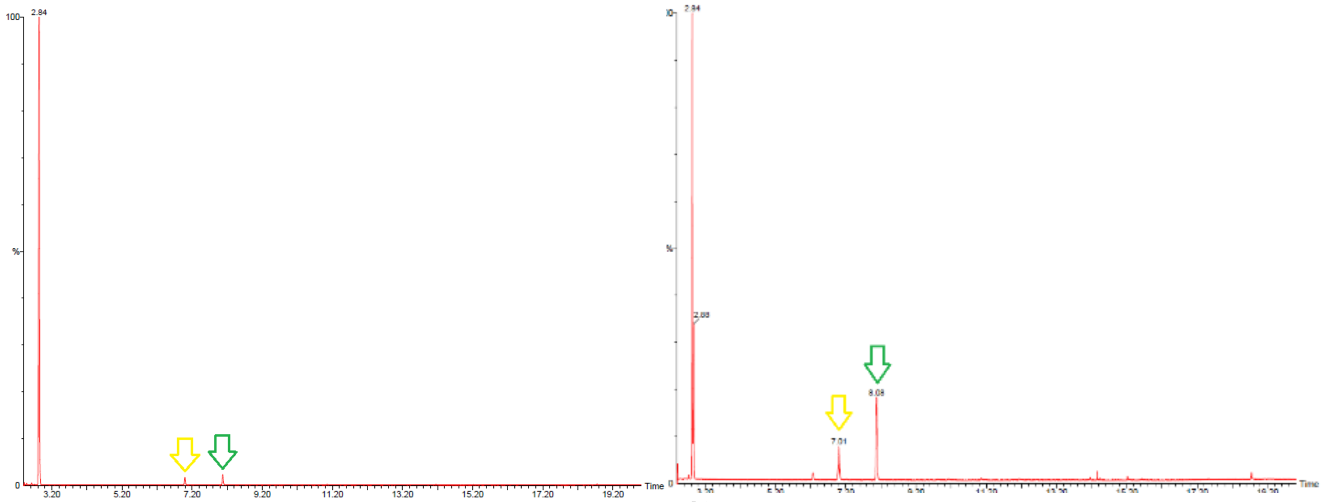
The reactions have been performed in MW, at 50 °C for 30 minutes. Reactant and oxidant are added in a molar ratio of 1:3. Parameters and conditions are resumed in Appendix B (reaction 73 and 74).

Table 4. 5 *Experimental values for the cyclohexene oxidation (reactions 73, 74)*

Entry	Reaction number	Oxidant	Method	T [°C]	RT (min)	Yield %		TON	TOF (h^{-1})
						Cyclo-hexenol	Cyclo-hexenone		
1	73	H_2O_2	microwave	50	30	0.71	1.42	9	17
2	74	H_2O_2	microwave	50	30	3.53	6.36	40	79

Reaction conditions, unless stated otherwise are presented in appendix B. TON = moles of product per mol of catalyst. TOF (h-1) = TON/reaction time.

The reaction with [C_6mim][Ntf2] resulted biphasic, with the catalyst located in the ionic liquid, while in the reaction with [P66614][DCA], the catalyst moved to the organic phase, as revealed by the orange color of this phase. This probably means that the catalyst was decomposed. In both reactions, the organic phase was extracted with ether, centrifuged when needed and analyzed with GC-MS.
The results show that the reaction with [P66614][DCA] is more effective (Fig. 4.7 and Table 4.5), but since the catalyst is lost, there is no reason to use this ionic liquid.



a) reaction 73

b) reaction 74

Figure 4. 7 *Mass spectra of cyclohexene oxidation in MW, with $FeCl_2[HC(pz)_3]$ as catalyst, at 50 °C and 30 minutes, using different ionic liquids: [C_6mim][Ntf_2] (a) and [P66614][DCA] (b). Cyclohexenone is underlined by the green arrow, cyclohexenol by the yellow arrow.*

4.1.6 Cyclohexene oxidation with hydrogen peroxide using water as solvent: additive comparison

When speaking about green processes, one of the most obvious choice among solvents is water, if the process conditions and the involved chemicals allow its use. Water presents several advantages:

- low cost and high availability (however, not everywhere in the world);
- possible creation of biphasic systems;
- non-flammable and non-toxic;
- high specific heat capacity (exothermic reactions can be controlled more safely).

This last one can also represent a disadvantage, since it makes the system difficult to be heated up or cooled down rapidly. Moreover, water use can be limited by the following factors:

- low solubility of organic substrates;
- the necessary treatment of aqueous waste;
- the energy intensive distillation used to remove salts prior water use (salts can corrode industrial equipment).

Cyclohexene oxidation has been performed with water as solvent, since the catalyst $FeCl_2[HC(pz)_3]$ is soluble in this medium. In order to understand the benefit of the presence of water, the same reactions have been studied as solvent-free systems at the same conditions (30 minutes at 50 °C).

Since the use of an additive in the previous experiments revealed to improve the efficiency of the oxidation, three different additives have been compared: HNO_3, HPCA and $Na_2WO_4 \cdot 2H_2O$. The amount of additives was lowered with respect to previous experiments, in order to see if they improve the efficiency even when added in small quantity.

The quantities of the substances involved have been calculated with the molar ratios reported in Table 4.6.

***Table 4. 6** Molar ratios used in the cyclohexene oxidation*

		HPCA	HNO_3	$Na_2WO_4 \cdot 2H_2O$
n(oxidant) / n(reactant)	1.5			
n(catalyst) / n(oxidant)	0.002			
n(additive) / n(catalyst)		2	10	2

Therefore, for 500 µL of cyclohexene (corresponding to 7.5 mmol), these amounts were used:

- Hydrogen peroxide (30%): 225 µL;
- $FeCl_2[HC(pz)_3]$: 5 mg;
- HNO_3: 6.2 µL;
- HPCA: 5.5 mg;
- $Na_2WO_4 \cdot 2H_2O$: 10 mg;
- Water: 3mL.

All the reaction parameters are listed in Appendix B (reactions 90÷101).

The reactions have been run first in MW equipment and then in a hot plate, to compare the alternative energy source with the conventional heating system.

After adding ether, in order to extract the products, the systems became biphasic and the organic phase has been analyzed in the gas chromatograph. The reactions using water presented of course a greater aqueous phase, making easier the phase separation.

It was not possible to analyze the reactions performed in the hot plate (reactions 96÷101), since the pressure in the vials increased consistently, making impossible to proceed with the reaction. This is another reason to choose the microwaves as energy source, since it controls and withstands the pressure (until its construction limit), and when it does not, it stops the reaction safely. The oxidant/reactant molar ratio was chosen equal to one for safety reason, but a lower one should be considered, when the hot plate is employed.

Results are very poor, for both solvent-free and water-solvent systems (Table 4.7). An increase in catalyst and additives quantities and in temperature should be investigated.

***Table 4. 7** Cyclohexenol and cyclohexenone yield for reactions 90÷95*

Entry	Reaction number	Oxidant	Additive	Solvent	T [°C]	Reaction Time (min)	Yield %		TON	TOF (h^{-1})
							Cyclo-hexenol	Cyclo-hexenone		
1	90	H_2O_2	HPCA	-	50	30	0.15	0.36	20	41
2	91	H_2O_2	HNO_3	-	50	30	0.03	0.03	2	5
3	92	H_2O_2	Na_2WO_4	-	50	30	0.12	0.34	18	37
4	93	H_2O_2	HPCA	water	50	30	0.03	0.06	4	7
5	94	H_2O_2	HNO_3	water	50	30	0.64	0.61	50	99
6	95	H_2O_2	Na_2WO_4	water	50	30	0.45	0.67	45	89

Reaction conditions, unless stated otherwise are presented in appendix B. TON = moles of product per mol of catalyst. TOF (h-1) = TON/reaction time.

Despite the low yields, it can be noticed that water improves the yield, except for the case using HCPA as additive. The best case is when sodium tungstate is used.

An interesting case can be the investigation of this additive in combination with the hydrogen peroxide when no catalyst is used, so when they are the only promoters of the reaction. A comparison between different systems has been made:

- system in which the sodium tungstate co-operates with the hydrogen peroxide and the catalyst;
- system with hydrogen peroxide and catalyst in which no additive is used;
- system with hydrogen peroxide and sodium tungstate in which the catalyst is not used to enhance the reaction (blank samples).

For each reaction, two experiments have been made: one using no solvent, one using 3 mL of water. Calculated yields are reported in Table 4.8.

Reaction parameters are:

- temperature: 80 °C
- reaction time: 4 hours
- sodium tungstate (when used): 10 mg
- hydrogen peroxide (30%): 0.25 mL
- cyclohexene: 1 g
- $FeCl_2[HC(pz)_3]$ (when used): 5 mg

Table 4. 8 *Cyclohexenol and cyclohexenone yield of reactions 102÷107*

Entry	Reaction number	Oxidant	Catalyst	Solvent	Yield %		TON	TOF (h^{-1})
					Cyclo-hexenol	Cyclo-hexenone		
1	102	H_2O_2	$FeCl_2[HC(pz)_3]$	Water	0.18	0.63	64	16
2	103	H_2O_2	$FeCl_2[HC(pz)_3]$	-	0.37	0.83	95	24
3	104	H_2O_2	$FeCl_2[HC(pz)_3]$	Water	0.07	0.19	21	5
4	105	H_2O_2	$FeCl_2[HC(pz)_3]$	-	0.22	0.76	78	19
5	106	H_2O_2	-	Water	1.29	2.74	0	0
6	107	H_2O_2	-	-	0.63	1.14	0	0

Reaction conditions, unless stated otherwise are presented in appendix B. TON = moles of product per mol of catalyst. TOF (h-1) = TON/reaction time. Additive: Na_2WO_4.

It is interesting to observe that the solvent free reactions in the presence of catalyst (Table 4.8, entries 2 and 4) show an increase of yield. This indicates that a greener process without the presence of a solvent will be favorable, and therefore it will be necessary to undertake further studies.

Reactions 102, 103 and 104 have been then repeated for 15 hours, in order to observe the catalyst behaviour for long reaction time (see Appendix B, reactions 108÷110).

The same trend regarding the absence of solvent is showed (Table 4.9, entry 2); moreover, it appears that the solvent free reaction is independent of reaction time, which could be an advantageous characteristic of these reactional systems.

Table 4. 9 *Cyclohexenol and cyclohexenone yields for reactions 108, 109, 110.*

Entry	Reaction number	Oxidant	Additive	Solvent	Yield %		TON	TOF (h^{-1})
					Cyclo-hexenol	Cyclo-hexenone		
1	108	H_2O_2	Na_2WO_4	Water	0.66	0.22	70	5
2	109	H_2O_2	Na_2WO_4	-	1.21	1.83	242	16
3	110	H_2O_2	-	Water	0.25	0.05	24	2

Reaction conditions, unless stated otherwise are presented in appendix B. ndition: stated in Appendix B. TON = moles of product per mol of catalyst. TOF (h-1) = TON/reaction time.

4.1.7 Cyclohexene oxidation using OXONE®

Recently, a work of Parida and Moorthy[33] showed the possibility of olefin oxidation into the corresponding carboxylic acids, using OXONE®. OXONE® is the registered trademark of DuPont for a blend of potassium peroxymonosulfate ($KHSO_5 \cdot 0.5KHSO_4 \cdot 0.5K2SO_4$), whose use as oxidant or co-oxidant in oxidative transformation is increasing, in virtue of its cheap availability and its environmentally benign characteristics.

Parida and Moorthy[33] tried to oxidize cyclohexene, using 3 equivalent of OXONE® in a mixture of water and acetonitrile 1:1 v/v, at 60 °C under reflux and with a reaction time of 11 hours, obtaining adipic acid with an yield of 58%. This procedure was repeated (reaction 112), also performing the reaction in the microwave equipment (reaction 113): to 1 mmol of cyclohexene, corresponding to 100 µL, 0.92 g of OXONE®, corresponding to 3 mmol, was added.

At the end of the reactions, the products have been extracted with 4 mL of ethyl acetate and to the extracted part benzaldehyde was added.

No product was detected in the reaction with the hot plate, while the mass spectrum of the reaction in the microwave shows the presence of cyclohexanediol (Table 4.10, entries 1 and 2).

With the presence of the iron scorpionate complex (Table 4.10, entries 3 and 4), an increase in cyclohexanediol yield is observed.

Table 4. 10 *Cyclohexene oxidation using OXONE®*

Entry	Reaction number	Solvent	Additive	Method	T [°C]	Reaction Time (min)	Yield % Cyclo-hexanediol	TON	TOF (h^{-1})
1	112	ACN-H2O	-	hot plate	60	660	0	0	0
2	113	ACN-H2O	-	MW	60	660	1.94	0	0
3	114	ACN-H2O	-	MW	60	660	3.5	23	2
4	115	ACN-H2O	HPCA	MW	60	660	8.3	55	5

Reaction conditions, unless stated otherwise are presented in appendix B. TON = moles of product per mol of catalyst. TOF (h-1) = TON/reaction time.

As observed in entry 4, the presence of an additive further increases the yield. In all cases where there is product detection, there is 100% selectivity towards cyclohexanediol. This result is promising, but more research is required in order to assemble an industrial procedure.

4.2 Molybdenum-based complexes as catalysts for cyclohexene oxidation

Molybdenum(VI)-based catalysts are very versatile in olefin epoxidation, although titanium is industrially more used, since it is more stable in heterogeneous systems.

The most recent studies on molybdenum complexes for cyclohexene oxidation with TBHP regard bis-oxomolybdenum acetylacetonate supported on silica gel[29] and oxidation with hydrogen peroxide applying octamolybdate and tetraperoxodimolybdate[7].

In the past years, scientific research focused more on finding effective ways to support the molybdenum catalyst, testing them on cyclohexene oxidation, since homogeneous systems are very promising but they have the drawback of the difficult separation and the unrecoverable catalyst. Goto *et al.*[15] studied complexes of molybdenum hexacarbonyl on polymeric masters (polystyrene), employing TBHP as oxidant and benzene as solvent. The reaction was 100% selective towards the epoxide. Barradas *et al.*[5] applied supports of silica bearing ethylenediamine ligands to immobilize $Mo(CO)_6$ and $MoO_2(acac)_2$; the oxidation was conducted with TBHP, in dichloroethane. The major success was the fact that the molybdenum did not leach from the surface in which it was supported, but these silica systems caused a decrease in the epoxidation rate with respect to other supports.

Other work to mention are from Gnecco *et al.*[13] and from Wang *et al.*[50]: although the studies on molybdenum complexes reveal to be promising in terms of catalytic activity, several drawbacks are always present, such as the use of hazardous organic solvents and halides.

In this project, molybdenum(II) carbonile complexes have been applied in the cyclohexene oxidation, trying to perform the reaction with conditions as greener as possible, thus employing hydrogen peroxide as oxidant, no solvents and no additives, and using microwaves as energy source.

4.2.1 Use of Mo-based catalysts at low reaction times, with hydrogen peroxide, without solvents and additives

The tested catalysts are (see §1.4):

- MS11 ($MoBrO_2N_4C_{23}H_{15}$)
- MS14 ($MoBrO_2N_2C_{17}H_{13}$)
- MS104 ($MoBrO_2N_2C_{23}H_{29}$)
- MS154 ($MoPF_6N_3O_4C_{25}H_{22}$)

Each catalysts have been tried at 50 °C, at two different reaction times, 10 minutes and 30 minutes, and the molar ratio employed is the following: [Reactant : additive : catalyst = 100 : 1 : 0.2]. The reactions have been conducted without additives, in order to verify if these catalysts are effective for cyclohexene oxidation without using any other additional substance. Therefore, for 1 mL of cyclohexene (corresponding to 9.87 mmol), the following quantities have been calculated:

- MS11: 10.5 mg;
- MS14: 14.3 mg;
- MS104: 10.2 mg;
- MS154: 8.6 mg.

The catalysts have been dissolved in the reactant, so as no additional solvent was used.

The amount of hydrogen peroxide was calculated as follows:

$$\frac{moles\ (oxidant)}{moles\ (reactant)} = 3$$

The figures 4.8÷4.11 and Table 4.11 show the presence of products even with 10 minutes of reaction time.

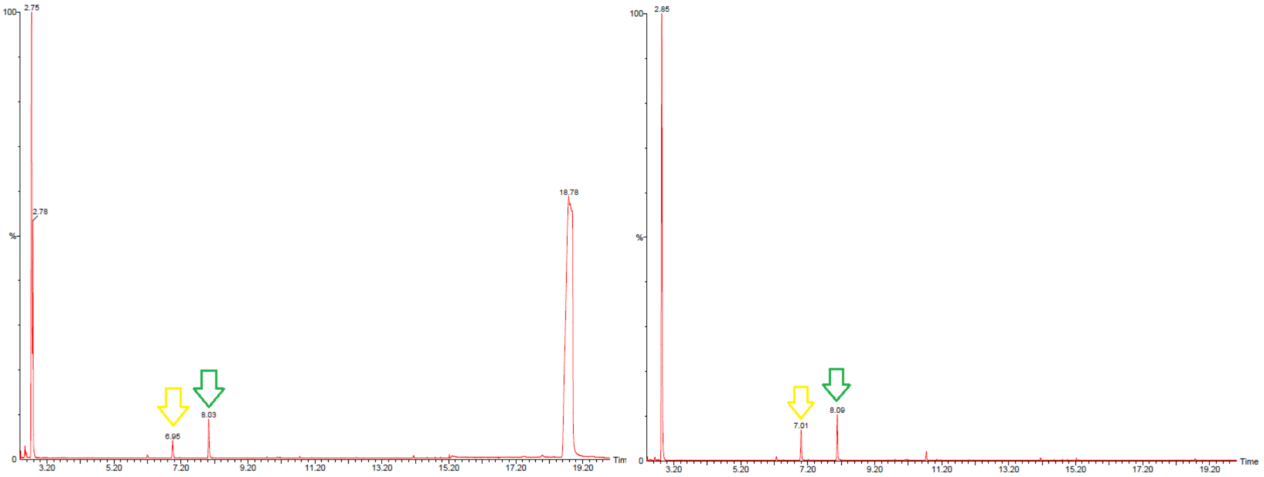


Figure 4. 8 *Mass spectra of cyclohexene oxidation with hydrogen peroxide, catalyzed by MS11, at 50 °C, at different reaction time: 10 (left) and 30 (right) minutes. Yellow and green arrows indicate respectively cyclohexenol and cyclohexenone.*

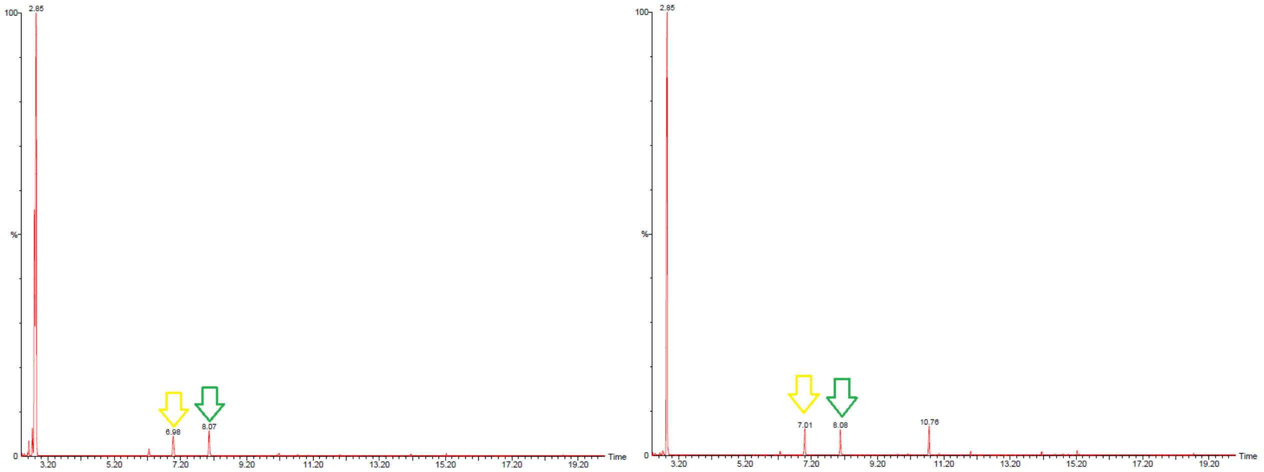


Figure 4. 9 *Mass spectra of cyclohexene oxidation with hydrogen peroxide, catalyzed by MS14, at 50 °C, at different reaction time: 10 (left) and 30 (right) minutes. Yellow and green arrows indicate respectively cyclohexenol and cyclohexenone.*

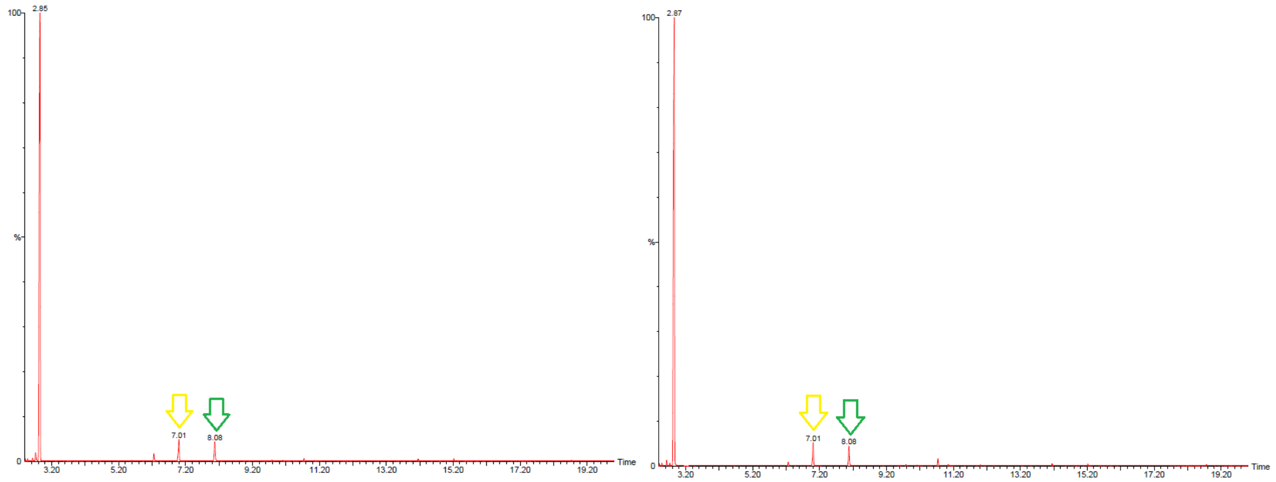


Figure 4. 10 *Mass spectra of cyclohexene oxidation with hydrogen peroxide, catalyzed by MS104, at 50 °C, at different reaction time: 10 (left) and 30 (right) minutes. Yellow and green arrows indicate respectively cyclohexenol and cyclohexenone.*

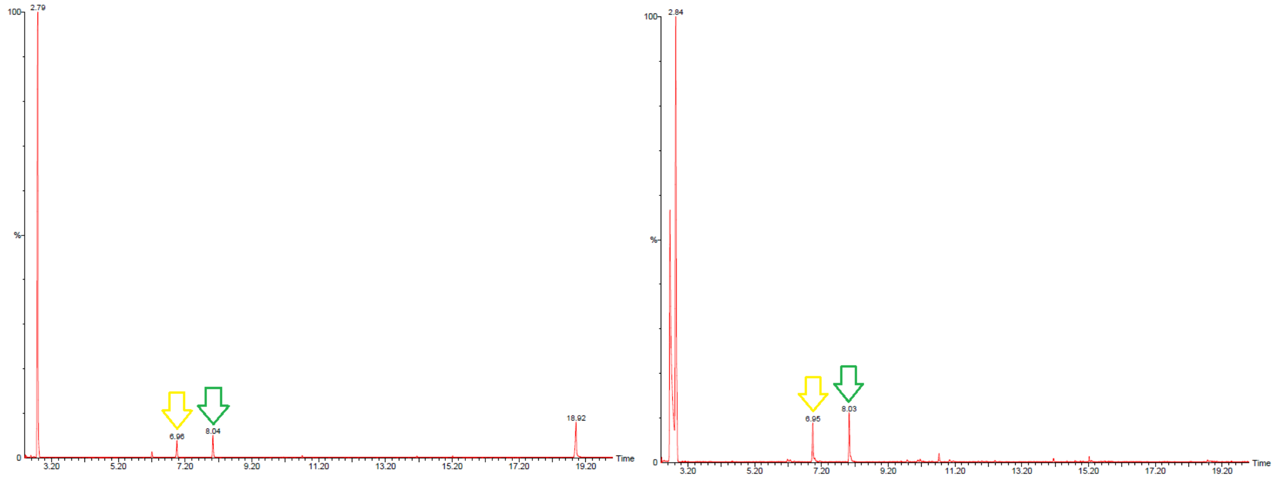


Figure 4. 11 *Mass spectra of cyclohexene oxidation with hydrogen peroxide, catalyzed by MS154, at 50 °C, at different reaction time: 10 (left) and 30 (right) minutes. Yellow and green arrows indicate respectively cyclohexenol and cyclohexenone.*

Table 4. 11 *Cyclohexene oxidation using Mo-based catalysts*

Entry	Reaction number	Catalyst	Method	T [°C]	Reaction Time (min)	Selectivity %	
						Cyclohexenol	Cyclohexenone
1	65	MS11	MW	50	10	35.3	64.7
2	66	MS11	MW	50	30	42.1	57.9
3	67	MS14	MW	50	10	43.8	56.3
4	68	MS14	MW	50	30	52.9	47.1
5	69	MS104	MW	50	10	54.5	45.5
6	70	MS104	MW	50	30	55.0	45.0
7	71	MS154	MW	50	10	58.3	41.7
8	72	MS154	MW	50	30	42.9	57.1

Reaction conditions, unless stated otherwise are presented in appendix B. Selectivity = production rate of one component per production rate of overall components

4.3 Temperature screening for iron and molybdenum catalysts

A temperature screening has been done on the reactions that applied $FeCl_2[HC(pz)_3]$, MS14, MS104 and MS 154, in order to optimize this parameter for each case.

The evaluated cases (Table 4.12) are all performed in MW, employing the conditions analyzed in the previous experiments. All parameters and quantities are reported in Appendix B.

Table 4. 12 *Evaluated cases in the temperature screening*

Catalyst	**Additive**	**Oxidant**	**Solvent**	**Time [min]**	**Reaction #**
		CASE 1			
$FeCl_2[HC(pz)_3]$	$Na_2WO_4 \cdot 2H_2O$	H_2O_2 (30%)	None	30	78, 79
		CASE 2			
$FeCl_2[HC(pz)_3]$	HPCA	H_2O_2 (30%)	None	10	80-82
		CASE 3			
MS14	None	H_2O_2 (30%)	None	30	83, 84
		CASE 4			
MS104	None	H_2O_2 (30%)	None	30	85, 86
		CASE 5			
MS154	None	H_2O_2 (30%)	None	30	87, 88

Case 1 was evaluated at 30 °C and 50 °C, since 80 °C was already tried in previous experiments.

On the contrary, case from 3 to 5, were evaluated at 30 °C and 80 °C, being performed already at 50 °C. Case 2 was evaluated for all the three temperatures.

The products have been extracted using diethyl ether, allowing a better separation from the catalyst and the water produced by the reaction.

An interesting fact occurred in Case 2. The extracted phase of reaction at 30 °C was transparent, but yellow at 50 °C and orange at 80 °C, letting assumed that at 80 °C the catalyst was dispersed in all the reaction mixture. Therefore, a centrifugation was necessary before injecting the solution in the gas chromatograph, but the samples were destroyed in the centrifuge, probably due to the high amount of oxidant still present.

The reactions could not be analyzed in the gas chromatograph, since it was discovered that nitromethane, which was added at the end of the reactions, was not a proper internal standard for cyclohexene oxidation (see § 4.5). Therefore, this reaction series has to be repeated, when a suitable internal standard will be found.

4.4 Magnetization of the $FeCl_2[HC(pz)_3]$ as recycle technique

The synthesized $FeCl_2[HC(pz)_3]$ was magnetized using titanium dioxide core shell, in order to allow an easy recycle of the catalyst from the reaction mixture, by using a magnet to remove it.

The catalyst was applied in cyclohexene oxidation with hydrogen peroxide, without using additives nor solvents. The usual molar ratios were employed: [Reactant : Catalyst = 100 : 0.5], [Oxidant : Reactant = 3 : 1].

Since previous experiments showed better efficiency at short reaction time, 30 minutes has been chosen as reaction time.

At 30 °C, the system resulted biphasic, with the catalyst in the lower phase. It was not possible to recover the catalyst with a magnet since the wet particles were too small. Therefore, the lower phase was separated and centrifuged, and the recovered catalytic powder has been let drying under the fumehood. However, the loss of the magnetic property from the supported catalyst was quite evident in this case, and no recycling experiment was performed.

Both phases were diluted with ether but the lower one was not miscible, and still presented dispersed catalyst particles.

4.5 Search of proper internal standard for GC analysis

In order to obtain the value of the yield, the reaction is analyzed in a gas chromatograph that produces a chromatogram in which each volatile substance has its own peak, defined by the retention time and area. To determine the exact amount of a substance, an internal standard is added. The substance chosen to be the internal standard cannot react with any of the compounds and should be inert to the experimental conditions where it will be used. For non-mechanistic experiments, the internal standard is added to the reaction before the analysis; knowing the exact amount of internal standard, the calculation of the concentration of the other substances (reactant and desired products) is possible (see the method in Appendix A).

Some odd yield/conversion results revealed that nitromethane might be not the right internal standard for cyclohexene oxidation, in fact, it has been proven that is not inert in the reaction mixture. The adopted procedure was preparing different flasks in which the standard solution has been built step by step and analyzed with the gas chromatography. The first step is to analyze the solvent of the

reaction with the internal standard, then a mixture composed by solvent, internal standard and reactant, and at the end the complete solution (solvent, internal standard, reactant, desired product).
To be inert, the internal standard has to show a peak, whose area is always constant (a little decreasing is acceptable, because the dilution in the different steps has to be considered).
The first analyzed solution, composed by 3 mL of ether and 50 µL of nitromethane, reported a peak for the internal standard at 2.60 minutes, with an area of 34907 mm^2. The second solution was made of 3 mL of ether, 50 µL of nitromethane and 100 µL of cyclohexene and gave a peak at 2.60 minutes, with an area of 21431 mm^2 for nitromethane. The difference between the two values is considered too high, and although other proofs are not necessary, the complete reference solution (3 mL of ether, 50 µL of nitromethane, 100 µL of cyclohexene, 50 µL of cyclohexenol and 50 µL of cyclohexenone) was also analyzed, giving a peak area of 22378 mm^2 for the nitromethane.
The same procedure was applied to study the cycloheptanone as internal standard.
At first, a solution of 3 mL of diethyl ether and 50 µL of cycloheptanone was analyzed. Then the same components plus 100 µL of cyclohexene were analyzed. The peak areas of cycloheptanone were 45639 mm^2 and 147569 mm^2, respectively, letting assume that cycloheptanone is present in cyclohexene as an impurity. Hence, not even cycloheptanone is a good internal standard in this case.
Octane, nonane and bromobenzene were also studied; octane was used by Carrasco *et al.*[7], nonane by Gnecco *et al.*[13] and bromobenzene by Barradas *et al.*[5].
Three solution were prepared as usual, for each internal standards:

- Solution 1: 3 mL of ether + 50 µL of internal standard;
- Solution 2: 3 mL of ether + 50 µL of internal standard + 100 µL of cyclohexene;
- Solution 3: 3 mL of ether + 50 µL of internal standard + 100 µL of cyclohexene + 50 µL of cyclohexenone + 50 µL of cyclohexenol.

The peak areas of the internal standards in the different solutions are reported in Table 4.13.

Table 4. 13 *Retention times and peak areas of octane, nonane and bromobenzene in the three different solution*

	Octane retention time [min]	Octane peak area [mm^2]	Nonane retention time [min]	Nonane peak area [mm^2]	Bromobenzene retention time [min]	Bromobenzene peak area [mm^2]
Solution 1	10.93	24742	8.03	36339	9.12	151121
Solution 2	10.94	26158	8.08	166047	9.16	159610
Solution 3	10.95	52669	8.12	359991	9.17	353377

Octane presents a quite constant peak area when cyclohexene is added, but the area increases when the complete solution is analyzed. However, since an increase in the cyclohexene peak was also noticed, this can be due to mixing issue: the solution should be well mixed before being injected, but mixing can heat the sample causing ether evaporation.

Nonane and bromobenzene cannot be used as internal standards, since the former has the same retention time of the cyclohexenol and the latter has the same retention time of the cyclohexenone. This is also demonstrated by the big increase of the areas when analyzing the complete solutions.

At last, benzaldehyde and cyclopentanone have been also analyzed, since they are used as internal standards in alkane oxidation. Their peak areas are reported in Table 4.14.

Table 4. 14 *Benzaldehyde and cyclopentanone peak areas for the different solutions*

	Benzaldehyde retention time [min]	Benzaldehyde peak area [mm^2]	Cyclopentanone retention time [min]	Cyclopentanone peak area [mm^2]
Solution 1	9.82	32975	5.85	102797
Solution 2	9.81	39106	5.87	68452
Solution 3	9.85	166264	-	-

In the case of the benzaldehyde, the big peak increase in solution 3 could also be seen for cyclohexenol and cyclohexenone with respect to former analyzed reference solutions at the same concentration. This suggests that ether has partially evaporated: the evaporation causes higher concentrations of the other substances in the mixture and therefore bigger peak areas in the chromatogram.

An ice bath was then employed, in order to prevent ether loss, but this hindered a good mixing of the substances (verifiable by the very low peaks obtained in the chromatogram). Of course, low temperature does not favor the mixing, so a good compromise has to be chosen. The best procedure was found to be the following: as soon as the reference solution is prepared, it has to be mixed in a vial with a tightly closed cap for some minutes and it has to stay some minutes at room temperature (20 °C), before injection. The same procedure has to be adopted when adding the internal standard to the reactions to be tested.

From solution 1 to solution 2, cyclopentanone presents already a peak that decreases consistently. For this reason, it could not be considered a good internal standard for cyclohexene oxidation and solution 3 was not prepared.

Concluding, benzaldehyde seems to be the most suitable internal standard for the case.

Another interesting fact is that in the GC-Fisons (see Appendix C), cyclohexenol and cyclohexenone exit the column at the same time, so they give only one indistinct peak. This is due to their boiling points, which are very close: 164 °C for cyclohexenol, 171 °C for cyclohexenone. Therefore, in order to have two distinct peaks and evaluate the single yields in the cyclohexene oxidation, the GC-MS (see Appendix C) has to be used.

Chapter 5

Cyclohexane oxidation experimental section

5.1 Reaction mechanism of peroxidative oxidation

The peroxidative oxidation of cyclohexane is believed to proceed via radical mechanism, which involves oxygen, carbon radicals and a metal-based oxidant (as MOOH or M=O)[45]. The metal-peroxo intermediates can act on the product formation, through the following different reactions:

- Direct attack of the alkane, thus aging like a metal-based oxidant producing the corresponding alcohol (4.1) or the corresponding ketone (4.2);
- homolytic bond O-O break (4.3), producing $M^{n+1}=O$ and radical HO·. Both react with the alkane, giving radicals R· (4.4 and 4.5);
- heterolysis of O-O bond (4.6), giving the $M^{n+2}=O$ which attacks the alkane, giving radical R· (4.7);
- hemolysis of M-O bond (4.8), producing radicals HOO· that can undergo disproportionation to H_2O_2 and O_2 (4.9);
- reaction with formed radical R·, that gives the peroxide (4.10), or the alcohol ROH (4.11).

The mechanism proposed is:

$$M^nOOH + RH \rightarrow M^nOH + ROH \tag{4.1}$$

$$M^nOOH + RH \rightarrow M^{n+1} + [R = O] + H_2O \tag{4.2}$$

$$M^nOOH \rightarrow [M^{n+1} = O] + HO\cdot \tag{4.3}$$

$$HO\cdot + RH \rightarrow R\cdot + H_2O \tag{4.4}$$

$$[M^{n+1} = O] + RH \rightarrow R\cdot + M^nOH \tag{4.5}$$

$$M^nOOH \rightarrow [M^{n+2} = O] + HO^- \tag{4.6}$$

$$[M^{n+2} = O] + RH \rightarrow R\cdot + M^{n+1}OH \tag{4.7}$$

$$M^nOOH \rightarrow M^{n-1} + HOO\cdot \tag{4.8}$$

$$HOO\cdot + HOO\cdot \rightarrow H_2O_2 + O_2 \tag{4.9}$$

$$R\cdot + M^nOOH \rightarrow ROOH + M^{n-1} \tag{4.10}$$

$$R\cdot + M^nOOH \rightarrow ROH + [M^{n+1} = O] \tag{4.11}$$

Scheme 5. 1 *Cyclohexane oxidation mechanism*

In order to get an insight into the mechanism of the catalytic reaction, the oxidation of cyclohexane was performed in the presence of a radical trap ($CBrCl_3$ or Ph_2NH as a trap for C- or O-centred radicals, respectively) also used in homogeneous conditions[39]. The drastic decrease in the yield (by *ca.* 95−87%) suggests that the reaction proceeds mainly *via* a radical mechanism[39].

5.2 Cyclohexane oxidation applying $FeCl_2[HC(pz)_3]$ as catalyst

Synthetized $FeCl_2[HC(pz)_3]$ (see § 1.3) has been applied in cyclohexane oxidation. Expected products are cyclohexanol and cyclohexanone.

Silva *et al.*[45], using acetonitrile a solvent, a reaction time of 6 hours and an inert atmosphere of nitrogen as reaction environment, have already employed this catalyst in cyclohexane oxidation with hydrogen peroxide. In this project, several changes have been made in order to obtain a greener reaction: microwave irradiation, shorter reaction time, organic solvent replacement and no inert atmosphere have been adopted. HPCA has been applied as additive, in all the experimented reactions.

5.2.1 Use of different ionic liquids as solvents

Cyclohexane oxidation has been conducted with different ionic liquids as solvents and using alternatively the hot plate and the microwave irradiation as energy sources.

At first attempt, cyclohexane has been oxidized by TBHP, at 50 °C, for one hour, employing 0.5 g of ionic liquid $[C_4mim][NTf_2]$. Proper TBHP/cyclohexane molar ratio range is between 2 and 5. A molar ratio of 3.2 has been chosen, therefore, for 0.25 mL of cyclohexane (corresponding to 2.3×10^{-3} moles), 0.72 mL of TBHP (10 mmol) has been added. For an amount of 8 mg of catalyst, 50 mg of additive has been added, corresponding to a HPCA/catalyst molar ratio of 10.

The procedure is the following:

- <u>REACTION 9</u>: Cyclohexane oxidation in MW with ionic liquid and TBHP.
  First, solubility of the ionic liquid in ether has to be checked. Proceed with these chemicals only if two phases are created. Add 0.5 g of $[C_4mim][Ntf_2]$ to 8 mg of catalyst, stir for 5 minutes, add 50 mg of HPCA and stir again for 5 minutes. Then add the reactant and the oxidant: 250 µL of cyclohexane and 720 µL of TBHP, in this order. Let it stir for one hour at 50 °C in the microwave equipment. When the reaction is over, add 5 mL of ether to form a biphasic system and let it stir for 5 minutes in the fumehood. Let the vial cool down, and then extract the ether, that will contain the reaction products. Add to them 50 µL of standard (nitromethane).
- <u>REACTION 10</u>: Cyclohexane oxidation in normal heating with ionic liquid with TBHP.
  The procedure is the same of reaction 9, the only difference is that MW is not used.

Resumed parameters and quantities can be found in Appendix B.

Both reactions have to be diluted with ether in order to make GC analysis. Since addition of triphenylphosphine prior to the GC analysis can increase in the amount of the expected alcohol, due to reduction of the peroxide by PPh_3 (Shul'pin method)[26], a little amount of PPh_3 has been added

gradually to the samples, until the phosphine can no longer dissolve. The reason why the phosphine is not poured all in once is that the peroxide reduction is a high exothermic reaction.
GC analysis and relative calculations provide the results reported in Table 5.1 (the method to calculate yield and conversion from GC data is reported in Appendix A).

Table 5. 1 *Cyclohexane conversion and product yields of reaction 9 and 10.*

Entry	Reaction number	IL	Method	T [°C]	Reaction Time (min)	Cyclohexane conversion (%)	Yield %		TON	TOF (h^{-1})
							Cyclo-hexanol	Cyclo-hexanone		
1	9	[C_4mim][Ntf_2]	MW	50	60	97.17	0.48	29.83	291	291
2	10	[C_4mim][Ntf_2]	hot plate	50	60	98.13	2.56	10.18	122	122

Reaction conditions, unless stated otherwise are presented in appendix B. Conversion (%) = production rate of products component per substrate. TON = moles of product per mol of catalyst. TOF (h-1) = TON/reaction time.

Next step was replacing the TBHP with the greener oxidant hydrogen peroxide (30%), using alternatively hot plate and microwaves and the following ionic liquids (see §3.1.1):

- [C_4mim][Ntf_2]
- CYPHOS 105®
- [C_8mim][Ntf_2]

The procedures are reported below:

- REACTION 11: Cyclohexane oxidation in hot plate with ionic liquid: [C_4mim][Ntf_2].
  Add 0.5 mL of [C_4mim][Ntf_2] to 3 mg of catalyst, stir for 5 minutes, add 20 mg of HPCA and stir again for 5 minutes. Then add the reactant and the oxidant: 250 µL of cyclohexane and 500 µL of H_2O_2 (30%). Stir for 6 hours at 30 °C on a hot plate. When the reaction is over, add 5 mL of ether to form a biphasic system and let it stir for 5 minutes in the fumehood. Let the vial cool down, then extract the ether, that will contain the reaction products. Add 50 µL of standard (nitromethane).
- REACTION 12: Same procedure of reaction 11, but using microwaves and reducing reaction time to 2 hours.
- REACTION 13: Same procedure of reaction 11, changing ionic liquid: CYPHOS 105®.
- REACTION 14: Same procedure of reaction 13, but using microwaves and reducing reaction time to 2 hours.
- REACTION 15: Same procedure of reaction 11, changing ionic liquid: [C_8mim][Ntf_2].
- REACTION 16: Same procedure of reaction 15, but using microwaves and reducing reaction time to 2 hours.

Resumed parameters and quantities can be found in Appendix B.

The reason why the molar ratio oxidant/reactant has been reduced to two is to diminish the oxidant amount in order to prevent pressure problems in the microwave equipment while using hydrogen peroxide. This is also the reason why the temperature is set to 30 °C instead of 50 °C, and the reaction time is 6 hours for the hot plate, but 2 hours for the microwaves.

All products formed were identified by GC and their retention times confirmed with those of commercially available products. Nitromethane (0.05 mL) was used as GC internal standard.

The reaction mixtures were analyzed twice by GC: with and without adding an excess of solid triphenylphosphine. The addition of this phosphine to the final organic phase reduces cyclohexyl hydroperoxide, if present, to the corresponding alcohol, and hydrogen peroxide to water. Comparison of the results of both analyses allows estimate the amount of cyclohexyl hydroperoxide, following a method developed by Shul'pin[44]. Blank experiments in ionic liquid were performed and confirmed that no alkane oxidation products (or only traces, below 1%) were obtained in the absence of the metal catalyst. The catalytic activity of the ligand was also tested and no products were detected[44].

Regarding reactions in microwaves (12, 14 and 16) the system resulted triphasic after ether extraction. Therefore, NMR analysis has been done before the GC analysis, in order to understand what every phase contains (Fig. 5.1).

Figure 5. 1 *Triphasic mixture (reaction 12): the upper layer is the ether phase, in the middle there is the water phase, while the lowest layer is the IL phase*

Product yields were calculated from the GC data (see Appendix A) and results are reported in Table 5.2.

Table 5. 2 *Cyclohexane oxidation using ILs*

Entry	Reaction number	IL	Method	T [°C]	Reaction Time (min)	Yield %		TON	TOF (h^{-1})
						Cyclo-hexanol	Cyclo-hexanone		
1	11	[C_4mim][Ntf_2]	hot plate	30	360	2	21	220	37
2	12	[C_4mim][Ntf_2]	MW	30	120	4.2	36.1	386	193
3	13	CYPHOS 105	hot plate	30	360	4.6	7.2	113	19
4	14	CYPHOS 105	MW	30	120	0.5	18.4	181	91
5	15	[C_8mim][Ntf_2]	hot plate	30	360	1.2	18.1	185	31
6	16	[C_8mim][Ntf_2]	MW	30	120	1.3	22.4	227	114

Reaction conditions, unless stated otherwise are presented in appendix B.

The presence of different ionic liquids in the reactions tends to produce very different results. This is possibly due to their different density and viscosity.

It is also interesting to see, from the differences between reactions using hot plate and reactions using microwave, how the heating source is a crucial component: the type of heating is one of the key elements in a new and greener process.

5.3 Molybdenum-based complexes as catalysts in cyclohexane oxidation

Molybdenum is widely used in catalytic complexes for alkenes epoxidation, but they are not used for the less reactive alkanes. In this project, some Mb-based catalysts that were synthesized in the laboratory of Group V have been tested in cyclohexane oxidation reaction. These five different catalysts are (see §1.4):

- MS11 ($MoBrO_2N_4C_{23}H_{15}$)
- MS104 ($MoBrO_2N_2C_{23}H_{29}$)
- MS154 ($MoPF_6N_3O_4C_{25}H_{22}$)
- MS155 ($MoPF_6N_3O_4C_{31}H_{38}$)
- MS14 ($MoBrO_2N_2C_{17}H_{13}$)

The goal is to investigate if these catalysts are effective for cyclohexane oxidation, therefore, at first attempt, all the reactions have been conducted with the same parameters and no additive. These are:

- temperature: 50 °C
- reaction time: 2 hours in MW

- 3 mL of solvent (acetonitrile)[25]
- 10 mmol of oxidant
- amount of catalyst according to the amount of oxidant[25]:

$$\frac{moles\ (oxidant)}{moles\ (catalyst)} * 10^{-3} = 2.5$$

- amount of reactant according to the amount of oxidant[25]:

$$\frac{moles\ (oxidant)}{moles\ (reactant)} = 2$$

Reaction 18-22 apply hydrogen peroxide (30%) as oxidant, reactions 23-27 apply TBHP (all parameters are reported in Appendix B). In the table 5.3, the corresponding catalyst for each reaction is shown.

Table 5. 3 *Type of catalyst and quantity for each reaction.*

Reaction	**Catalyst**	**Qt [mg]**
18, 23	MS 11	2.2
19, 24	MS 104	2.2
20, 25	MS 154	2.7
21, 26	MS 155	3
22, 27	MS 14	1.8

Reactions 19 and 20 gave expected products, but with very low yield, while reaction 24, 26 and 27 seemed to give promising results. However, it has been verified with GC analysis and mass spectroscopy that the resulted peak in 24, 26 and 27 is not corresponding to cyclohexanone, but to the tert-butyl alcohol coming from TBHP molecule, used as oxidant, that has a retention time similar to cyclohexanone. In the table 5.4, reaction yields are shown.

In order to see the effect of reaction time on the yield, a reaction time screening has been conducted applying both the oxidants.

Table 5. 4 *Cyclohexane oxidation applying Mo-based catalysts*

Entry	Reaction number	Oxidant	Method	T [°C]	Reaction Time (min)	Yield %		TON	TOF (h^{-1})
						Cyclo-hexanol	Cyclo-hexanone		
1	17	H_2O_2	hot plate	50	120	0.00	0.00	0	0
2	18	H_2O_2	MW	50	120	0.00		0	0
3	19	H_2O_2	MW	50	120	0.00	0.06	1	0
4	20	H_2O_2	MW	50	120	0.22	0.11	5	2
5	21	H_2O_2	MW	50	120	0.00	0.00	0	0
6	22	H_2O_2	MW	50	120	0.00	0.00	0	0
7	23	TBHP	MW	50	120			0	0
8	24	TBHP	MW	50	120	0.01	0.09	1	0
9	25	TBHP	MW	50	120	0.20	0.08	4	2
10	26	TBHP	MW	50	120	0.00	0.00	0	0
11	27	TBHP	MW	50	120	0.90	0.10	25	13

Reaction conditions, unless stated otherwise are presented in appendix B.

5.3.1 Effect of reaction time on reactions applying TBHP.

The study was made repeating the same conditions of reactions 24, 26 and 27, but varying the reaction time from 2 hours to 15 minutes:

- REACTION 30: cyclohexane oxidation in microwaves for 15 minutes. Add 2.2 g of MS104 to 3 mL of acetonitrile and stir the mixture. Add the reactant (540 µL of cyclohexane) and the oxidant (1 mL of TBHP) in this order. Put the reaction in microwaves for 15 minutes a 50 °C.
- REACTION 31: cyclohexane oxidation in microwaves for 15 minutes. Add 3 g of MS155 to 3 mL of acetonitrile and stir the mixture. Add the reactant (540 µL of cyclohexane) and the oxidant (1 mL of TBHP) in this order. Put the reaction in microwaves for 15 minutes a 50 °C.
- REACTION 32: cyclohexane oxidation in microwaves for 15 minutes. Add 1.8 g of MS14 to 3 mL of acetonitrile and stir the mixture. Add the reactant (540 µL of cyclohexane) and the oxidant (1 mL of TBHP) in this order. Put the reaction in microwaves for 15 minutes a 50 °C.

Later, the study proceed with different reaction time: 30 minutes, 1 hour, 3 hours, 24 hours. Other reaction conditions as well as chemicals quantities have been kept constant (see Appendix B, reactions 33÷44).

Results from GC analysis showed that there was no effect of reaction time on the yield, in fact, the peak corresponding to TBHP always appears nearby cyclohexanone retention time, but no cyclohexanone or cyclohexanol are detected.

5.3.2 Effect of reaction time on reactions applying H_2O_2 (30%)

At first attempt, as for TBHP, a reaction time of 15 minutes has been tried on reaction 19 and 20 (those using MS 104 and MS 154 respectively), keeping the other parameters at the same conditions. Resuming them:

- REACTION 28: cyclohexane oxidation in microwaves for 15 minutes. Add 2.2 g of MS104 to 3 mL of acetonitrile and stir the mixture. Add the reactant (540 µL of cyclohexane) and the oxidant (1 mL of hydrogen peroxide 30%) in this order. Put the reaction in microwaves for 15 minutes a 50 °C.
- REACTION 29: cyclohexane oxidation in microwaves for 15 minutes. Add 2.7 g of MS154 to 3 mL of acetonitrile and stir the mixture. Add the reactant (540 µL of cyclohexane) and the oxidant (1 mL of hydrogen peroxide 30%) in this order. Put the reaction in microwaves for 15 minutes a 50 °C.

Other reaction times have been tried for both catalysts: 30 minutes, one hour, two hours, three hours (see Appendix B, reactions 45÷52). Any product has been detected by GC analysis in any reaction.

Conclusions

Green chemistry is nowadays a central issue in the innovation of chemical industry, with which our daily life is strictly related. This approach means to pursue industrial sustainability, finding eco-friendly processes but maintaining a good efficiency and productivity, two aspects that it is not always simple to keep together.

In this project, some green techniques have been applied in the study of cyclohexene and cyclohexane oxidation, catalyzed by a complex made of a scorpionate ligand and iron ($FeCl_2[HC(pz)_3]$) and by molybdenum-based complexes. Among the used techniques, microwave irradiation, organic solvent replacement and application of hydrogen peroxide as oxidant agent, have been the most studied and discussed.

In the cyclohexane oxidation, $FeCl_2[HC(pz)_3]$ was first studied with $[C_4mim][Ntf_2]$ and TBHP, to allow a comparison between microwave irradiation and conventional heating source. The results showed that microwave irradiation enhances the reaction yield in all cases (*e.g.* 30% against 12%, entries 1 and 2 from Table 5.1). The TBHP was then replaced with the greener H_2O_2 (30%), and a ILs survey was made ($[C_4mim][Ntf_2]$, $[C_8mim][Ntf_2]$, CYPHOS105®). In all cases, small amounts or no products were detected in the reactions performed with conventional heating.

Although molybdenum is not as employed in alkane oxidation as iron, five different molybdenum complexes (MS11, MS14, MS104, MS154, MS155) were also tested with cyclohexane, comparing TBHP and H_2O_2 (30%). A reaction time screening has also been done, but only small amounts of products were observed. From the studies performed, it can be concluded that these molybdenum-based complexes gave no benefits in the different conditions tested.

Although in this project more attention was given to cyclohexene, due the fact that few published results were found, it is worth to mention that cyclohexane oxidation is considered a "hot topic" in chemistry.

Application of iron-based catalysts on cyclohexene oxidation is scarcely reported and $FeCl_2[HC(pz)_3]$ (or scorpionate compounds in general) has never been tried. As reported, several conditions were studied using this catalyst; namely the effect of oxidant, time, solvent and quantity. At first, the catalyst was tried with hydrogen peroxide and sodium tungstate as additive, to compare the microwave irradiation with the conventional heating: with the hot plate, only cyclohexanediol was obtained, while with MW, also cyclohexenol and cyclohexenone were observed. Comparing the mass spectra of the MW reactions, long residence time did not bring any advantage.

The sodium tungstate, previously used as additive, was also tried as only oxidant. From the analyzed mass spectra, longer time seems to be more effective, a behavior that was found to be opposite with hydrogen peroxide. However, selectivity decreased for longer times.

Shorter times were chosen to make a comparison between oxidants, TBHP and hydrogen peroxide, using HPCA as additive and no solvent. One of the first thing to notice is that the resulted biphasic system is less developed when using TBHP, as there is no water (that instead comes from the reaction with the peroxide); this makes the phase separation more difficult, therefore, since the results are similar, hydrogen peroxide is preferable. Another interesting result is that even in 10 minutes, products can be obtained.

Two ionic liquids were tried as solvents in the cyclohexene oxidation with hydrogen peroxide: $[P_{66614}][DCA]$ and $[C_6mim][Ntf_2]$. The former was more effective but it did not retain the catalyst, therefore it was considered useless.

Since $FeCl_2[HC(pz)_3]$ is water-soluble, a comparison between solvent-free systems and water-systems was studied, evaluating also microwave irradiation vs. conventional heating and different additives. Reactions in hot plates were not completed because of pressure problems. Results were very poor, both for solvent-free systems and water-systems. Those systems were also studied applying the combined effect of sodium tungstate and hydrogen peroxide, with and without the catalyst: the system water/peroxide/tungstate gave better yield (although quite low) with respect to water/catalyst/peroxide and water/catalyst/peroxide/tungstate systems and to all the solvent-free cases. Reactions with the catalyst were repeated for longer time, but the slightly yield improvement does not justify the employment of such long time.

Cyclohexene oxidation with OXONE® was also performed: the presence of the catalyst $FeCl_2[HC(pz)_3]$ improves the product yield, which is further enhanced by the additive HPCA.

Magnetization of $FeCl_2[HC(pz)_3]$ was investigated as recycle technique, however the recovery of the catalyst failed because the wet particles were too small and with loss of the magnetic moment. The centrifugation of the sample and the drying of the recovered catalyst also failed because the catalyst loss was too consistent.

Since molybdenum catalysts are versatile and much used in olefin oxidation, some complexes (MS11, MS14, MS104, MS154) were tried in cyclohexene oxidation with hydrogen peroxide, without solvents or additives. Products were already present after 10 minutes and there were not substantial differences between the mass spectra at 10 and 30 minutes.

A search of a proper internal standard for cyclohexene oxidation was also conducted: among cycloheptanone, octane, nonane, bromobenzene benzaldehyde and cyclopentanone, benzaldehyde was chosen.

Future works on this project should be considered according to the cases: for the most effective reaction conditions a decrease in the oxidant/catalyst molar should be investigated. A temperature screening is also advised, in order to understand the activity range of the catalysts, as well as a study on the additive/catalyst molar ratio.

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Appendix A

Gas chromatography

In order to be able to identify the peaks from a GC analysis and to do the relative calculation of yield and conversion, a reference solution is needed. This reference solution is called *standard solution* and it has to contain, in known amounts, the reactant, the expected products, the solvent used in the reaction and an internal standard component. This internal standard component has to be added to the reaction mixture as well, just before the GC injection, in order to avoid possible additional reactions. By examining the results of the standard solution, it is possible to ascribe to a component its relative peak, because every component has a different residence time in the GC column. Since GC analysis provides also the area of the peaks, which is proportional to the amount of the component in the mixture, the reaction mixture is analyzed to evaluate yield, conversion and selectivity.
Therefore, the concentration of the product in the reaction mixture has been calculated through the following equation:

$$C(product) = \frac{A(product\ in\ reaction) * A(int.st\ in\ standard) * C(product\ in\ standard) * C(int.st\ in\ reaction)}{A(int.st\ in\ reaction) * A(product\ in\ standard) * C(int.st\ in\ standard)}$$

C = concentration of the substance
A = area of the peak
int.st = component used as internal standard

Once the product concentration is known, the reactant concentration is calculated in the same way:

$$C(remaining\ reactant) = \frac{A(reactant\ in\ reaction) * A(product\ in\ standard) * C(react.in\ standard) * C(\ prod.in\ reaction)}{A(product\ in\ reaction) * A(reactant\ in\ standard) * C(product\ in\ standard)}$$

Now that the remaining reactant concentration and the product concentration are known, conversion, yield and selectivity can be obtained:

$$Y = \frac{C(product)}{C°(reactant)} * 100$$

$$X = \frac{C°(reactant) - C(remaining\ reactant)}{C°(reactant)} * 100$$

$$S_A = \frac{C(product\ A)}{C(all\ products)} * 100$$

Y = product yield
X = reactant conversion
S_A = selectivity with respect to product A
C° = initial concentration

Appendix B

Reaction list

B.1 Cyclohexane oxidation

Entry	React.n°	reactant	Qt [µL]	oxidant	Qt [µL]	Catalyst	Qt [mg]
1	9	cyclohexane	250	TBHP	720	$FeCl_2[HC(pz)_3]$	8
2	10	cyclohexane	250	TBHP	720	$FeCl_2[HC(pz)_3]$	8
3	11	cyclohexane	250	H_2O_2	500	$FeCl_2[HC(pz)_3]$	3
4	12	cyclohexane	250	H_2O_2	500	$FeCl_2[HC(pz)_3]$	3
5	13	cyclohexane	250	H_2O_2	500	$FeCl_2[HC(pz)_3]$	3
6	14	cyclohexane	250	H_2O_2	500	$FeCl_2[HC(pz)_3]$	3
7	15	cyclohexane	250	H_2O_2	500	$FeCl_2[HC(pz)_3]$	3
8	16	cyclohexane	250	H_2O_2	500	$FeCl_2[HC(pz)_3]$	3
9	17	cyclohexane	540	H_2O_2	1000	MS11	2,2
10	18	cyclohexane	540	H_2O_2	1000	MS11	2,2
11	19	cyclohexane	540	H_2O_2	1000	MS104	2,2
12	20	cyclohexane	540	H_2O_2	1000	MS154	2,7
13	21	cyclohexane	540	H_2O_2	1000	MS155	3
14	22	cyclohexane	540	H_2O_2	1000	MS14	1,8
15	23	cyclohexane	540	TBHP	1000	MS11	2,2
16	24	cyclohexane	540	TBHP	1000	MS104	2,2
17	25	cyclohexane	540	TBHP	1000	MS154	2,7
18	26	cyclohexane	540	TBHP	1000	MS155	3
19	27	cyclohexane	540	TBHP	1000	MS14	1,8
20	28	cyclohexane	540	H_2O_2	1000	MS104	2,2
21	29	cyclohexane	540	H_2O_2	1000	MS154	2,7
22	30	cyclohexane	540	TBHP	1000	MS104	2,2
23	31	cyclohexane	540	TBHP	1000	MS155	3
24	32	cyclohexane	540	TBHP	1000	MS14	1,8
25	33	cyclohexane	540	TBHP	1000	MS104	2,2
26	34	cyclohexane	540	TBHP	1000	MS155	3
27	35	cyclohexane	540	TBHP	1000	MS14	1,8

28	36	cyclohexane	540	TBHP	1000	MS104	2,2
29	37	cyclohexane	540	TBHP	1000	MS155	3
30	38	cyclohexane	540	TBHP	1000	MS14	1,8
31	39	cyclohexane	540	TBHP	1000	MS104	2,2
32	40	cyclohexane	540	TBHP	1000	MS155	3
33	41	cyclohexane	540	TBHP	1000	MS14	1,8
34	42	cyclohexane	540	TBHP	1000	MS104	2,2
35	43	cyclohexane	540	TBHP	1000	MS155	3
36	44	cyclohexane	540	TBHP	1000	MS14	1,8
37	45	cyclohexane	540	H_2O_2	1000	MS104	2,2
38	46	cyclohexane	540	H_2O_2	1000	MS154	2,7
39	47	cyclohexane	540	H_2O_2	1000	MS104	2,2
40	48	cyclohexane	540	H_2O_2	1000	MS154	2,7
41	49	cyclohexane	540	H_2O_2	1000	MS104	2,2
42	50	cyclohexane	540	H_2O_2	1000	MS154	2,7
43	51	cyclohexane	540	H_2O_2	1000	MS104	2,2
44	52	cyclohexane	540	H_2O_2	1000	MS154	2,7

Entry	React.n°	Additive	Qt [mg]	Solvent	Qt [µL]	Method	T [°C]	RT [min]
1	9	HPCA	50	C_4mim Ntf$_2$	0,5 (g)	MW	50	60
2	10	HPCA	50	C_4mim Ntf$_2$	0,5 (g)	HP	50	60
3	11	HPCA	20	C_4mim Ntf$_2$	500	HP	30	360
4	12	HPCA	20	C_4mim Ntf$_2$	500	MW	30	120
5	13	HPCA	20	CYPHOS 105	500	HP	30	360
6	14	HPCA	20	CYPHOS 105	500	MW	30	120
7	15	HPCA	20	C_8mim Ntf$_2$	500	HP	30	360
8	16	HPCA	20	C_8mim Ntf$_2$	500	MW	30	120
9	17	-		ACN	3000	HP	50	120
10	18	-		ACN	3000	MW	50	120
11	19	-		ACN	3000	MW	50	120
12	20	-		ACN	3000	MW	50	120
13	21	-		ACN	3000	MW	50	120
14	22	-		ACN	3000	MW	50	120
15	23	-		ACN	3000	MW	50	120
16	24	-		ACN	3000	MW	50	120

17	25	-		ACN	3000	MW	50	120
18	26	-		ACN	3000	MW	50	120
19	27	-		ACN	3000	MW	50	120
20	28	-		ACN	3000	MW	50	15
21	29	-		ACN	3000	MW	50	15
22	30	-		ACN	3000	MW	50	15
23	31	-		ACN	3000	MW	50	15
24	32	-		ACN	3000	MW	50	15
25	33	-		ACN	3000	MW	50	30
26	34	-		ACN	3000	MW	50	30
27	35	-		ACN	3000	MW	50	30
28	36	-		ACN	3000	MW	50	60
29	37	-		ACN	3000	MW	50	60
30	38	-		ACN	3000	MW	50	60
31	39	-		ACN	3000	MW	50	180
32	40	-		ACN	3000	MW	50	180
33	41	-		ACN	3000	MW	50	180
34	42	-		ACN	3000	MW	50	1440
35	43	-		ACN	3000	MW	50	1440
36	44	-		ACN	3000	MW	50	1440
37	45	-		ACN	3000	MW	50	30
38	46	-		ACN	3000	MW	50	30
39	47	-		ACN	3000	MW	50	60
40	48	-		ACN	3000	MW	50	60
41	49	-		ACN	3000	MW	50	120
42	50	-		ACN	3000	MW	50	120
43	51	-		ACN	3000	MW	50	180
44	52	-		ACN	3000	MW	50	180

B.2 Cyclohexene oxidation

Entry	n°	reactant	Qt [µL]	oxidant	Qt [µL]	Catalyst	Qt [mg]
1	4	cyclohexene	1200	H_2O_2	500	$FeCl_2[HC(pz)_3]$	5
2	5	cyclohexene	1200	H_2O_2	250	$FeCl_2[HC(pz)_3]$	5
3	7	cyclohexene	1200	H_2O_2	250	$FeCl_2[HC(pz)_3]$	5
4	53	cyclohexene	1200	H_2O_2	1000	$FeCl_2[HC(pz)_3]$	5
5	54	cyclohexene	1200	H_2O_2	1000	$FeCl_2[HC(pz)_3]$	5
6	55	cyclohexene	1200	H_2O_2	1000	$FeCl_2[HC(pz)_3]$	5
7	56	cyclohexene	1200	H_2O_2	1000	$FeCl_2[HC(pz)_3]$	5
8	57	cyclohexene	1200	H_2O_2	1000	$FeCl_2[HC(pz)_3]$	5
9	58	cyclohexene	600	H_2O_2	500	$FeCl_2[HC(pz)_3]$	10
10	59	cyclohexene	600	H_2O_2	500	$FeCl_2[HC(pz)_3]$	10
11	60	cyclohexene	600	TBHP	500	$FeCl_2[HC(pz)_3]$	10
12	61	cyclohexene	600	TBHP	500	$FeCl_2[HC(pz)_3]$	10
13	62	cyclohexene	600	Na_2WO_4	(20 mg)	$FeCl_2[HC(pz)_3]$	10
14	63	cyclohexene	600	Na_2WO_4	(20 mg)	$FeCl_2[HC(pz)_3]$	10
15	64	cyclohexene	600	Na_2WO_4	(20 mg)	$FeCl_2[HC(pz)_3]$	10
16	65	cyclohexene	1000	H_2O_2	1000	MS11	11
17	66	cyclohexene	1000	H_2O_2	1000	MS11	11
18	67	cyclohexene	1000	H_2O_2	1000	MS14	14
19	68	cyclohexene	1000	H_2O_2	1000	MS14	14
20	69	cyclohexene	1000	H_2O_2	1000	MS104	10
21	70	cyclohexene	1000	H_2O_2	1000	MS104	10
22	71	cyclohexene	1000	H_2O_2	1000	MS154	9
23	72	cyclohexene	1000	H_2O_2	1000	MS154	9
24	73	cyclohexene	1000	H_2O_2	1000	$FeCl_2[HC(pz)_3]$	10
25	74	cyclohexene	1000	H_2O_2	1000	$FeCl_2[HC(pz)_3]$	10
26	75	cyclohexene	1200	H_2O_2	250	$FeCl_2[HC(pz)_3]$	5
27	76	cyclohexene	1200	H_2O_2	250	$FeCl_2[HC(pz)_3]$	5
28	77	cyclohexene	1200	H_2O_2	250	$FeCl_2[HC(pz)_3]$	5
29	78	cyclohexene	1200	H_2O_2	250	$FeCl_2[HC(pz)_3]$	5
30	79	cyclohexene	1200	H_2O_2	250	$FeCl_2[HC(pz)_3]$	5
31	80	cyclohexene	600	H_2O_2	500	$FeCl_2[HC(pz)_3]$	10
32	81	cyclohexene	600	H_2O_2	500	$FeCl_2[HC(pz)_3]$	10
33	82	cyclohexene	600	H_2O_2	500	$FeCl_2[HC(pz)_3]$	10
34	83	cyclohexene	1000	H_2O_2	1000	MS14	14
35	84	cyclohexene	1000	H_2O_2	1000	MS14	14

36	85	cyclohexene	1000	H_2O_2	1000	MS104	10
37	86	cyclohexene	1000	H_2O_2	1000	MS104	10
38	87	cyclohexene	1000	H_2O_2	1000	MS154	9
39	88	cyclohexene	1000	H_2O_2	1000	MS154	9
40	89	cyclohexene	600	H_2O_2	600	$FeCl_2[HC(pz)_3]$	10
41	90	cyclohexene	500	H_2O_2	225	$FeCl_2[HC(pz)_3]$	5
42	91	cyclohexene	500	H_2O_2	225	$FeCl_2[HC(pz)_3]$	5
43	92	cyclohexene	500	H_2O_2	225	$FeCl_2[HC(pz)_3]$	5
44	93	cyclohexene	500	H_2O_2	225	$FeCl_2[HC(pz)_3]$	5
45	94	cyclohexene	500	H_2O_2	225	$FeCl_2[HC(pz)_3]$	5
46	95	cyclohexene	500	H_2O_2	225	$FeCl_2[HC(pz)_3]$	5
47	96	cyclohexene	500	H_2O_2	225	$FeCl_2[HC(pz)_3]$	5
48	97	cyclohexene	500	H_2O_2	225	$FeCl_2[HC(pz)_3]$	5
49	98	cyclohexene	500	H_2O_2	225	$FeCl_2[HC(pz)_3]$	5
50	99	cyclohexene	500	H_2O_2	225	$FeCl_2[HC(pz)_3]$	5
51	100	cyclohexene	500	H_2O_2	225	$FeCl_2[HC(pz)_3]$	5
52	101	cyclohexene	500	H_2O_2	225	$FeCl_2[HC(pz)_3]$	5
53	102	cyclohexene	1200	H_2O_2	250	$FeCl_2[HC(pz)_3]$	5
54	103	cyclohexene	1200	H_2O_2	250	$FeCl_2[HC(pz)_3]$	5
55	104	cyclohexene	1200	H_2O_2	250	$FeCl_2[HC(pz)_3]$	5
56	105	cyclohexene	1200	H_2O_2	250	$FeCl_2[HC(pz)_3]$	5
57	106	cyclohexene	1200	H_2O_2	250	-	
58	107	cyclohexene	1200	H_2O_2	250	-	
59	108	cyclohexene	600	H_2O_2	250	$FeCl_2[HC(pz)_3]$	5
60	109	cyclohexene	600	H_2O_2	250	$FeCl_2[HC(pz)_3]$	5
61	110	cyclohexene	600	H_2O_2	250	$FeCl_2[HC(pz)_3]$	5
62	111	cyclohexene	600	H_2O_2	250	$FeCl_2[HC(pz)_3]$-CNT	6
63	112	cyclohexene	100	OXONE	(920mg)	-	
64	113	cyclohexene	100	OXONE	(920mg)	-	
65	114	cyclohexene	100	OXONE	(920mg)	$FeCl_2[HC(pz)_3]$	6
66	115	cyclohexene	100	OXONE	(920mg)	$FeCl_2[HC(pz)_3]$	6

Entry	React.n°	Additive	Qt [mg]	Solvent	Qt [µL]	Method	T [°C]	RT [min]
1	4	Na_2WO_4	10	-	-	HP	80	240
2	5	Na_2WO_4	10	-	-	MW	80	240
3	7	Na_2WO_4	10	-	-	MW	80	480
4	53	-		-		MW	50	30
5	54	-		-		MW	50	60
6	55	-		-		MW	50	120
7	56	-		-		MW	50	180
8	57	-		-		MW	50	900
9	58	HPCA	11	-		MW	50	10
10	59	HPCA	11	-		MW	50	30
11	60	HPCA	11	-		MW	50	10
12	61	HPCA	11	-		MW	50	30
13	62	-		-		MW	50	10
14	63	-		-		MW	50	30
15	64	-		-		MW	50	60
16	65	-		-		MW	50	10
17	66	-		-		MW	50	30
18	67	-		-		MW	50	10
19	68	-		-		MW	50	30
20	69	-		-		MW	50	10
21	70	-		-		MW	50	30
22	71	-		-		MW	50	10
23	72	-		-		MW	50	30
24	73	-		C_6mim Ntf_2	1500	MW	50	30
25	74	-		P_{66614}DCA	1500	MW	50	30
26	75	Na_2WO_4	10	-		MW	80	10
27	76	Na_2WO_4	10	-		MW	80	30
28	77	Na_2WO_4	10	-		MW	80	60
29	78	Na_2WO_4	10	-		MW	30	30
30	79	Na_2WO_4	10	-		MW	50	30
31	80	HPCA	11	-		MW	30	10
32	81	HPCA	11	-		MW	50	10
33	82	HPCA	11	-		MW	80	10
34	83	-		-		MW	30	30
35	84	-		-		MW	80	30
36	85	-		-		MW	30	30
37	86	-		-		MW	80	30

38	87	-		-		MW	30	30
39	88	-		-		MW	80	30
40	89	-		-		MW	30	30
41	90	HPCA	5,5	-		MW	50	30
42	91	HNO_3	6,2 (µL)	-		MW	50	30
43	92	Na2WO4	10	-		MW	50	30
44	93	HPCA	5,5	H_2O	3000	MW	50	30
45	94	HNO_3	6,2 (µL)	H_2O	3000	MW	50	30
46	95	Na_2WO_4	10	H_2O	3000	MW	50	30
47	96	HPCA	5,5	-		HP	50	30
48	97	HNO_3	6,2 (µL)	-		HP	50	30
49	98	Na_2WO_4	10	-		HP	50	30
50	99	HPCA	5,5	H_2O	3000	HP	50	30
51	100	HNO_3	6,2 (µL)	H_2O	3000	HP	50	30
52	101	Na_2WO_4	10	H_2O	3000	HP	50	30
53	102	Na_2WO_4	10	H_2O	3000	MW	80	240
54	103	Na_2WO_4	10	-		MW	80	240
55	104	-		H_2O	3000	MW	80	240
56	105	-		-		MW	80	240
57	106	Na_2WO_4	10	H_2O	3000	MW	80	240
58	107	Na_2WO_4	10	-		MW	80	240
59	108	Na_2WO_4	10	H_2O	3000	MW	80	900
60	109	Na_2WO_4	10	-		MW	80	900
61	110	-		H_2O	3000	MW	80	900
62	111	-		ACN	3000	MW	80	240
63	112	-		ACN-H_2O	1500-1500	HP	60	660
64	113	-		ACN- H_2O	1500-1500	MW	60	660
65	114	-		ACN- H_2O	1500-1500	MW	60	660
66	115	HPCA	10	ACN- H_2O	1500-1500	MW	60	660

Appendix C

General materials and procedures

For Tpm and $FeCl_2[HC(pz)_3]$:
Pyrazole (Sigma-Aldrich), tetra-n-butylammonium bromide (Fluka), sodium carbonate (Sigma-Aldrich), chloroform (Fischer Scientific), diethyl ether (Fischer Scientific), active carbon (Panreac), hexane (Fischer Scientific), iron chloride (ACROS), ethanol (Fischer Scientific) were used as received. Sodium chloride (ACROS) was used in a saturated solution.
Heidolph rotating evaporator was used for Tpm purification.

For cyclohexane and cyclohexene oxidation:
Cyclohexane (Sigma-Aldrich), cyclohexene (ACROS), TBHP (ACROS), Hydrogen peroxide (30%) (ACROS), $Na_2WO_4{\cdot}2H_2O$ (M&B), silica gel (ACROS), HPCA, diethyl ether (Fischer Scientific), acetonitrile (Fischer Scientific), $[C_6mim][Ntf_2]$, $[P_{66614}][DCA]$, $[C_4mim][Ntf_2]$, $[C_8mim][Ntf_2]$, CYPHOS105 (CYPHOS®), triphenylphosphine (ACROS), molybdenum acetylacetonate (Sigma-Aldrich). $FeCl_2[HC(pz)_3]$ was synthesized following the procedure of Silva *et al.* (ref), using the ligand prepared with Reger's procedure (ref). MS11, MS14, MS104, MS154, MS155 were prepared in the laboratory of Group 5 of CQE.
Reactions carried out under microwave irradiation were performed in an Anton Paar Microwave Synthesis Reactor: Monowave 300 (max pressure: 32 bar, max power: 850 W).

For ionic liquid synthesis:
1-methylimidazole (Sigma-Aldrich), 1-chlorobutane (Sigma-Aldrich), ethyl acetate (Fluka).
Heidolph rotating evaporator was used for [bmim][Cl] purification.

For reference solutions:
Cyclohexane (Sigma-Aldrich), cyclohexanol (ACROS), cyclohexanone (Sigma-Aldrich), nitromethane (ACROS), benzaldheyde (Sigma-Aldrich), acetonitrile (Fischer Scientific), cyclohexene (ACROS), 2-cyclohexen-1-ol (ACROS), 2-cyclohexen-1-one (ACROS), cycloheptanone (ACROS), diethyl ether (Fischer Scientific), n-octane (Sigma-Aldrich), nonane (Fluka), Bromobenzene (Fluka).

For analysis:
^{1}H NMR and ^{13}C NMR spectra were recorded at 22 °C on a Bruker 300 Ultrashield spectrometer. Deuterated Chloroform was used as solvent.

Infrared spectra (4000–400 cm_1) were recorded on a Nicolet Impact 400D, a Perkin–Elmer 1330 or a Jasco FT/IR-430 spectrophotometer.

Gas chromatographic and mass spectroscopy measurements were carried out using a Perkin-Elmer Clarus 600 gas chromatograph, with two capillary columns (SGE BPX5, column length: 30 m; internal diameter: 0.32 mm), one having EI-MS (electron impact) and the other one with FID detectors. Helium was used as the carrier gas.

Other gas chromatographic (GC) measurements were carried out using a Fisons Instruments GC 8000 series gas chromatograph with a FID detector, with one capillary column (DBWAX, column length: 30 m; internal diameter: 0.32 mm). Helium was used as the carrier gas

List of abbreviations

ACN: acetonitrile
C_4mim NTf_2: 1-Butyl-3-methylimidazolium bis(trifluoromethanesulfonyl)imide
C_6mim NTf_2: 1-Hexyl-3-methylimidazolium bis(trifluoromethanesulfonyl)imide
C_8mim NTf_2: 1-Octyl-3-methylimidazolium bis(trifluoromethanesulfonyl)imide
CNT: carbon nanotubes
GC: gas chromatography
HC(pz)$_3$: tris(pyrazolyl)methane
HP: hot plate
HPCA: pyrazine-carboxylic acid
IL: ionic liquid
IR: infrared
KA oil: ketone-alcohol oil
MS: mass spectroscopy
MW: microwaves
NMR: nuclear magnetic resonance
P66614DCA: Trihexyl(tetradecyl)phosphonium dicyanamide
RT: reaction time
SILP: supported ionic liquid phase
TBHP: tert-butyl hydroperoxide
TEMPO: tetramethylpiperidin-oxyl
TOF: turn over frequency
TON: turn over number
TPA: tris(pyridylmethyl)amine
Tpm: tris(pyrazolyl)methane
VOCs: volatile organic compounds.