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Doctoral Thesis

Chemo-catalytic Conversion of Vegetable Oils for Sustainable Production of Chemicals and Biofuels

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A Vincenzo A., che ha lottato fino alla fine

Ai dottori Di Lorenzo G., Ferro M., Imbimbo, C., Nettuno R., Puglia L.
che mi hanno permesso di esser qui a raccontare questa storia

A mamma, papà, Andrea e Alessandra
per esserci sempre stati

A Franx e i Metor, la mia seconda famiglia

A Gene Roddenberry per avermi insegnato
che il sogno, la fantasia e la curiosità sono il mezzo
per arrivare là dove nessuno è mai giunto prima

To Vincenzo A., that fought 'till the end

To doctors Di Lorenzo G., Ferro M., Imbimbo, C., Nettuno R., Puglia L.
that allowed me to stay here and tell this story

To mom, dad, Andrea and Alessandra
for being with me, ever

To Franx and Metors, my second family

To Gene Roddenberry for teaching me
that dreams, fantasy and curiosity are the means
to boldly go where no one has gone before

In recent years use of biomass as a source of energy and raw materials has become a central theme in academic and industrial debate. Biomass indicates “the biodegradable fraction of products, waste and residues of synthetic origin from agriculture (including vegetal and animal substances), forestry and related industries, as well as the biodegradable fraction of industrial and municipal waste”.[1]

Two are the main modes of reuse: as it is, to produce energy, or via its chemical conversion. The related concept of biorefinery is defined by NREL as “an integrated structure for the conversion of biomass into fuels, energy and chemicals”.[2]

This PhD research project fits in this area and aims at obtaining the following classes of chemicals, starting from waste vegetable oils, as well as to design and/or optimize industrially transferable procedures:

- Biofuels through esterification and transesterification of oils and free fatty acids with small chain alcohols.

- Monomers for polyester synthesis, like long chain di-carboxylic acids, obtainable through oxidation of unsaturated free fatty acids.

- Chemicals: base products, solvents or surfactants.

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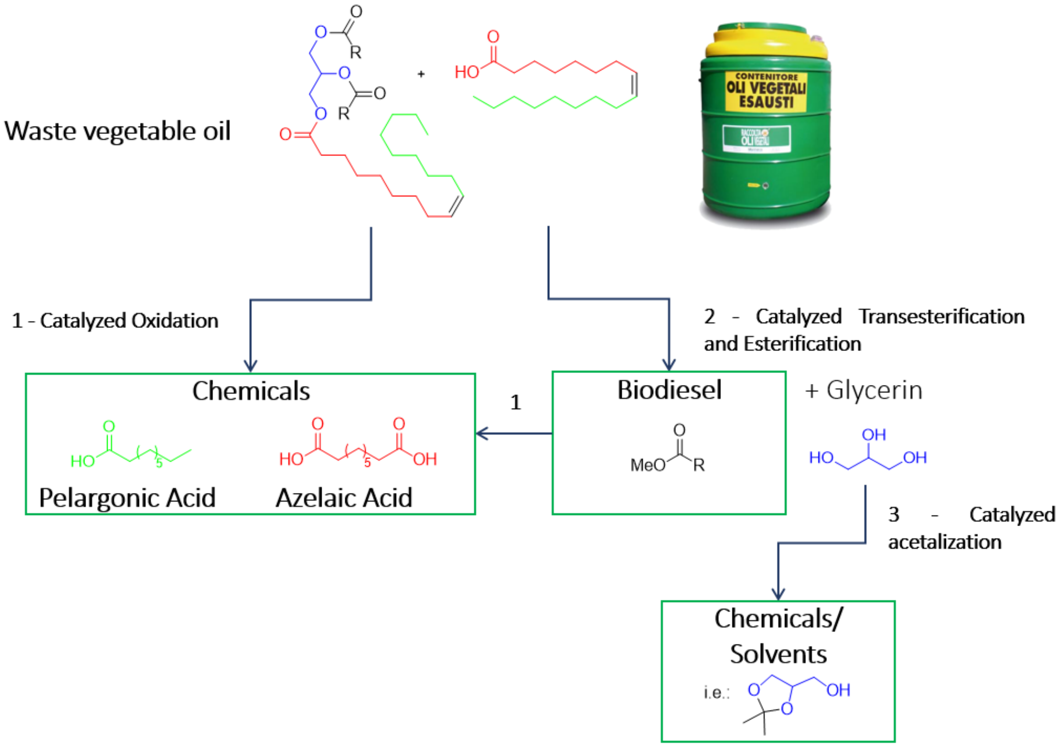
[1] Decreto Legilsativo 29 dicembre 2003, n. 387, Art. 2

[2] National Renewable Energy Laboratory.
http://www.nrel.gov/biomass/biorefinery.html

Catalytic methods (scheme 1.1) to obtain biofuel,[3] mono and di-carboxylic acids[4] and valorize the byproduct glycerol[5] were successfully developed.



Scheme 1.1 – Conversion of waste vegetable oil

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[3] Benessere, V.; Cucciolito, M. E.; Esposito, R.; Lega, M.; Turco, R.; Ruffo, F.; Di Serio, M. *Fuel*, **2016**, *171*, 1.
[4] Benessere, V.; Cucciolito, M. E.; De Santis, A.; Di Serio, M.; Esposito, R.; Ruffo, F.; Turco, R. *J. Am. Oil Chem Soc*, **2015**, *92*, 1701.
[5] Esposito, R.; Cucciolito M. E.; D'Amora, A.; Di Guida, R.; Montagnaro, F.; Ruffo, F. *Fuel Process. Technol.* **2017**, *167*, 670.

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Chapter 1

Introduction

1.1 – Sustainable development

Sometimes one could forget that we all live on a planet. A planet with a tiny blue blanket that protects all the life from the cold inhabitable space. A planet with very precarious equilibria that let an animal, descending from apes, to be alive, study, discover the nature and the universe, manipulate the reality in such a way that allows him to live longer and better. This planet has finite resources, finite matter and finite energy.

Figure 1.1 – Our finite planet and Italy view from International Space Station[6]

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[6] https://www.nasa.gov/sites/default/files/iss040e080967.jpg

Since the civilization appeared, humans started to consume resources but the consumption rate was such that every generation satisfied their needs. This rate enormously increased with the industrial revolution. With the discover of fossil fuels, the mankind started to consume resources faster than their renewal rate. The acceleration of consumption can be appreciated looking at the world energy consumption per year (figure 1.2). The awareness that this could be a problem arose only in the second half of 90's.

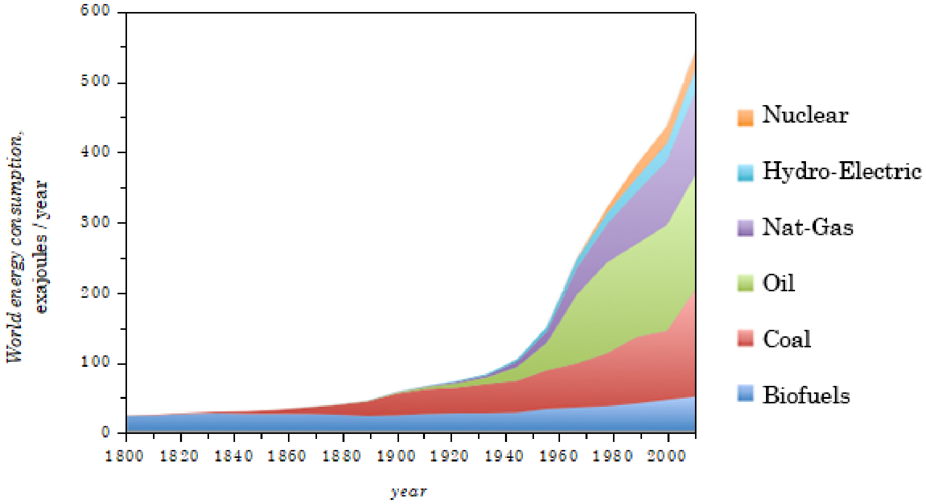

Figure 1.2 – World Energy Consumption by Source, based on Vaclav Smil estimates from Energy Transitions: History, Requirements and Prospects together with BP Statistical Data for 1965 and subsequent.

The idea of sustainability was born in 1969 by the IUCN, the International Union for Conservation of Nature. This concept developed through the time in different international conferences: The United Nations Conference on the Human Environment in Stockholm in 1972, the World Conservation Strategy in 1980, the Brundtland Report in 1987, and the United Nations Conference on environment and Development in Rio in 1992. It was coined explicitly to suggest that it was possible to achieve economic growth and industrialization without environmental damage.

The wide used definition of sustainability, or more precisely of *sustainable development*, is: the development that "meets the needs of the present without compromising the ability of future generations to meet their own needs."[7] That is not far from the Native American proverb: "We do not inherit the earth from our ancestors; we borrow it from our children."

An effective graphical description (figure 1.3), shows how sustainability is founded on three pillars. Only when the social, the economic and the environment needs are satisfied there is a sustainable development.

Figure 1.3 – Venn diagram of sustainable development at the confluence of three constituent parts

The problem of global sustainability started to be widely recognized by world leaders, academical research, journalism and public opinion as well, at the beginning of the twenty-first century. Most of governments and businesses responded to the challenge to some extent.[8]

Together with the energy consumption, the other major challenge for our future is the waste production and the pollution that it causes.[9] In this sense a solution could be found in this newborn concept: the circular economy. It's defined as "a regenerative system in which resource input and waste, emission, and energy leakage are minimized by slowing, closing, and narrowing material and energy loops. This can be achieved

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[7] *Our Common Future* also known as the Brudtland report, Report of the World Commission on Environment and Development **1987**.

[8] Adams, W.M. "The Future of Sustainability: Re-thinking Environment and Development in the Twenty-first Century." *Report of the IUCN Renowned Thinkers Meeting*, 29–31 January **2006**.

[9] See for example: https://svs.gsfc.nasa.gov/4174

through long-lasting design, maintenance, repair, reuse, remanufacturing, refurbishing, and recycling."[10]

Figure 1.4 – Graphical representation of Circular Economy

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[10] Geissdoerfer, M. et al. *Journal of Cleaner Production* **2017**, *143*, 757-768.

1.2 – Green Chemistry

Chemistry plays a crucial role in the development of a more sustainable future. Chemical industry is one of the most important industries in the world and has an important impact on economic, environmental and social fields.

Since 1991, with the creation of the term "Green Chemistry" by P. Anastas, chemists officially took an active role in contributing to the cause. The ecologic economy concept was born in the same year.[11] In 1998 logistical guidelines were published to suggest chemists and engineers how to design their chemistry in terms of sustainability:[12]

1. **Prevent waste:** Design chemical syntheses to prevent waste, leaving no waste to treat or clean up.

2. **Maximize atom economy:** Design synthetic methods to maximize the incorporation of all materials used in the process into the final product.

3. **Design less hazardous chemical syntheses:** Design syntheses to use and generate substances with little or no toxicity to humans and the environment.

4. **Design safer chemicals and products:** Design chemical products to be fully effective, yet have little or no toxicity.

5. **Use safer solvents and auxiliaries:** Avoid using solvents, separation agents, or other auxiliary chemicals. If these chemicals are necessary, use innocuous chemicals.

6. **Increase energy efficiency:** Run chemical reactions at ambient temperature and pressure whenever possible.

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[11] Daly, H. E. Steady-state: economics, (2nd ed.) Washington, D.C.: Island Press, **1991**.

[12] Anastas, P. T.; Warner, J. C. Green Chemistry: Theory and Practice, Oxford University Press: New York, **1998**, p.30.

7. **Use renewable feedstocks:** Use raw materials and feedstocks that are renewable rather than depleting. Renewable feedstocks are often made from agricultural products or are the wastes of other processes; depleting feedstocks are made from fossil fuels (petroleum, natural gas, or coal) or are mined.

8. **Avoid chemical derivatives:** Avoid using blocking or protecting groups or any temporary modifications if possible. Derivatives use additional reagents and generate waste.

9. **Use catalysts, not stoichiometric reagents:** Minimize waste by using catalytic reactions. Catalysts are used in small amounts and can carry out a single reaction many times. They are preferable to stoichiometric reagents, which are used in excess and work only once.

10. **Design chemicals and products to degrade after use**: Design chemical products to break down to innocuous substances after use so that they do not accumulate in the environment.

11. **Analyze in real time to prevent pollution:** Include in-process real-time monitoring and control during syntheses to minimize or eliminate the formation of by-products.

12. **Minimize the potential for accidents:** Design chemicals and their forms (solid, liquid, or gas) to minimize the potential for chemical accidents including explosions, fires, and releases to the environment.

More than defining a new branch of chemistry, those rules should be an ethical instrument to make a good use of chemical knowledge. In the only possible future in which the mankind still survives, this ethical chemistry would be the only way to do chemistry. With the global warming growing year by year, it is not alarmistic to say that the non-ethical, non-green use of chemistry would only make humans made a step toward the extinction.

Wisely, nowadays the application of a more sustainable chemistry is becoming a priority for chemical industries and academic community.[13]

This doctoral thesis was developed trying to fit as much as possible with these twelve principles as will be shown in the next paragraph.

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[13] Jessop, P. G. et al. *Green Chem.* **2015**, *17*, 2664.

1.3 – Biomass, biorefinery and vegetable oils

The need of renewable resources brought the attention on materials, renewable or better if wastes, that could be transformed into base chemicals, finding an alternative to petrochemistry. In recent years attention was drawn to an important concept: the *biomass*.

Biomass is: "the biodegradable fraction of products, waste and residues of synthetic origin from agriculture (including vegetal and animal substances), forestry and related industries, as well as the biodegradable fraction of industrial and municipal waste."[14]

This definition includes a great variety of chemical compounds and mixtures and the use that could be done with these different materials is as wide as their number.[15]

Another important concept that unifies the sustainable development, the circular economy and green chemistry raised up: the *biorefinery*. It is defined as "an integrated structure for the conversion of biomass into fuels, energy and chemicals"[16]

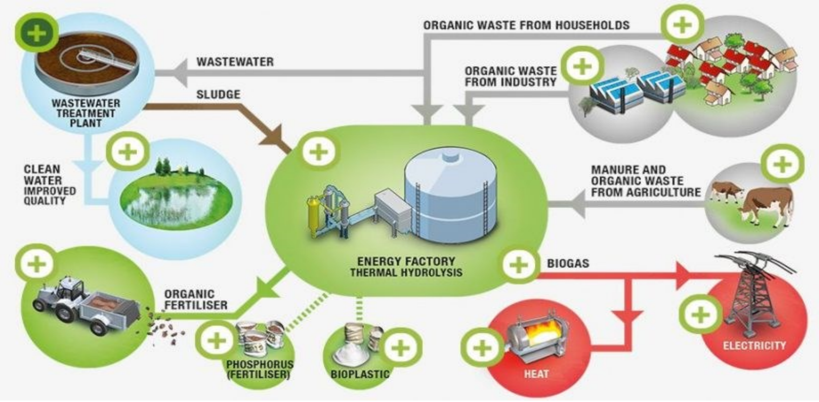

Figure 1.5 – Biorefinery.

This brand-new concept of industry, that uses a renewable raw material instead of fossil oil, opens infinite possibilities of discoveries and chemical investigations.

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[14] Decreto Legilsativo 29 dicembre 2003, n. 387, Art. 2.

[15] a) Demirbas, A. *Prog. Energy Combust. Sci.* **2007**, *33*, 1–18;
b) Corma, A. et al. *Chem. Rev.* **2007**, *107*, 2411-2502; c) Cherubini, F. *Energy Convers. Manage.* **2010**, *51*, 1412-1421.

[16] National Renewable Energy Laboratory:
http://www.nrel.gov/biomass/biorefinery.html

Today the main use of biomass is still the transformation in energy, directly through combustion or indirectly through the production of many types of biofuels.

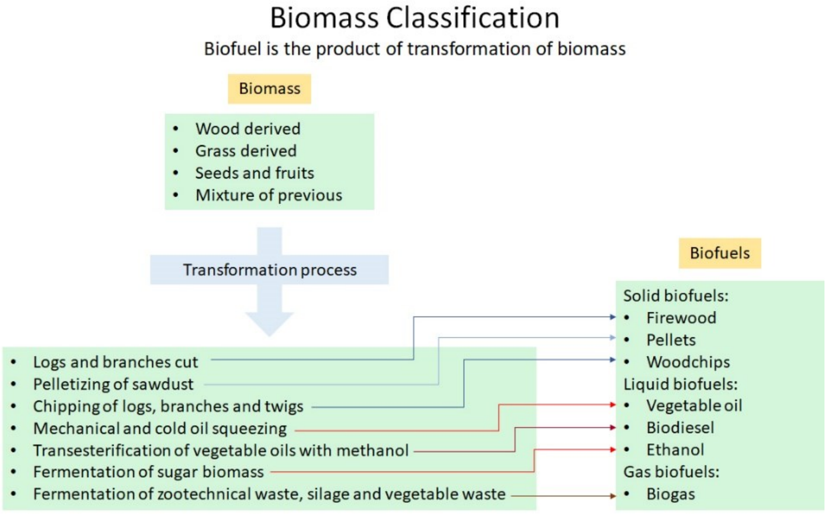

Figure 1.6 – Common uses of biomass to produce biofuels.[17]

However, academic and industrial chemistry efforts are addressed to develop a new chemistry, based on biomass instead of petroleum, to obtain both raw and fine chemicals from the great diversity of substrates that biomass offers.

Among all classes of compounds (from cellulose to terpenes, from aminoacids to careen), that are included in this waste materials, one is of a particular interest: the vegetable oils.

Avelino Corma dedicates an entire chapter to vegetable oils in his 92 pages review of 2007[14b] about the biomass transformation into chemicals. The relevance of this class of compounds is attributable to:

- their long paraffinic or olefin chains make them chemically similar to some petroleum fraction;

- their functionality makes them attractive for chemical transformations and for commercial uses;

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[17] Panvini, A. Seminario UNACOMA Bologna, 27 aprile **2006**, Comitato Termotecnico Italiano. http://slideplayer.it/slide/190325/

- they are renewable;

- they are cheap and worldwide distributed, another perk that pushes towards the sustainable development.

The applications of vegetable oils as chemical substrates are many: *biodiesel*, plasticizers, monomers, cosmetic products, surfactants, lubricants and coatings (Figure 1.7 taken from Biermann, U. et al. *Angew. Chem. Int. Ed.* **2011**, *50*, 3854-3871).[18]

Figure 1.7 – Vegetable oils as a chemical platform

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[18] Biermann, U. et al. *Angew. Chem. Int. Ed.* **2011**, *50*, 3854-3871 and references therein

A recent example is given by the Matrìca process, born in 2014 in Porto Torress (Sardinia). This process transforms the cardo oil (rich in oleic acid), obtained from cultivation of cardo flower, into azelaic and pelargonic acids.[19]

This PhD thesis fits into this contest. Here it will be proposed:

- A catalytic system for the production of azelaic acid and pelargonic acid from oleic acid that makes use of hydrogen peroxide as oxidant. It will be also investigated the use of methyl oleate as starting material since this could be efficiently obtained from Olive Oil Wastewater (Chapter 2).

- A supported homogeneous catalyst for the production of biodiesel directly from non-pretreated acid waste vegetable oils (Chapter 3).

- Valorization of glycerol through its transformation in *solketal* with the use of a simple and highly efficient catalysts (Chapter 4).

These processes have been designed to fits as much as possible with the principles of Green Chemistry:

- they are designed to transform waste materials into useful substances, in line with principle 7;

- they make use of catalytic reagents, in line with principle 9;

- they are developed to substitute industrial existent processes that make use of hazardous and toxic reagents (*i.e.* ozone), in line with principles 3 and 12;

- they make use of non-toxic solvents, in line with principle 5;

- they transform byproducts into precursors of chemicals and non-toxic solvents, in line with principles 1, 2 and 4.

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[19] www.matrica.it

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Chapter 2

Oleic Acid

2.1 – Oleic acid oxidation in industry

The Mediterranean area is rich of countries that produce and consume vegetable oils. The first three producers of olive oil in the world are Spain, Italy and Greece.[20] Oleic acid (OA), *cis*-9-octadecenoic acid, is the main fatty acid contained in this oil and in high oleic oils.

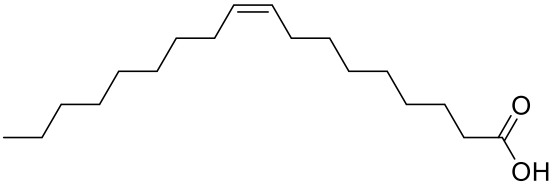

Figure 2.1 – Oleic acid (OA)

Wastes of olive oil production (*sansa* oil, that is a semi-solid residue of the grinding processing) and oils coming from disposal oils are rich in this free fatty acid. Many processes exist for the recovery of this acid from oil and from its wastes.[21] It can be also derived from different oils and animal fats such as tallow.[22]

This fatty acid is a very interesting reagent for industry. Its double bond can be transformed to lead to different products. The main transformations are hydroxylation,

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[20] Food and Agriculture Organization of the United Nations Statistics 2012, 2013, 2014

[21] See for example: Elkacmi, R. et al. *J. Mater. Environ. Sci.* **2016**, 7, *5*, 1485-1494 and references therein

[22] Swern, D.; Knight, H.B.; Scanlan, J.T. et al. *Oil Soap* **1945**, *22*, 302.

epoxidation and oxidative cleavage. The latter reaction produces two interesting products: a monoacid, nonanoic acid, also known as pelargonic acid (PA), and a diacid, nonanedioic acid or azelaic acid (AA).

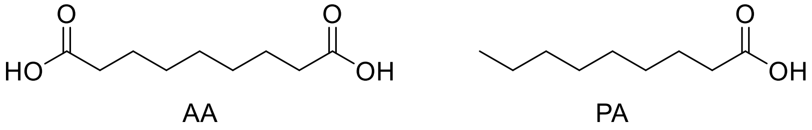

Figure 2.2 – Azelaic Acid (AA) and Pelargonic Acid (PA)

Azelaic acid is a commodity with an industrial output of about 1000 tons/year and finds many applications in which it has the role of: monomer in *Nylon*-6,9, polymerized with hexamethylendiamine; monomer in biodegradable polymers (*i.e.*: Mater Bi); antibacterial agent in anti-acne creams; hair growth factor and it's used in hair loss disease's cure.[23]

Industrially it is produced via ozonolysis of OA.[24] The reaction occurs into two steps (scheme 2.1):

- Ozone reacts with the double bond, at a temperature comprised between 293 K and 313 K for ten minutes, in water or PA as solvent; there is the formation of a 1,2,3-trioxolane intermediate (**1**), that then rearranges to a 1,2,4-trioxolane species (**2**).

- The 1,2,4-trioxolane intermediate (**2**) is cleaved with molecular oxygen between 70 and 110°C.

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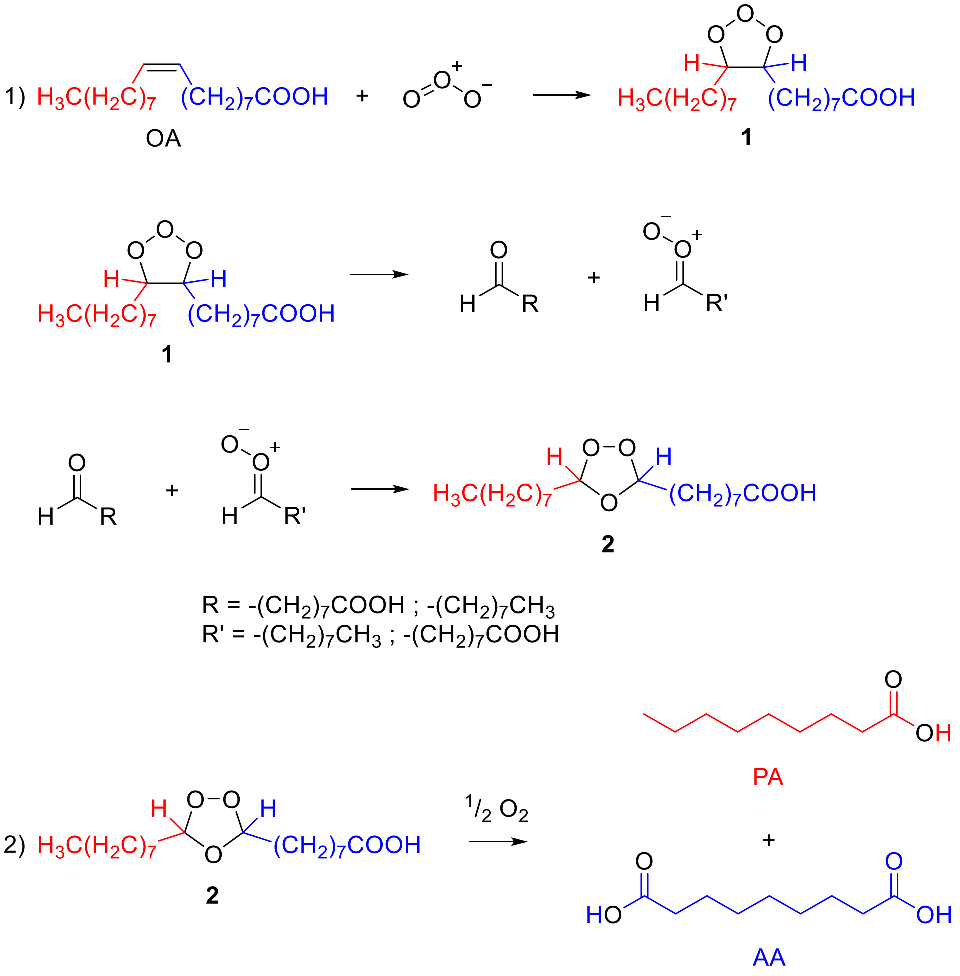
[23] a) Turnwald, S. E.; Lorier, M. A.; Wright, L. J.; Mucalo, M. R. *J Mater Sci Lett* **1998**,17, *15*, 1305-1307.
b) Telos, S. R. L.; Bader, S.; Masiello, S. **1999** Cosmetic composition containing azelaic acid. WO Patent 9,917,714
c) Sefton, J. **2001** Method and composition for treating acne. US Patent 6,262,117

[24] Brown, A. C.; Goebel C. G.; Oehlschlaeger, H.F.; Rolfes, R.P. Method of making azelaic acid. **1957**, US Patent 2,813,113



Scheme 2.1 – Oleic Acid ozonolysis reaction mechanism

The yield of azelaic acid is 78%. However, use of ozone and molecular oxygen at high temperatures represents a serious drawback of the process. These oxidants are very hazardous to manipulate at high temperatures, due to their flammability, and their production and purification processes are expensive.

A valid alternative is hydrogen peroxide because it is capable of oxidizing with excellent atom economy and is safer than gaseous reactants.[25] Many of the known strategies couple H_2O_2 with catalytic systems such as RuO_2, $Na_3PO_4\{[WO(O_2)_2]\}$,

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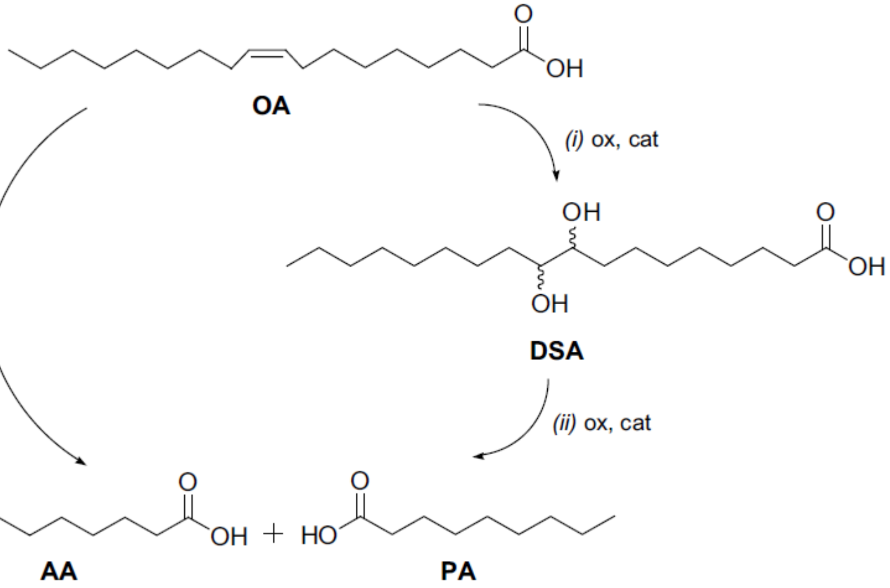
[25] Noyori, R.; Aoku, M.; Sato, K. *Chem Commun* **2003**, *16*, 1977.

$H_2WO_4/Co(OAc)_2$, and Re_2O_7.[26] These synthetic routes (path *i* in scheme 2.2) typically include a first step of dihydroxylation that gives 9,10-dihydroxystearic acid (DSA).



Scheme 2.2 – Oxidative cleavage of oleic acid

In a second step (*ii*) a new catalyst is introduced, either in the same reaction environment[27] or on the purified diol,[28] for the oxidative cleavage of the CH(OH)–CH(OH) bond. Recently, an efficient one-pot strategy (*iii* in scheme 2.2) was proposed with a catalyst based on the quaternary ammonium salt $Q_3\{PO4[WO(O_2)_2]_4\}$.[29] The reaction yield is high, 81%, comparable to the ozonolysis. However, even in this case, there are some disadvantages, namely the high catalyst loading (7% in moles based on

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[26] a) Köckritz, A.; Martin, A. *Eur J Lipid Sci Technol,* **2011**, 113:83–91. b) Warwel, S.; Rüsch gen. Klaas, M. *Lipid Technol* **1997**, *9*, 10–14. c) Antonelli, E.; D'Aloisio R.; Gambaro M.; Fiorani T.; Venturello, C. *J Org Chem*, **1998**, *63*, 7190–7206.
d) Santacesaria E.; Ambrosio M.; Sorrentino A.; Tesser R.; Di Serio M.; *Catal Today*, **2003**, *79–80*, 59–65. e) Behr, A.; Tenhumberg, N.; Wintzer, A. *RSC Adv*, **2013**, *3*, 172–180.

[27] Oakley, M. A.; Woodward, S.; Coupland, K.; Parker, D.; Temple-Heald, C. *J Mol Catal A Chem*, **1999**, *150*, 105–111.

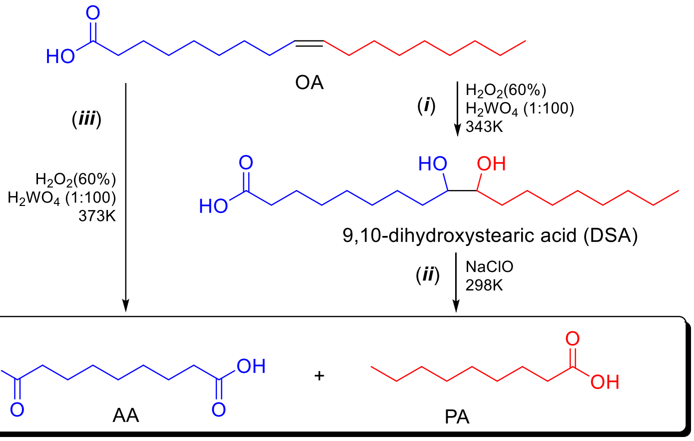
[28] Köckritz, A.; Blumenstein, M.; Martin, A. *Eur J Lipid Sci Technol*, **2010**, *112*, 58–63.

[29] Godard, A.; De Caro, P.; Thiebaud-Roux, S.; Vedrenne, E.; Mouloungui, Z. *J Am Oil Chem Soc*, **2013**, 90, 133–140.

W), use of phase-transfer agents, and addition of hydrochloric acid for product recovery. Thus, it is clear that, in terms of sustainability, the goal is not yet reached.

2.2 – Oxidation of Oleic Acid

In this thesis, two new pathways for the oxidation of oleic acid are proposed:

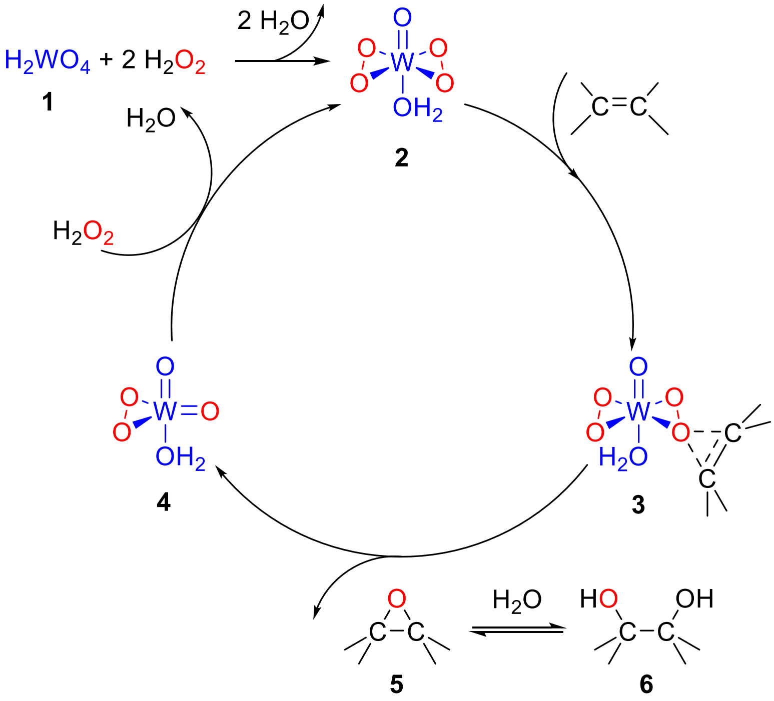


Scheme 2.3 – Procedures to obtain AA and PA

- A two-step reaction, that uses mild conditions and a relatively fast oxidation of oleic acid to 9,10-dihydroxystearic acid (DSA, step *i* in scheme 2.3), using commercially available H_2WO_4 as the only catalytic ingredient and H_2O_2 (60 % v/v). Than the DSA is oxidized with a stoichiometric amount of NaClO (*ii*) at room temperature.

- A single step reaction that uses higher temperatures and longer reaction time, but has the advantages of: (i) using a unique oxidant (hydrogen peroxide) and catalyst; (ii) absence of solvents or transferring agents; (iii) high yields of products.

In the presence of hydrogen peroxide, tungstic acid (**1**) forms a diperoxo-complex also called "butterfly" complex (**2**) for its structure. This complex is capable of oxidizing olefins to give epoxides (scheme 2.4).[30]



Scheme 2.4 – Epoxydation catalyzed by diperoxo-tungsten complex

The key-step (**3**) is the oxygen atom transfer from the "butterfly" complex to the double bond to give the epoxide (**5**) and an "half-buterlfy" that is capable of oxidizing another double bond or to be oxidized again into the species **2**.

In the acid conditions of the reaction media, the epoxide opens to give a vicinal diol (**6**). This can be further oxidized to a carboxylic acid and an aldehyde and scheme 2.5 illustrates a reworked reaction mechanism based on literature.[25, 31]

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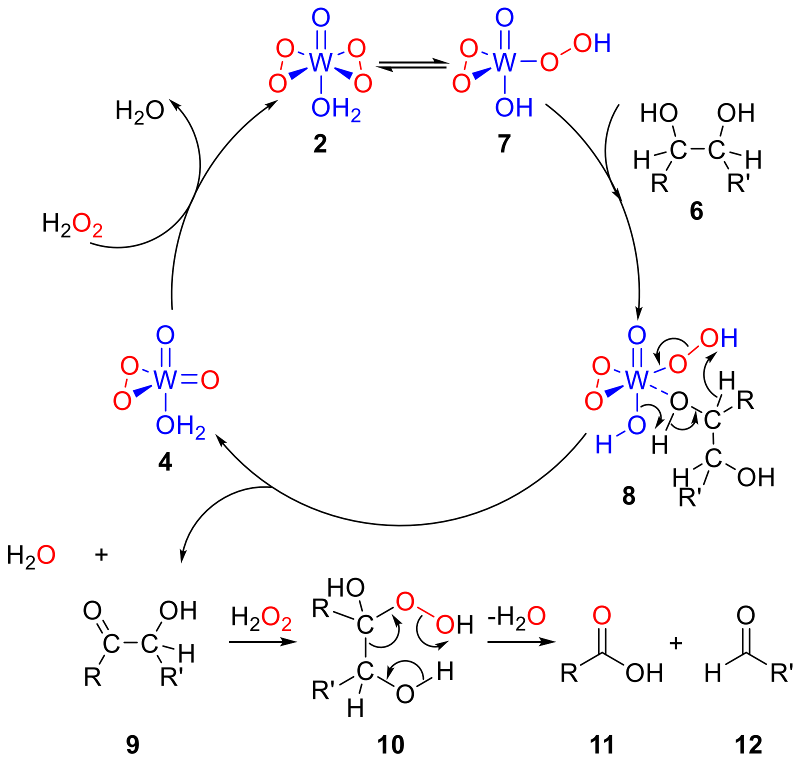
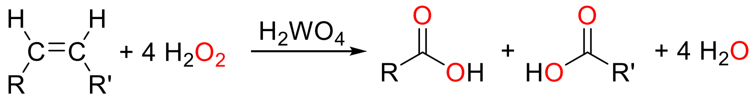
[30] Catalytic oxidations with hydrogen peroxideas oxidant, Strukul, G. *Kluwer Academic Publishers*, **1992**, 191.

[31] a) Venturello, C.; Ricci, M. *J. Org. Chem.* **1986**, *51*, 1599-1602. b) Turnwald, S.E.; Lorier, M. A.; Wright, L. J. et al. *J. Mater. Sci. Lett.* **1998**, *17*, 1305.



Scheme 2.5 – Oxidation of diols

The "butterfly" complex (**2**) is in equilibrium with a hydroperoxocomplex (**7**). This is capable of oxidizing the diol (**6**) to an α-hydroxy ketone (**9**) and gives the species **4** that is again oxidized by hydrogen peroxide. The hydroxyketone **9** is further oxidized to an acid (**11**) and an aldehyde (**12**). The aldehyde is then cleaved by hydrogen peroxide to obtain carboxylic acid. The stoichiometry of the overall reaction is:



OA: R = $-(CH_2)_7COOH$; $-(CH_2)_7CH_3$
R' = $-(CH_2)_7CH_3$; $-(CH_2)_7COOH$

Scheme 2.6 – Stoichiometry of the oxidation of OA to PA and AA

In the case of oleic acid, it is possible to control the oxidation by modulating the oxidant quantity and the temperature: one can isolate DSA or go further and obtain PA and AA.

In addition, in this thesis, the possibility to produce a homogeneous supported catalyst for the oxidation of oleic acid and the extension of the single-step procedure to the oxidation of the methyl oleate will be explored.

2.2.1 – Two-steps oxidation

As stated before, one of the proposed procedure is a one-pot/two-steps reaction. The two steps are:

(i) Oxidation of the double bond of OA: the pre-catalyst H_2WO_4 is dissolved in hydrogen peroxide (60% v/v) at 343 K for ten minutes, then oleic acid (OA) is added. A biphasic mixture is obtained and the reaction is carried out for 2h to give 9,10-dihydroxystearic acid (DSA);

(ii) this diol is subsequently oxidized, in the same reaction batch, with sodium ipochlorite at room temperature.

In step (*i*), the catalyst (the butterfly species in scheme 2.4) is prepared *in situ* suspending tungstic acid pre-catalyst in hydrogen peroxide at 343 K. After ten minutes, when the suspension becomes a colorless solution, oleic acid is added.

To optimize the process, a screening on step (*i*) was carried out. The optimization of the oxidant/substrate ratio was performed evaluating the reaction time for the complete conversion of oleic acid (table 2.1).

Entry	**OA : H_2WO_4, mol / mol**	***T*, K**	***Conversion*,^{a} %**	**H_2O_2 : OA, mol / mol**	***time*, min**
1	100 : 1	343	>99	1.1 : 1	30
2				1.5 : 1	60
3				2 : 1	120
4				4 : 1	240

a) Conversion evaluated with ^1H NMR

Table 2.1 – Oxidant/substrate ratio screening

It may seem counterintuitive that the higher the ratio is, the higher the reaction time. This effect may be simply due to the dilution of the catalyst upon increasing the amount of hydrogen peroxide. The reaction performed with a molar ratio oxidant/oleic acid of 1.1 to 1 (entry 1) shows the shorter reaction time. However, the high exothermicity is not balanced by the presence of enough bulk water, and the control of the reaction is difficult. For this reason, conditions of entry 2, with a molar ratio of 1.5 to 1, are identified as a good compromise between reaction time (60 minutes) and the control of the reaction.

Then a screening of catalyst loading was carried out (table 2.2).

Entry	**H_2O_2 : OA, mol / mol**	***T*, K**	***Conversion*,[a] %**	**OA : H_2WO_4, mol / mol**	***time*, min**
1	1.5 : 1	343	90 ± 4	100 : 1	30
2			>99	100 : 1	60
3			80 ± 4	200 : 1	60
4			>99	400 : 1	120
5			>99	1600 : 1	>240

a) Conversion evaluated with ^1H NMR

Table 2.2 – Catalyst loading screening

A drastic reduction of the catalyst loading increases too much the reaction time in perspective of an industrial application. So, the optimal loading is 0.25% mol (entry 4) that leads to a two hours reaction for the first step.

In all cases conversion can be evaluated by ^1H NMR considering the disappearance of the signal of the double bond protons of oleic acid that resonates at 5.32 ppm in $CDCl_3$.

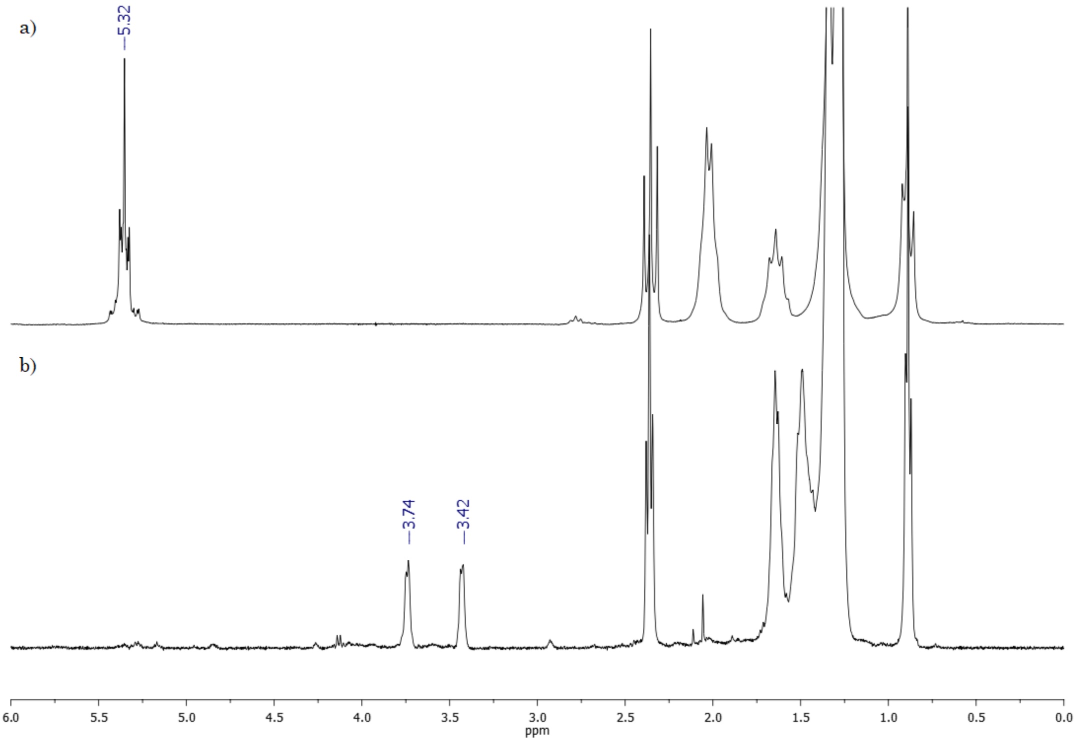


Figure 2.3 – ^{1}H NMR Spectra of: a) Oleic Acid b) Reaction crude.

The ^{1}H NMR spectra of the crude reaction mixtures show the presence of two oxidized species: DSA and another product, that has a proton geminal to a hydroxyl group (figure 2.3). Both have been isolated and characterized with ^{1}H and ^{13}C NMR, and mass spectrometry. The second species, which gives the signal at 3.74 ppm, is a mixture of hydroperoxo compounds analogue to the vicinal diol (PS, figure 2.4).

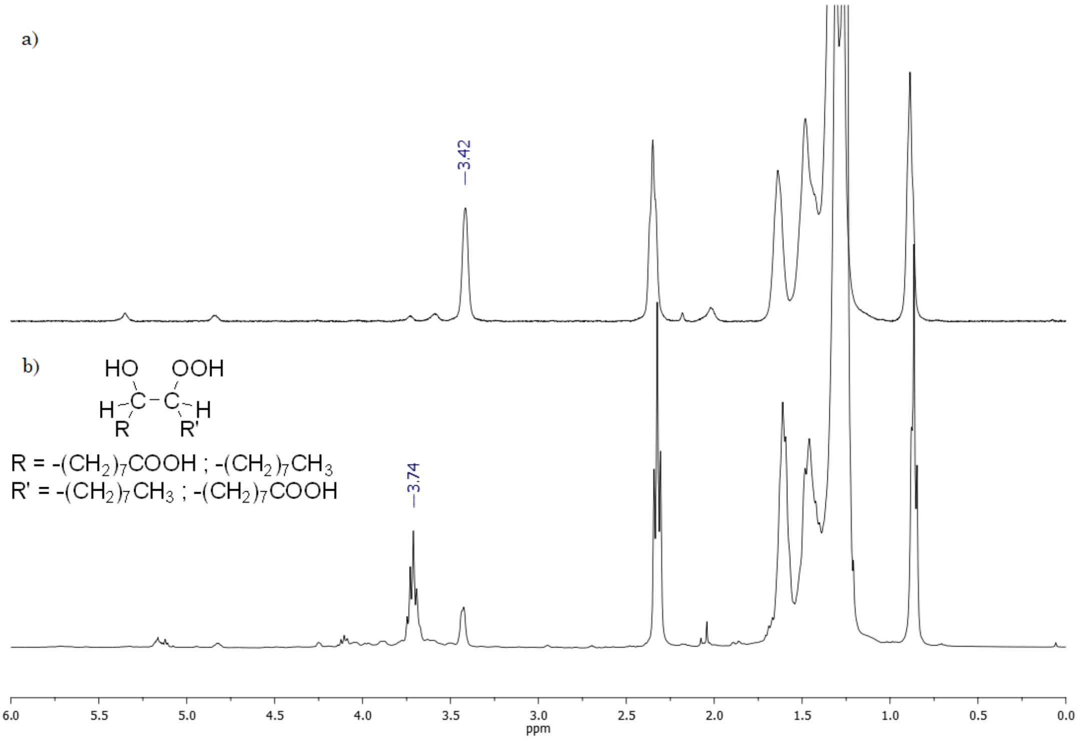


Figure 2.4 – ^{1}H NMR Spectra of: a) DSA b) Peroxide rich fraction.

The presence of this peroxo specie (PS) is not a problem for the second step of the reaction. This is equally oxidized to carboxylic acids by sodium hypochlorite.

After the optimization of the first step, the carbon-carbon sigma bond oxidation was conducted in the same reaction batch, adding sodium hypochlorite six times in moles (2 equivalents) with respect to the starting oleic acid. In two hours at room temperature complete conversion of DSA (and the peroxo species) was achieved. However, in these conditions, the chromatographic yield of azelaic acid did never exceed 54% (yield calculated via gas chromatography using undecane as internal standard, see page 47 for more information). The chromatogram shows the presence of many little peaks of byproducts that are still under investigation. The presence of uncomplete oxidation products (aldehydes) was observed. This result shows that the procedure is still not competitive with the industrial ozonolysis, even if it makes uses of milder condition and safer reactants.

2.2.2 – Single-step oxidation

This procedure differs from the previous one for the use of higher temperatures and a higher amount of oxidant, that is uniquely hydrogen peroxide. In this way the oxidative cleavage of the double bond is carried out in one single-step without adding other compounds. A new procedure for isolating azelaic acid has also been devised.

The catalyst is, again, prepared *in situ* suspending tungstic acid pre-catalyst in hydrogen peroxide at 343 K. After ten minutes, when the suspension becomes a colorless solution, oleic acid is added and the system is brought to about 373 K. In some experiments further hydrogen peroxide is added after two hours. The system is biphasic and necessitates of a vigorous stirring because it is solventless, and, the viscosity increases with the proceeding of the reaction.

The oleic acid conversion can be preliminarily evaluated via ^{1}H NMR, but the exact product yields are obtained via gas chromatography. The method used is the calibration curve with an internal standard. A generic reaction's chromatogram is reported in figure 2.5.

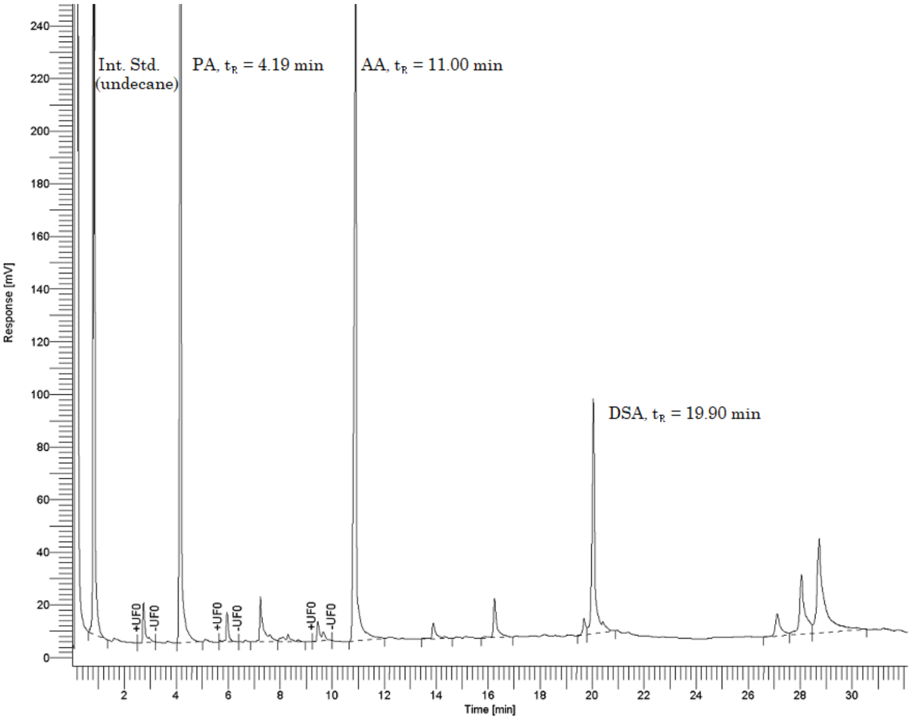


Figure 2.5 – Reaction chromatogram

First, a screening on catalyst loading was carried out (table 2.3).

Entry	**H_2O_2 : OA, mol / mol**	***T*, K**	***time*, min**	**OA : H_2WO_4, mol / mol**	**PA *Yield*,[a] %**	**AA *Yield*,[a] %**
1	4 : 1	373	240	-	14 ± 1.0	10 ± 1.1
2				100 : 1	36 ± 2	43 ± 1.3
3				50 : 1	24 ± 1.3	41 ± 2

a) Chromatographic yields, evaluated with GC.

Table 2.3 – Catalyst loading screening

A run performed without any tungstic acid indicated that the presence of a catalytic ingredient is required to promote a significant conversion (entry 1). In the presence of the catalyst, conversion of oleic acid into pelargonic and azelaic acid was already significant within 4 h (entry 2). Increasing the catalyst loading was not beneficial for the performances (entry 2 versus 3). The complication of the chromatogram, in the experimental conditions of entry 3, also suggests that a higher concentration of the pre-catalyst possibly leads to the formation of different metal species, that catalyze side reactions. Therefore, a substrate/catalyst ratio of 100/1 was considered as a fair compromise between an acceptable reaction rate and minimization of the catalyst loading.

Subsequently, the effect of the amount of oxidant was evaluated, assuming that the high temperature degrades hydrogen peroxide (table 2.4).

Entry	***T*, K**	***time*, min**	**OA : H_2WO_4, mol / mol**	**H_2O_2 : OA, mol / mol**	**PA *Yield*,[a] %**	**AA *Yield*,[a] %**
1	373	240	100 : 1	4 : 1	36 ± 2	43 ± 1.3
2				8 : 1	52 ± 3	64 ± 3
3				(4 + 4) : 1	33 ± 2	72 ± 4

a) Chromatographic yields, evaluated with GC.

Table 2.4 – Oxidant/substrate ratio effect

The data reported in entries 1–2 clearly indicate that the yield of azelaic acid increases with the amount of oxidant, in line with the expectations.

The effects of the modality of addition of H_2O_2 were also considered. Therefore, a test was conducted in which hydrogen peroxide was added in two portions at an interval of 2 h (entry 3). The increase in yield of AA up to 72% proofs that the addition of fresh hydrogen peroxide enhances the performance of the system.

Finally, a significant increase in the yield of product was achieved by doubling the reaction time (table 2.5). After 8 h, an excellent yield of AA (91 %) was obtained by using the conditions described in entry 2. This is the higher chromatographic yield ever reported in literature.

Entry	***T*, K**	***time*, min**	**OA : H_2WO_4, mol / mol**	**H_2O_2 : OA, mol / mol**	**PA *Yield*,[a] %**	**AA *Yield*,[a] %**
1	373	480	100 : 1	4 : 1	55 ± 1.2	64 ± 2
2				8 : 1	69 ± 1.5	91 ± 2

a) Chromatographic yields, evaluated with GC.

Table 2.5 – Reaction time effect.

After the optimization of the reaction conditions, a convenient methodology for isolation and purification of azelaic acid was also developed (figure 2.6). The reaction was quenched by adding cold water to the reaction mixture, and the resulting suspension was extracted with hot ethyl acetate (AcOEt). The aqueous phase contained the catalyst and the residual H_2O_2, while the organic phase captured the crude reaction products. After evaporation under vacuum of the organic solvent, a white suspension was obtained, which was extracted with boiling water. On cooling, azelaic acid crystallized into white microcrystals.

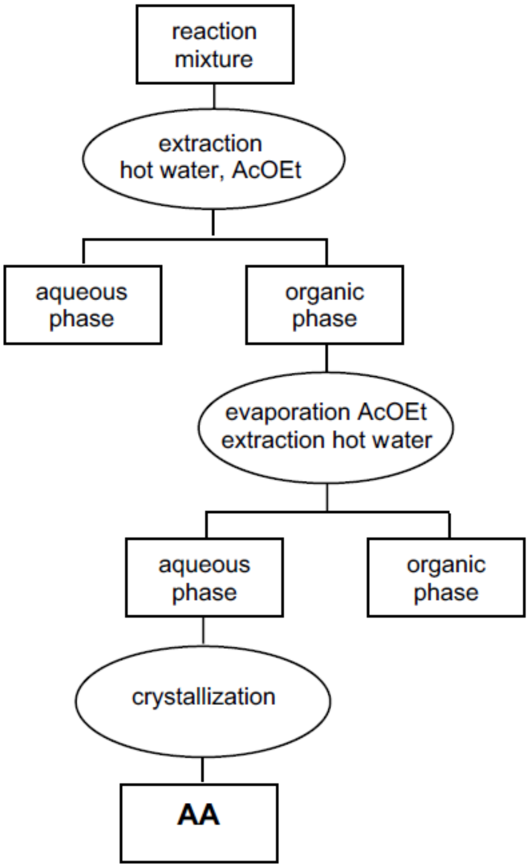


Figure 2.6 – Work-up procedure

^{1}H NMR (figure 2.7) and GC confirmed a high degree of product purity (figure 2.8). It should be noted that this convenient procedure for isolation of azelaic acid was found less feasible when applied to the crude reaction mixture of the oxidative cleavage in two steps.

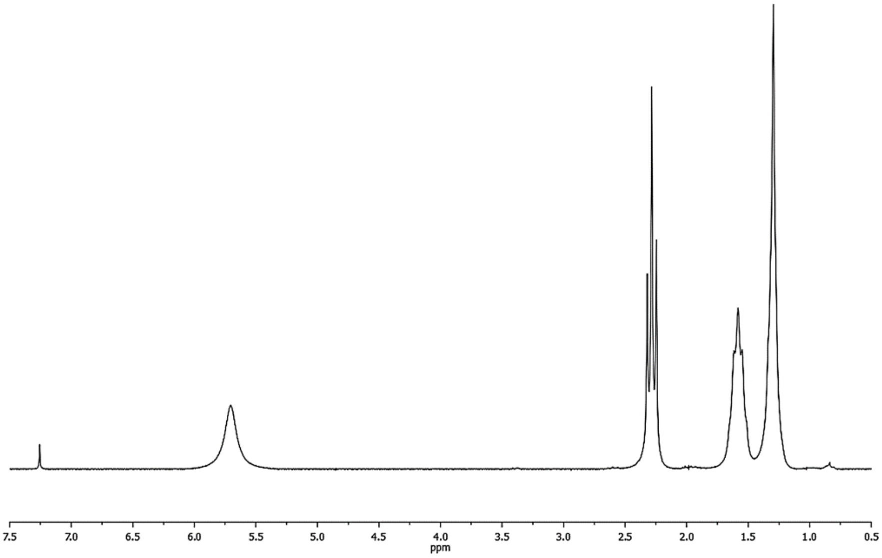


Figure 2.7 – Obtained azelaic acid ^{1}H NMR spectrum

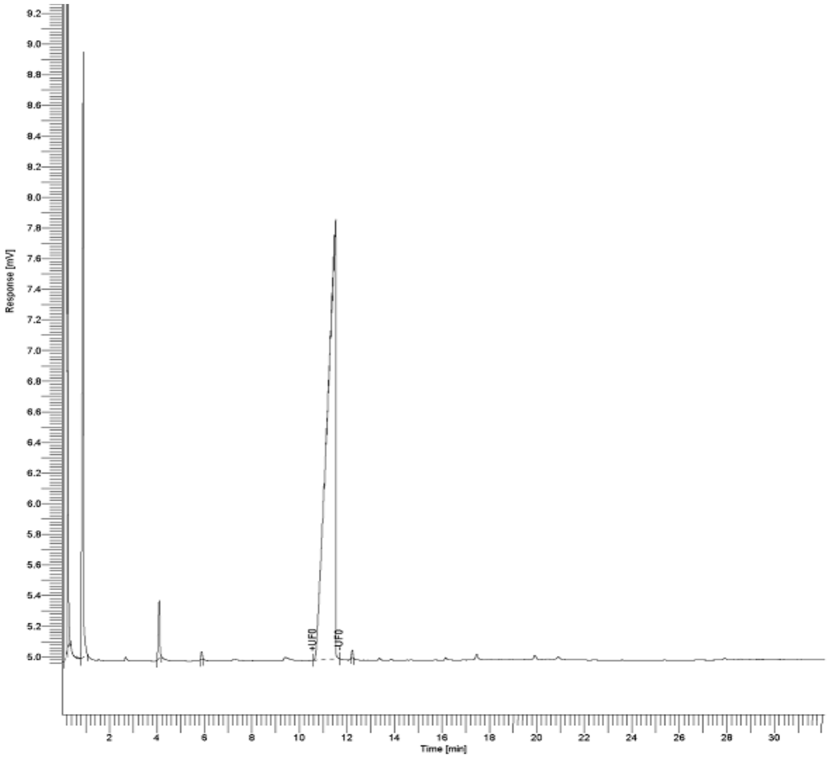


Figure 2.8 – Obtained azelaic acid GC profile

2.2.3 – Heterogeneous catalysis: searching for a solid support.

The possibility of supporting the catalyst on a solid was investigated in order to help separation and recycle of the catalyst. This methodology adopts the principles of *homogeneous supported catalysis*, that combines both advantages of homogeneous and heterogeneous catalysis. The objective is to obtain a finely disperse solid where discrete molecules of catalyst operate as homogeneous species on its surface and in contact with the liquid phase were the reagents are located. The solid support is chosen so that its surface does not affect the stereochemical properties of the metal center.

The catalyst can be supported in various ways (a, b and c in figure 2.9). It can be anchored through a bifunctional linker that binds the surface and possesses a ligand moiety L' that coordinates the metal (a), or can be incapsulated in the pores of the solid (b), or immobilized in a film of solvent (for example hydrophilic in cases of a polar support) deposited on a solid (c).

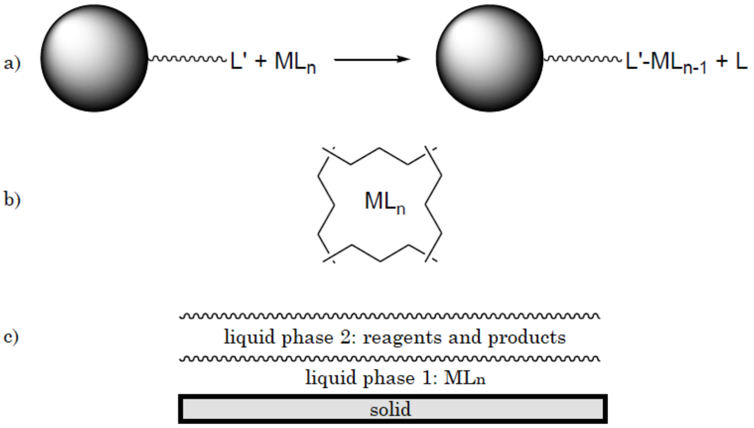


Figure 2.9 – Supporting catalyst methods.[32]

Several advantages can be recognized for this technique:

- Their reactivity is often comparable to that of corresponding homogeneous catalysts, and the reaction mechanisms are equivalent.

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[32] Ruffo F. *Metodi innovativi in Catalisi Omogenea*.

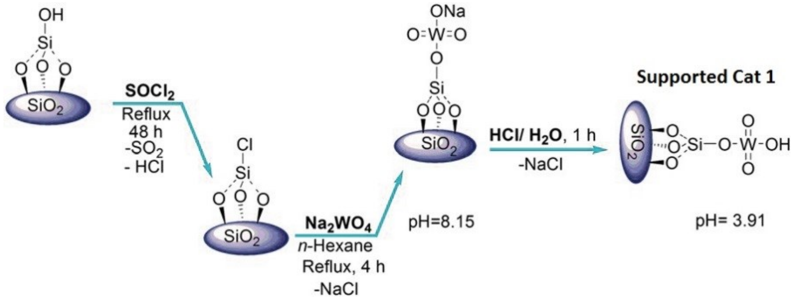
- The catalyst can be recovered by a simple filtration and reused many times, thus lowering the environmental impact of the process.

- If the homogeneous catalyst has corrosive effect on the reactor (the case of many Lewis acid catalysts), the supported counterpart often does not display the same undesired action.

Method (a) was selected to produce three different supported W catalysts, varying the nature of the solid support or the ligand: silica and organic polymers (polystyrene) were selected as candidates.

2.2.3.1 – Supported cat 1

Anchoring the catalyst H_2WO_4 on SiO_2 was carried out according to the synthetic path of scheme 2.7.[33]



Scheme 2.7 – Preparation of supported tungstic acid.

Silica is treated with thionyl chloride to substitute the superficial hydroxyl groups with chlorides. The resulting solid is treated with sodium tungstate to operate a nucleophilic substitution where the chloride is the leaving group and a W-O-Si bond is formed. This powder is then neutralized to obtain a supported tungstic acid (**Supported Cat 1**).

This catalyst was characterized by SEM-EDS microscopy and x-ray diffraction (figure 2.10). The X-ray pattern and the elemental analysis indicated the presence of a high crystalline species with a tungsten content of 44 ± 3 % w/w.

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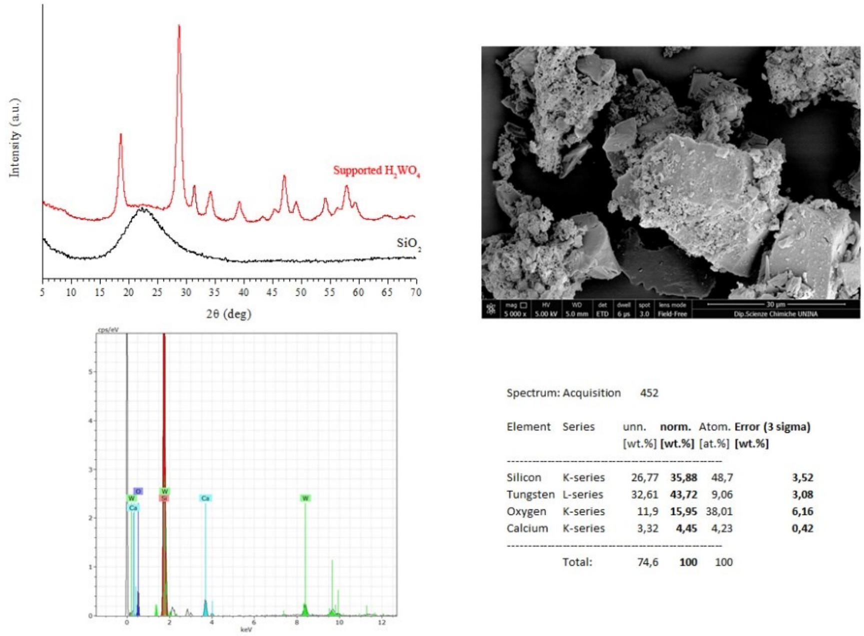
[33] Karami, B.; Ghashghaee, V.; Khodabakhshi, S. *Catalysis Communications* **2012**, 20, 71.



Spectrum: Acquisition 452

Element	Series	unn. [wt.%]	**norm. [wt.%]**	Atom. [at.%]	**Error (3 sigma) [wt.%]**
Silicon	K-series	26,77	**35,88**	48,7	**3,52**
Tungsten	L-series	32,61	**43,72**	9,06	**3,08**
Oxygen	K-series	11,9	**15,95**	38,01	**6,16**
Calcium	K-series	3,32	**4,45**	4,23	**0,42**
	Total:	74,6	**100**	100	

Figure 2.10 – XR and SEM-EDS characterization.

The solid catalyst showed a lower activity with respect to the homogeneous counterpart (entry 4 vs 2 in table 2.6). This result is also a consequence of the inhibitive action of silica: a comparison of entries 1 and 3 discloses a reduction of conversion in the presence of the sole silica gel with respect to the blank. This effect (reproducible also in four subsequent recycles of the catalyst) did not encourage further studies with this solid support, that is not innocent in the reaction system. The interaction between silica gel and hydrogen peroxide is under study in literature, and both degradation or absorption of the peroxide seems to be possible.[34]

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[34] see for example: a) Penner, S. S. *J. Am. Chem. Soc.*, **1952**, *74*, 11, 2754–2757; b) Zeglinski, J.; Piotrowski, G. P.; Piekos, R. *J. Mol. Struc.* **2006**, *794*, 83–91.

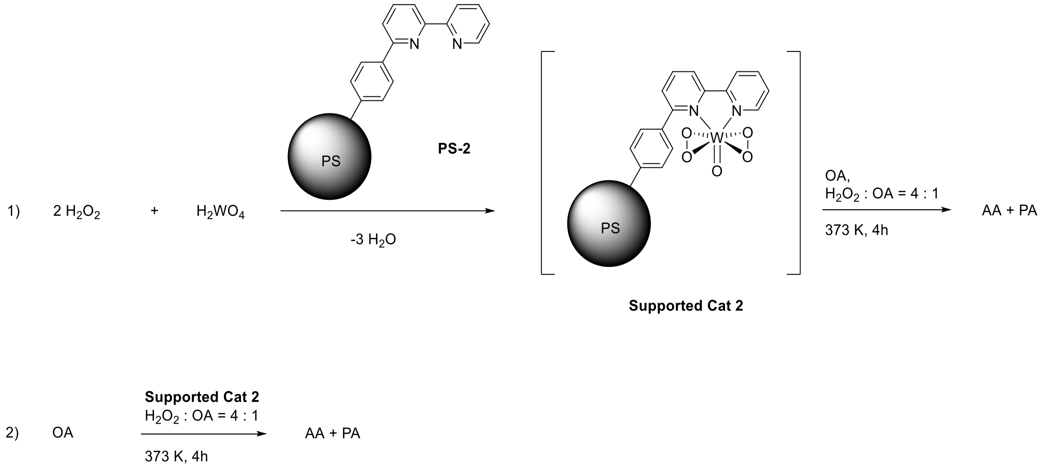
Entry[a]	Catalyst	AA Yield[b], %	PA Yield[b], %
1	**none**	10 ± 1	14 ± 1
2	**H_2WO_4** 1% mol	43 ± 1	36 ± 2
3	**Silica Gel** 5% w/w	<1	<1
4	**Supported Cat 1** 2% mol W 5% w/w	10 ± 1	12 ± 2

a) Reaction conditions: H_2O_2 : OA = 4 : 1 mol/mol; T = 373 K; time = 480 minutes
b) Chromatographic yields, evaluated with GC.

Table 2.6 – **Supported cat 1** acid and silica gel activities.

2.2.3.2 – Supported cat 2

Taking inspiration by literature data,[35] an alternative solid support was selected in a commercially available bipyridine functionalized polystyrene (**PS-2** in scheme 2.8).



Scheme 2.8 – In situ complexation and use as catalyst of **Supported Cat 2**.

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[35] Amini, M.; Haghdoost, M. M.; Bagherzadeh, M. *Coordination Chemistry Reviews* **2014**, 268, 83.

The oxidation of oleic acid was carried out in presence of **PS-2**. In this way, at the formation, the butterfly species can be complexed by the bi-pyridine ligand *in situ*. After the reaction the solid, **Supported Cat 2**, was filtered and re-used for further runs (scheme 2.8).

This catalyst showed a mild activity (entry 4 of table 2.7), but the substantial loss of activity, probably also due to leaching of the metal, within three recycles (first recycle in entry 5) did not encourage further studies with this support.

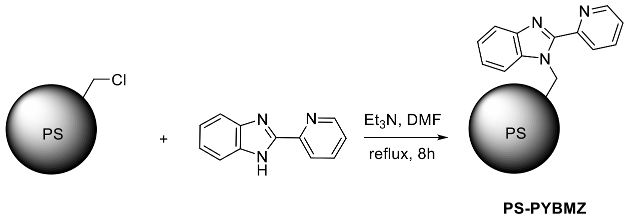
Entry[a]	**Catalyst**	**AA *Yield*,**[a] **%**	**PA *Yield*,**[a] **%**
1	**none**	10 ± 1	14 ± 1
2	**H_2WO_4** 1% mol	43 ± 1	36 ± 2
3	**PS-2** 5% w/w	5 ± 1	12 ± 1
4	**Supported Cat 2** 2% mol W 5% w/w	28 ± 2	22 ± 1
5	Recycle 1 **Supported Cat 2** 2% mol W 5% w/w	16 ± 1	25 ± 1

a) Reaction conditions: H_2O_2 : OA = 4 : 1 mol/mol; T = 373 K; time = 480 minutes
b) Chromatographic yields, evaluated with GC.

Table 2.7 – Supported cat 2 and polystyrene resin activities.

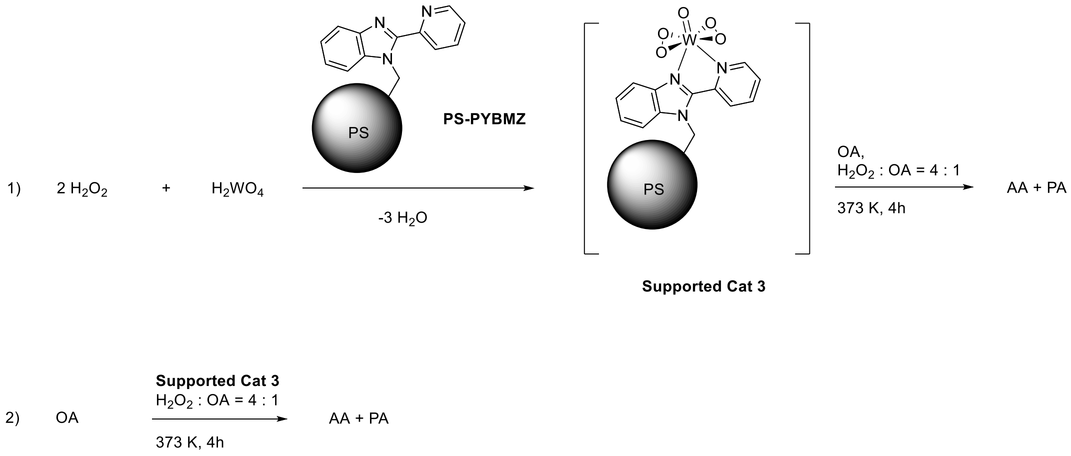
2.2.3.3 – Supported cat 3

Another modified polystyrene was considered to support tungstic acid. Following a literature procedure, the polymer-anchored 2-(2-pyridyl)benzimidazole (**PS-PYBMZ**) was synthetized (scheme 2.9).[36]



Scheme 2.9 – Polymer-anchored 2-(2-pyridyl)benzimidazole (**PS-PYBMZ**) synthesis.

A commercially available chlorine modified polystyrene was allowed to react with 2-(2-pyridyl)benzimidazole to obtain **PS-PYBMZ**. This was used in a similar fashion of **PS-2,** as described in the previous paragraph, to afford **Supported Cat 3** *in situ* (scheme 2.10).



Scheme 2.10 – In situ complexation and use as catalyst of **Supported Cat 3**.

The catalyst showed no activity in the first run (entry 3 in in table 2.8), where the complexation occurred. This can be due to a changed activation kinetic and may

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[36] Maurya, M.R.; Kumar, M.; Sikarwar, S. *Reactive & Functional Polymers* **2006**, *66*, 808–818.

indicate that a change of the activation modality for this first run is needed. However, from the first recycle run, a good activity, comparable to homogeneous catalyst was observed (entry 4 vs. entry 2)

Entry^{a}	**Catalyst**	**AA *Yield*,**^{a} **%**	**PA *Yield*,**^{a} **%**
1	**none**	10 ± 1	14 ± 1
2	**H_2WO_4** 1% mol	43 ± 1	36 ± 2
3	**Supported Cat 3** 2% mol W 6% w/w	13 ± 1	11 ± 1
4	Recycle 1 **Supported Cat 3** 2% mol W 6% w/w	39 ± 2	17 ± 2

a) Reaction conditions: H_2O_2 : OA = 4 : 1 mol/mol; T = 373 K; time = 480 minutes
b) Chromatographic yields, evaluated with GC.

Table 2.8 – Supported cat 3 and activity.

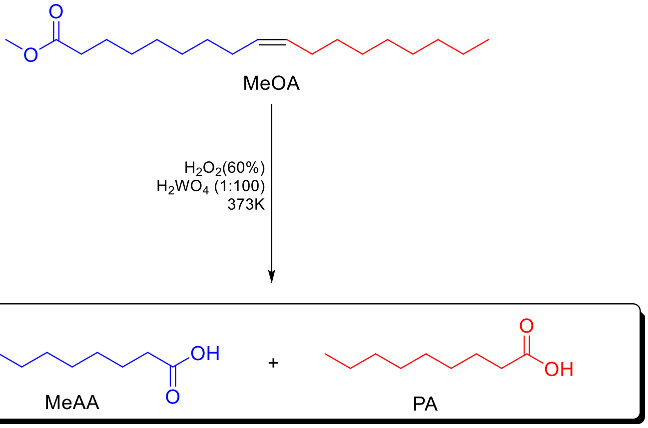
The successive recovers of the catalyst were difficult. The powder darkened, changed in morphology and showed a consistent loss in weight. These findings may indicate degradation of the support itself, as polystyrene might not be completely inert under these reaction conditions.

The ensemble of these results show that the design of a successful supported catalyst must rely in finding an inert and innocent support, and, therefore, further investigations are needed in this field.

2.2.4 – Oxidation of oleate methyl ester.

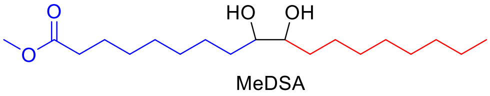
Many recovering processes of oleic acid, from oils or fats, reckon on transesterification processes that provide, in first instance, the oleate methyl ester (MeOA).[21, 22]

Thus, the homogeneous catalyst of paragraph 2.2.2 was applied to this substrate (scheme 2.11).



Scheme 2.11 – Oxidation of metyl oleate (MeOA)

The reaction mechanism of the oxidation can be considered analogous to that of oleic acid. The difference is in the products and the intermediate, that is methyl 9,10-dihydroxystearate (scheme 2.12).



Scheme 2.12 – Methyl 9,10-dihydroxystearate

The optimization of the process was carried out varying the time of the reaction and the oxidant/substrate ratio.

Entry[a]	***time*, h**	**H_2O_2 : OA, mol / mol**	**PA *Yield*,**[a] **%**	**MeAA *Yield*,**[a] **%**
1	2	4 : 1	9 ± 1	14 ± 1
2		8 : 1	10 ± 1	6 ± 1
3	4	4 : 1	29 ± 2	28 ± 2
4		8 : 1	27 ± 2	31 ± 2
5	8	4 : 1	33 ± 2	39 ± 2
6		8 : 1	35 ± 2	40 ± 2
7	24	4 : 1	27 ± 2	31 ± 2
8		8 : 1	50 ± 2	57 ± 2

a) Reaction condition: MeOA : H2WO4 = 100 : 1 mol/mol; T = 373 K
b) Chromatographic yields, evaluated with GC.

Table 2.9 – Oxidant/substrate optimization

From the data it can be inferred that at two and four hours, with oxidant/substrate ratios of either 4 : 1 or 8 : 1, the yields are not satisfying if compared to the oxidation of oleic acid (entry 1-4 in table 2.9).

Better results are obtained raising the reaction time to eight hours (entry 5-6). In this case the yields don't change significantly with the oxidant/substrate ratio probably because of the slower kinetic of the reaction compared to the oxidation of oleic acid. The difference in yields with different oxidant loadings can be appreciated with the longer reaction time of 24 hours (entry 7-8). Acceptable yields are obtained when the oxidant/substrate ratio is 8 : 1.

The lower yield obtained in entry 7, compared to entries 5 and 6, suggests that with this longer reaction time some degradation and/or side reaction occurs.

In general, the yields are lower to those obtained with oleic acid. This is probably due to the different polarity of the substrates, that makes the mixing more difficult in the case of methyl ester, without the use of any transfer agent or solvent.

However, the results are good enough to push the research in this field, to find a procedure capable of being used on oleic acid esters and/or directly on waste oils.

2.3 – Materials and method

General

Solvents, oleic acid (90%) and the other reagents were purchased from Sigma-Aldrich. Aqueous hydrogen peroxide (aqueous solution 60 %) was supplied by Solvay (Rosignano, Italy).

The collected samples were quantified by gas chromatography on a Perkin-Elmer instrument coupled to a flame ionization detector (FID), equipped with a capillary column Perkin Elmer Elite Series 5 (0.10 μm, 0.32mm ID, 15 m). The carrier gas was helium at a pressure of 1.72 bar at the head of the column. The injector temperature was 423 K and the detector temperature was 523 K. The oven temperature was held at 313 K for 1 min, then ramped to 453 K at 7 K/min and kept for 1 min, finally increased to 503 K at 7 K/min kept for 4 min.

All samples (25 mg mixture dissolved in 500 μL THF) were derivatized with BSTFA (300 μL). *n*-Undecane was added as the internal standard (1% v/v) to 5 mL of hexane.

^{1}H NMR spectra were recorded in $CDCl_3$ at 400 MHz.

Oxidative cleavage in two steps

In a 250-mL round-bottom flask equipped with a condenser, tungstic acid (0.040 g, 0.160 mmol) was suspended in an aqueous solution of H_2O_2 (60% w/w, 1.36 g, 24 mmol) and the system was stirred at 343 K. Oleic acid (5.1 mL, 16 mmol) was added as soon as the completely dissolution of tungstic acid was observed. After 2h, the mixture was allowed to cool down to room temperature and NaOCl (4.5% active Cl_2, 150 mL, 95.4 mmol) was added. The system was stirred at room temperature for 2 h, and pH was then adjusted to 1 with an aqueous hydrochloric acid solution (37% w/w). The reaction mixture was extracted with ethyl acetate (4×200 mL). The combined organic layers were dried with anhydrous sodium sulfate and evaporated under reduced pressure. The products were analyzed by ^1H NMR without further purification of the crude material and through GC after derivatization. (t_r AA = 11 min; t_r PA = 4.2 min).

Procedure for obtaining a fraction enriched in the intermediate peroxo species PS.

In a 250-mL round-bottom flask equipped with a condenser, tungstic acid (0.040 g, 0.160 mmol) was suspended in an aqueous solution of H_2O_2 (60% w/w, 1.36 g, 24 mmol) and the system was stirred at 343 K. Oleic acid (5.1 mL, 16 mmol) was added as soon as the completely dissolution of tungstic acid was observed. After 2h, the mixture was allowed to cool down to room temperature. The oily residue was melted and hexane was added. After cooling at 273 K, the resulting white solid was filtered (mainly DSA), and washed with hexane. The solvents were removed under vacuum from the liquor mother, and hexane was added at 273 K to the resulting oily residue. The resulting white solid was again filtered (mainly DSA), and washed with hexane. The solvents were removed under vacuum from the liquor mother, affording a fraction enriched in PS. *Caution: evaporation of solutions which may contain hydrogen peroxide or peroxo species at a rotary evaporator represents a serious safety risk and can hazard people and cause an explosion and destruction of equipment.* The peroxides value was 550 mmol O_2/Kg (NFT 60-220).

Oxidative cleavage in a single step

In a 250-mL round-bottom flask equipped with a condenser, tungstic acid (0.283 g, 1.13 mmol) was suspended in an aqueous solution of H_2O_2 (60% w/w, 51.2 g, 904 mmol) and the system was stirred at 343 K. Oleic acid (36.3 mL, 113 mmol) was added as soon as the completely dissolution of tungstic acid was observed. The reaction mixture was stirred under reflux. After 8h, the mixture was allowed to cool down to room temperature and cool water (50 mL) was added. The reaction mixture was extracted with hot ethyl acetate (4×100 mL). The combined organic layers were dried with anhydrous sodium sulfate and evaporated under reduced pressure. The products were analyzed by ^{1}H NMR without further purification of the crude material and by GC after derivatization. (t_r AA = 11 min; t_r PA = 4.2 min, t_r DSA = 20 min).

Separation and purification of azelaic acid (single step)

The reaction mixture was extracted with cool water (100 mL) and then with hot ethyl acetate (3×200 mL). The volume of the organic phase was reduced under vacuum and extracted with hot water (3×50 mL). On cooling the aqueous phase, a white precipitate of azelaic acid formed, which was collected, washed with cool water and dried (isolated yield: 60%).

Preparation of ***Supported cat 1***

A sample of silica-gel (20.9 g) was dried in an oven at 130 °C for 1.5 h and then in a round bottom flask (500 mL) in vacuum for 15 min at 130°C. The system was equipped with a condenser and a dying tube and 80 mL of thionil chloride was added. The stirred mixture was refluxed in presence of calcium chloride for 48 h. The resulting greyish powder was filtered; then was put in presence of sodium tungstate (31.8 g, 65.5 mmol), suspended and stirred in *n*-hexane (70 mL) and refluxed for 4 h. The reaction mixture was filtered and washed with distilled water, dried and that stirred for 1 h at room temperature in HCl 0.1 M. The mixture was filtered, washed with distilled water and dried in presence of P_2O_5 to afford the **supported cat 1** in the form of a white powder (36.8 g, loading estimation of W = 2.12 mmol/g, 39% w/w).

The solid was characterized by SEM-EDS microscopy and x-ray diffraction. The X-ray pattern and the elemental analysis indicated the presence of a high crystalline species with a tungsten content of 44 ± 3 % w/w.

Supported cat 1 was then used instead of tungstic acid in procedure: Oxidative cleavage in a single step. Then it was recovered by filtration, washed with distilled water and then with hot ethyl acetate and dried.

Preparation and recycle of ***Supported cat 2***

Commercially available pyridine functionalized polystyrene (0.330 g, n of pyridine 0.495 mmol) was suspended in H_2O_2 (11 g, 162.3 mmol). The mixture was stirred for 10 min at room temperature. Then tungstic acid (0.101 g, 0.406 mmol) is added and the mixture is kept at 343 K for 15 min. Oleic acid (7.5 mL, 6.7 g, 20.3 mmol) is added and the system is brought to reflux. After 4 hours the mixture was fitered. Mother liquor was treated as in *oxidative cleavage in a single step procedure*. The solid was washed with distilled water then with hot ethyl acetate and dried to afford **supported cat 2** as a yellow/brownish powder (0.367 g).

Supported cat 2 was then used instead of tungstic acid in procedure: *oxidative cleavage in a single step*. Then it was recovered by filtration, washed with distilled water and then with hot ethyl acetate and dried.

Preparation and recycle of ***Supported cat 3***

Commercially available chlorine functionalized polystyrene (2.37 g, chlorine loading 5.5 mmol/g) were suspended in a 100 mL round bottom flask in DFM (20 mL) and kept under stirring for 12 h at room temperature. Then a solution of 2-(2-pyridyl)benzimidazole (PYMBZ, 1.29 g) in DMF and a second solution of triethylamine (3.53g) in ethyl acetate (30 mL) were added. The system was kept at reflux for 8 h. Than the suspension is filtered, washed with hot DMF and hot ethanol and then dried to afford PS-PYBMZ (loading of PYMBZ 1.61 mmol/g).

In a 100 mL round bottom flask, PS-PYBMZ (0.738 g, 1.19 mmol of PYMBZ) was suspended in hydrogen peroxide (20 mL, 60% v/v) and stirred at room temperature. Tungstic acid (226.3 mg, 0.906 mmol) was added and the mixture was kept under stirring at 343 K for 15 min. Oleic acid (14 mL, 12.7 g, 45.3 mmol) was added and the system was brought to reflux. After 4 hours the mixture was fitered. Mother liquor was treated as in *oxidative cleavage in a single step procedure*. The solid was washed with distilled water then with hot ethyl acetate and dried to afford **supported cat 3**.

Supported cat 3 was then used instead of tungstic acid in procedure: *oxidative cleavage in a single step*. Then it was recovered by filtration, washed with distilled water and then with hot ethyl acetate and dried.

Oxidation of methyl oleate.

The procedure to oxidize methyl oleate was identical to o*xidative cleavage in a single step* using the proper quantities of methyl oleate and reaction time as reported in paragraph 2.2.4.

2.4 – Conclusions

In perspective of providing an alternative to ozonolysis, a sustainable process for the production of azelaic acid and pelargonic acid was proposed. The results of paragraph 2.2.2 and 2.2.3 were published as: *Sustainable Process for Production of Azelaic Acid Through Oxidative Cleavage of Oleic Acid* Benessere, V.; Cucciolito, M. E.; De Santis, A.; Di Serio, M.; Esposito, R.; Ruffo, F.; Turco, R. *J. Am. Oil Chem Soc*, 92, **2015**, 1701.

In addition, the application of the catalytic system on esters of oleic acid was evaluated and the application of this system to more complex matrix (*i.e.* triglycerides) was started to be examined.

Then, a design of the possibility to support the catalyst on a solid, to allow recover and reuse, was started to explore.

Chapter 3

Biodiesel

3.1 – Biodiesel in industry

Petrol is not a renewable source and sooner or later will be depleted. In addition, combustion of oil derivatives is a major source of pollution; in fact, CO_2, CO, sulfur and nitrogen oxides, volatile organic compounds and particulates are significantly harmful and the main cause of environmental problems, such as the greenhouse effect (in the case of nitrogen oxides and carbon dioxide) and acid rains (in the case of sulfur oxides).[37]

As stated in chapter 1, *biofuels* (figure 1.6) are alternative fuels derived from *biomass*, a renewable resource.

Some directives have been approved by the European Parliament: Directive 2005/55 / EC limits the environmental impact, which further reduces emissions of pollutants by 30% compared to the Kyoto Protocol; Directive 2009/28/EC states that a mandatory 10% minimum target for the share of biofuels in transport petrol and diesel consumption has to be achieved by all Member States by 2020.[38]

Biodiesel covers 80% of the entire European biofuel production, followed by 20% of bioethanol. In 2007, about 10 billion liters of biodiesel were produced, with an increase of +1100% from the beginning of 2000. The European Union is currently the world's leading producer with 6 billion liters of vegetable production in 2007. Following are the United States with 2 billion liters, Indonesia with 400 million liters and Malaysia with 300 million.[39]

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[37] P. Crosignani C. Bocchi*, Emissioni da traffico veicolare,diesel sotto esame* ARPA Rivista N. 6, **2005**

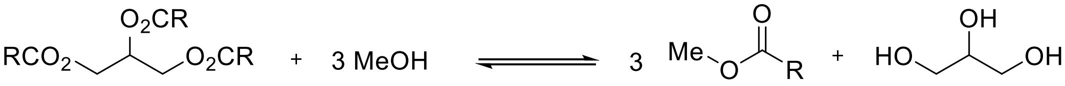
[38] http://eur-lex.europa.eu; European Biodiesel Board Report **2011**.

[39] www.ecoage.com, Produzione mondiale di Biodiesel.

Most of the merit comes from the role of Germany with 2861 million tons produced in 2010, followed by France, Spain and Italy, with 1910, 925 and 706 thousand tons, respectively. In 2010 there was an increase in European biodiesel manufactureof 5.5% compared to 2009, for a total of 9.570 million tons produced throughout Europe.[40]

First studies on alternative biofuels date back to the late 1800's and were conducted by the engineer Rudolf Diesel, who used a blend of vegetable oils. In fact, while being a good fuel (since its calorific value is about 90% that of fossil diesel), the vegetable oil did not provide satisfactory performance due to its low volatility and high viscosity. Since then, for decades, it has been worked with the aim of obtaining good fuel from natural substances; the studies carried out have identified different methodologies by which it is possible to lower the viscosity of vegetable or animal oils in order to make them suitable for diesel engines.[41]

Among them, the most widely used is the transesterification reaction of triglycerides with alcohols, also called alcoholysis (scheme 3.1), that significantly lowers the viscosity of the starting oil.



Scheme 3.1 – Transesterification reaction

The reaction is typically catalyzed by mixtures alkaline metal hydroxides and alcohols. Products of this reaction are fatty acid alkyl esters and glycerin. The obtained ester mixture is a good fuel and is more commonly known as biodiesel because it has properties comparable to fossil diesel.

The benefits of using biodiesel as fuel are many: first of all its low environmental impact, since it is a renewable energy source and is a biodegradable product; its possible dispersion in the environment is quickly absorbed and eliminated, as the bacteria in the

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[40] www.ebb-eu.org/index.php, Statistics.

[41] (a) Ma, F.; Hanna, M. A. *Bioresource Technology*, **1999**, *70*, 1-15. (b) Fukuda, H.; Kondo, A.; Noda, H. *J Biosci Bioeng*, **2001**, *92*, 405-416.

soil and in the water rapidly degrade it. Its biodegradability is 81% in 28 days, while diesel oil degrades, after the same number of days, at an extent of only 54%.[42]

Due to its high biodegradability, the use of biodiesel is particularly indicated in protected areas for nautical and transports on land, and wherever there is danger of leakage of fuel.

Biodiesel is safer to handle and store because it has a flash point higher than that of mineral diesel. Figure 3.1 shows the emissions of diesel engines fueled with conventional diesel and biodiesel, and in table 3.1 the chemical and physical parameters of biodiesel and diesel, defined in Italy by C.T.I.[43], are compared:

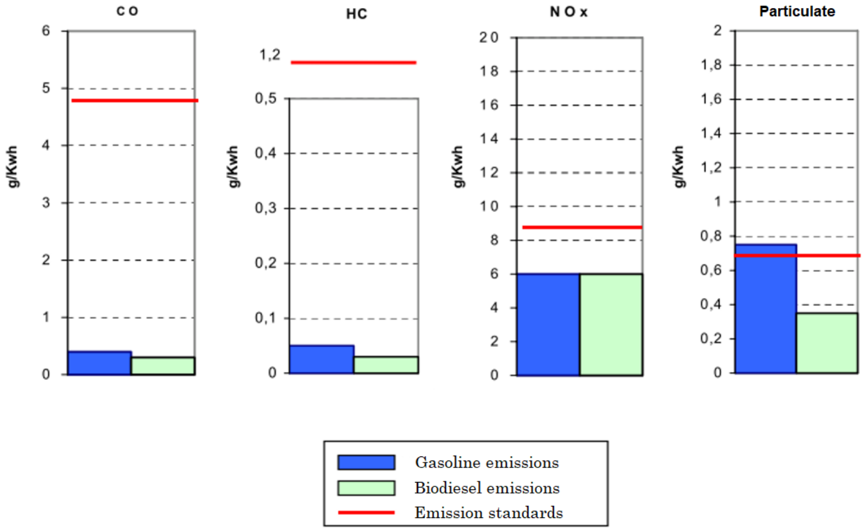

Figure 3.1 – Diesel and Biodiesel emissions

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[42] http://www.cti2000.it

[43] Manglaviti, A., *Biodiesel: il gasolio che nasce dai campi*, ICP ,**2001**, 144-146

Property	**Biodiesel**	**Gasoline**
Specific Weight at 15°C	0.880	0.845
Water content	0.03 max	0.05 max
Kinematic viscosity	5.0 CsT max	5.35 CsT max
Cetane number	52	47
Sulphur (% w/w)	None	0.1-0.2
Pour point	-24°C	-6°C
Flash point	118°C	55°C
Heating Value	33175 MJ/L	35700 MJ/L

Kinematic viscosity is the resistance that molecules encounter while flowing one respect to the other; it increases with the content of saturated fatty acids and the length of fatty acid chains. The cetane number indicates fuel readiness at power on, it affects cold start, engine noise, combustion and therefore gas and particulate emissions. The pour point is the temperature at which the fuel flow ceases due to the formation of solid fractions. The flash point indicates the minimum temperature at which the fuel vapors ignite in the presence of the flame; Low values of this parameter are indicative of the presence of volatile and flammable compounds. Heating value is the energy released by a fuel during the combustion process.

Table 3.1 – Biodiesel and Diesel chemical and physical parameters

The use of biodiesel as a fuel for cars does not require engine modifications, provided that it is mixed with small quantities (2 to 30%) of diesel fuel, while it is compatible with all diesel engines operating in thermal power plants, heating installations and on buses, without making any changes to the distribution system.

However, the production of biodiesel involves high costs compared to the production of petroleum products.

A solution to excessive biodiesel production costs may be the use of waste oils, such as waste cooking oils or oily residues from other productions. The use of these oils results in a substantial reduction in the cost of raw materials (the substrate purity affects 85% on the price), however, their high free fatty acid content contributes to increasing technology-related issues of the biodiesel production process.

3.1.2 – Catalysis

As mentioned before, biodiesel is produced by triglycerides transesterification reaction. These, by reaction with an alcohol, typically methanol, are converted into the corresponding alkyl esters. As by-product of this reaction, raw glycerin is obtained (scheme 3.1).

Specifically, transesterification is an equilibrium reaction that takes place according to a staging process in which the triglycerides are converted by reversible and consecutive reactions, first into diglycerides, then into monoglycerides and finally into glycerol. An equivalent of alkyl esters is released in each step.

The transesterification reaction is industrially conducted in stirred, batch reactors or in continuous reactors[44] mixing the oil with the alcohol and then adding the alkaline catalyst when the pre-setted temperature is reached. At the end of the reaction, the catalyst is neutralized, and the resulting mixture is distilled for the recovery of the excess alcohol, and then left to decant in order to separate the ester mixture from glycerol. The latter is further distilled to eliminate the residual alcohol.

The reaction rate depends on several variables: nature of substrate and alcohol, stoichiometric ratio between reagents, temperature, mixing rate and type of catalyst employed.

Generally, the reaction is conducted at the boiling temperature of the alcohol at atmospheric pressure. The oils used as substrate are made up of triglycerides with different types of esters and a certain fraction of free fatty acids. With respect to the alcohols to be used in this process, it has been experimentally observed that the alcoholysis of soybean oil is much slower with methanol than with butanol. This is because butanol and oil are miscible, while the methanol-oil system is heterogeneous. Instead, production of methyl esters with basic catalysis occurs more easily than that of ethyl esters. Indeed, the formation of stable emulsions occurs during the ethanolysis

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[44] Ster R. ; Hillion G. ; Rouxel J. J. ; *Noeveau procede de fabrication en continu d'esters methiliques d'uiles vegetales a usage carburant*, GECAT , **2002.**

process, caused in part by the formation of intermediates, diglycerides and monoglycerides, which compromises the separation of esters from glycerol.

In some cases, the use of a co-solvent favors conversions.[45] The co-solvent must be miscible with both alcohol and oily phases and must have boiling temperatures close to that of the alcohol to facilitate its removal from the reaction products.[46] The most commonly used cosolvents are tetrahydrofuran (THF) and *t*-butylmethylether (MTBE). One of the most important variables that influence the yield of the reaction is the molar ratio between alcohol and triglycerides. The stoichiometry of the process requires three moles of alcohol per mole of triglyceride. However, excess of alcohol is needed to shift the equilibrium and obtain complete conversion. The optimal molar ratio depends on the type of catalyst. In a reaction that occurs with alkaline catalysis, a molar ratio alcohol/oil of 6 : 1 is sufficient.

As for the temperature, direct proportionality has been observed with respect to conversion. It has also been found that when the reaction time increases, the temperature and concentration of the catalyst no longer influence the yield.[47]

Finally, because of the multi-phase nature of the system, the stirring rate is also a critical parameter.

One of the most efficient catalysts, also used in large-scale production, is sodium methoxide. This is produced in situ by addition of NaOH to the mixture. The reaction between NaOH and the alcohol also forms a small amount of water, which can be a problem due to the formation of soaps:

$$NaOH + CH_3OH = NaOCH_3 + H_2O$$

The mechanism proposed by Eckey[48] for the reaction of transesterification catalyzed by alkali involves the succession of three steps.

In the first stage there is an attack on the carbonyl carbon atom of the ester group by the alkoxide to form a tetrahedral intermediate. In the second step, the

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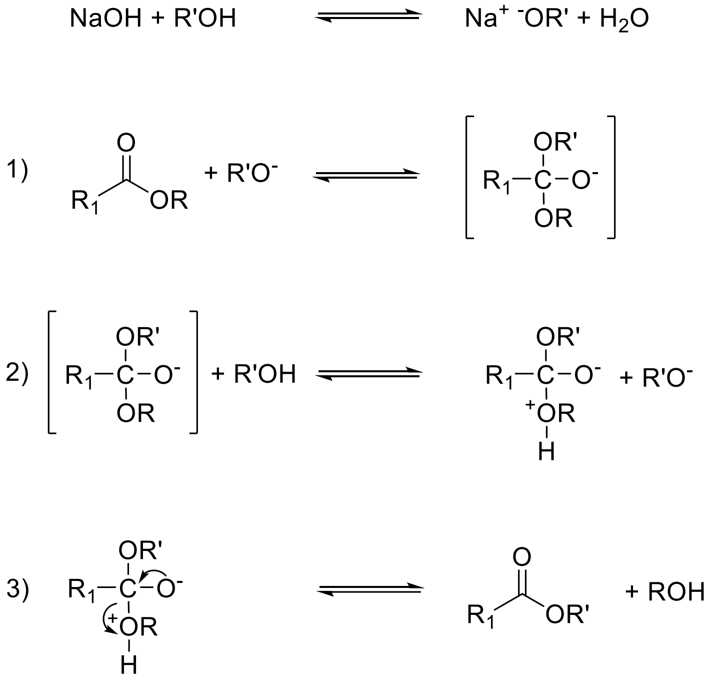
[45] Boocock, D.G.B., Konar, SK., Mao, V., Sidi, H., *Fast one-phase oil rich processes for the preparation of vegetable oil methyl esters, Biomass and bioenergy*, 1: **1996**, 43-50.
[46] D.G.B. Boocock, *Single phase process for production of fatty acid methyl esters from mixtures of triglycerides and fatty acids*, **2001**, WO0112581.
[47] Freedman, B.; Pryde, E. H.; Mounts, T. L. *J Am Oil Chem Soc*, **1984**, *61*, 1638-1643.
[48] E.W. Eckey, *J Am Oil Chem Soc*, **1956**, *33*, 575-579

tetrahedral intermediate reacts with a molecule of alcohol to regenerate the alkoxide. In the last step, a rearrangement of the tetrahedral intermediate produces a diglyceride molecule and one fatty acid ester. Scheme 3.2 below summarizes the steps of the alkaline transesterification described above.



Scheme 3.2 – Alkaline catalysis

One of the limitations of this procedure is the acidity of the system (due to free fatty acids present in the oil) leading to neutralization of the catalyst. Therefore, the free fatty acid content in the substrate is preliminary reduced by treating the oils before transesterification (pretreatment in scheme 3.3).

This process consists in the esterification of the substrates with methanol in the presence of acid catalysts (sulphuric acid),[49] through which the free fatty acids contained in the starting oil are converted into methyl esters.

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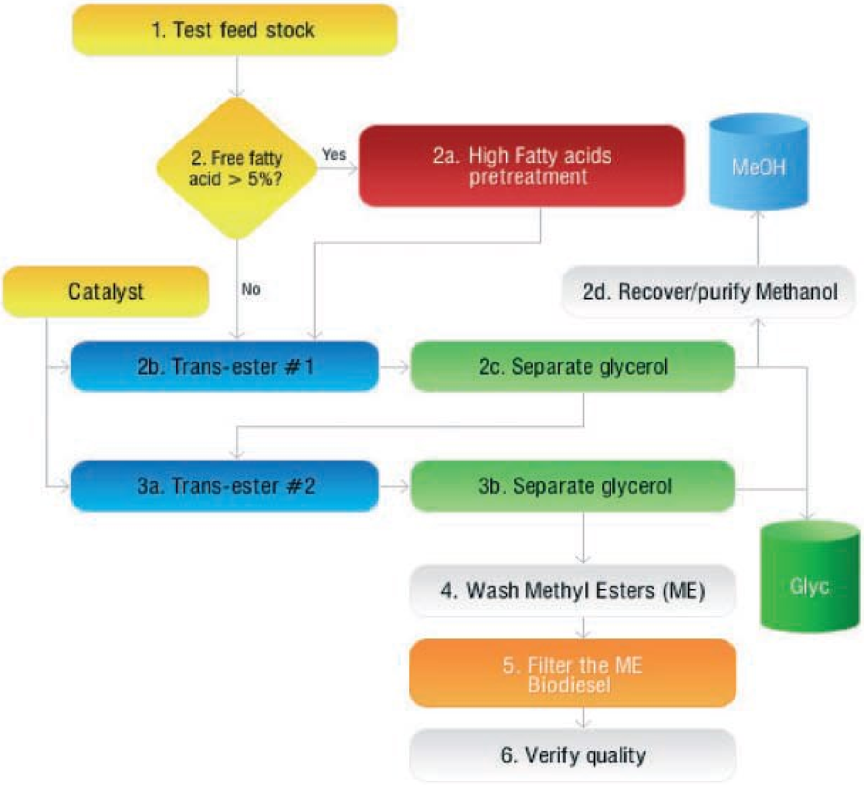
[49] Allinger, N. L.; Cava, M. P.; De Jongh, D. C.; Johnson, C. R.; Lebel, N. A.; Stevens, C. L. *Reazioni degli acidi carbossilici e loro derivati, Preparazione degli esteri, Chimica organica, Zanichelli*, **1993**, 498-499

$$RCOOH + MeOH = RCOOMe + H_2O$$

Subsequently, after a neutralization and anhydrification process, basic catalysis occurs. Based on the industrial process proposed by Jeromin,[50] the production of biodiesel from acid substrates can be schematized (scheme 3.3):



Scheme 3.3 – Biodiesel production scheme - alkaline catalysis

However, the esterification stage often is not sufficient to completely eliminate the acidity in the system; for this reason, it is still needed the identification of new catalysts, that are active in transesterification and at the same time are not affected by the acidity of the starting oil.

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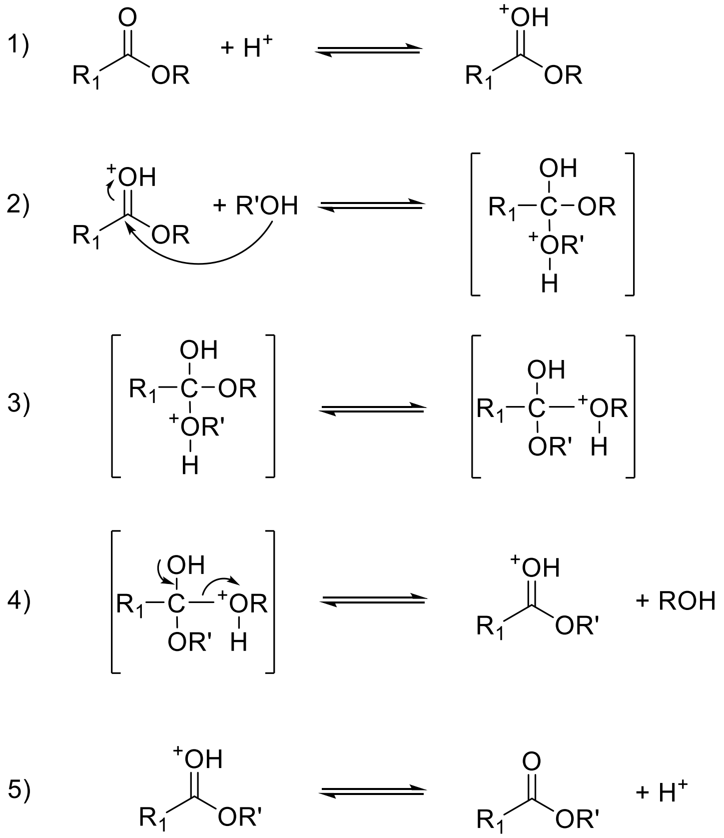
[50] Jeromin, Lutz, Gerhard, *Process for the pre-esterification of free fatty acids in fats and oils*, U.S. **1987**, 4,698,186

Protic acids may be used as catalysts, because they are active even in the presence of a consistent fraction of free fatty acids or moisture.

The mechanism involved in the transesterification of triglycerides catalyzed by Brønsted acids is that proposed by Fisher; it consists of the following reaction steps:



Scheme 3.4 – Brønsted acid catalyzed transesterification

Studies conducted by Alcantara[51] comparing the behavior of alkaline catalysts with that of acid catalysts showed that the reaction catalyzed by H_2SO_4 (1% by weight respect to the substrate) yields 13% conversions after 48 hours of reaction; instead, the

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[51] Alcantara, R.; Amores, J.; Canoira, L.; Fidalgo, E.; Franco, M. J.; Navarro, A. *Biomass Bioenergy* **2000**, *18*, 515-527.

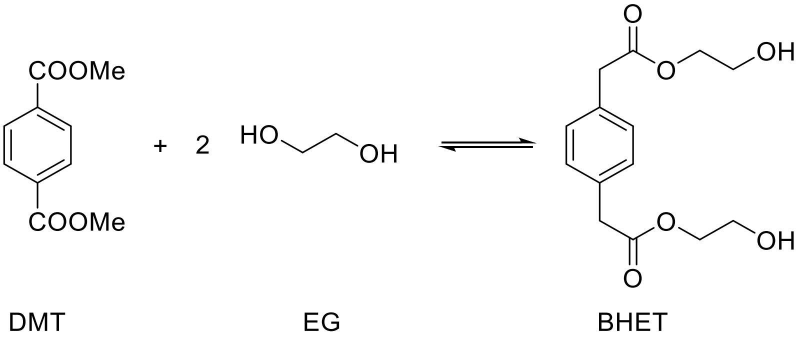
reaction promoted by sodium methoxide (1% by weight) reaches total conversions (equal to 95%) in less than three hours.

The processes catalyzed by Brønsted acids require considerably longer reaction times than those required in basic catalysis and generally higher temperatures that may favor secondary reactions.

In addition, while a reaction that occurs with alkaline catalysis requires only a molar ratio of 6 : 1 between alcohol and oil, acid catalysis requires a ratio equal to 30 : 1 to obtain the same yield.

In 1994 Basu et al,[52] proposed to use strong Lewis acids as catalysts for the transesterification reaction, specifically a mixture of calcium acetate and barium acetate in weight ratio of 3:1. The use of this mixture of acetates with strongly acidic metal ions has represented a remarkable improvement in the production of esters. It enables transesterification without prior esterification of substrates containing various impurities, such as highly acidic oils, greases, and oils with diglycerides, and monoglycerides.

It is expected that the catalytic activity of the metal ions is related to their Lewis acidity, and a criterion for expressing this property for divalent metals has been proposed[52] on the basis of the mechanism hypothesized for the transesterification of dimethylterphthalate (DMT) with 1,2-dihyroxyethane (scheme 3.5):



Scheme 3.5 – Transesterification of DMT

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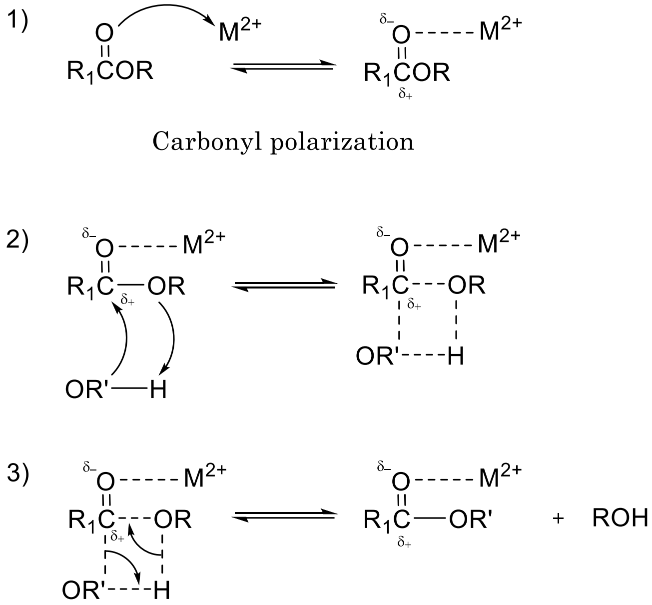
[52] Basu , Hemendra, Norris, *Process for production of esters for use as a diesel substitute using a non-alkaline catalyst*, U.S. **1996** 5,525,126

Coordination of the carbonyl group to the metal ion lowers the electronic density of the former one, which becomes activated towards the nucleophilic attack of the alcohol. Then a bonds exchange leads to the new ester and the leaving alcohol ROH. The catalytic cycle is completed by the dissociation of the carbonyl group from the metal ion (scheme 3.6).



Scheme 3.6 – Mechanism of the metal catalyzed transesterification

Tomita and Ida[53] correlated the acidity of several metal ions (expressed in function of the stability of their complexes with DMT), to the activity of the corresponding acetates in the transesterification of the same DMT.

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[53] Tomita, K.; Ida, H. *Polymer*, **1975**, *16*, 185-190.

A curve with a particular trend was obtained, defined as "volcano curve" (figure 3.2)

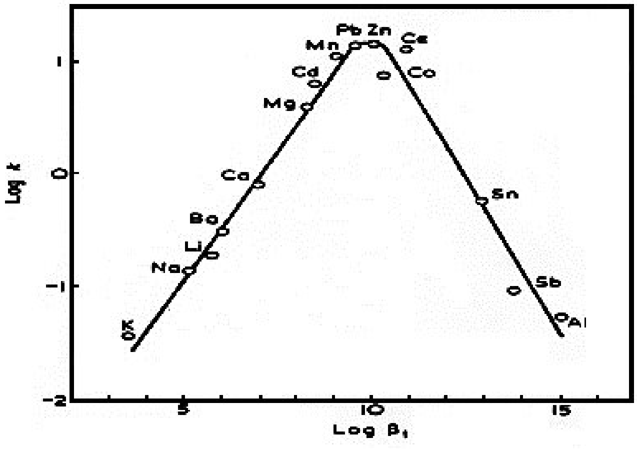

Figure 3.2 – Volcano curve

In this graph, the acidity of the metals is reported on the horizontal axis, expressed as the logarithm of the stability constant of the complexes formed with DMT (log β), whereas the ordinates report the total activity of the various acetates in the transesterification of DMT.

As it can be seen from the curve, the maximum values of catalytic activity concentrate on certain acidity values of the system, beyond which the activities decrease. This behavior can be explained by the fact that, as the acidic strength of the metal increases, the bond between the metal and the carbonyl becomes strong enough to prevent the release of the catalyst and its re-use in a subsequent catalytic cycle. As a result, there is a slowdown in the overall reaction rate.

This preliminary study paved the way for the use of Lewis acid catalysts in the production of biodiesel. In fact, over the years, numerous contributions have appeared, which describe the use of catalysts based on different metals for the transesterification reaction.[54]

Aiming to contribute to this emerging area, the present study has been devoted to the development of zinc(II) catalysts, in the light of the privileged position that this

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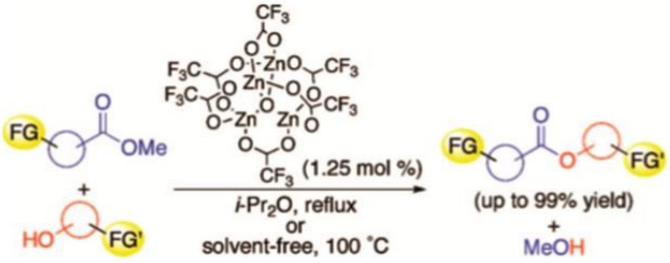
[54] Helwani, Z. et al. *Appl Catal A* **2009**, *363*, 1 and references therein.

ion occupies in the volcano curve, and also for its availability and low toxicity. In particular, the ability of simple salts to promote a model transesterification reaction has been preliminary verified, and subsequently the results have been used to design a homogeneous supported catalyst according to the principles mentioned in the previous chapter. This strategy has allowed to promote the contemporary transesterification and esterification even of acidic waste oils, with easy separation and immediate recycling of the catalyst.

3.2 – Lewis acid catalysis

3.2.1 – Screening of simple zinc (II) salts in a model transesterification reaction

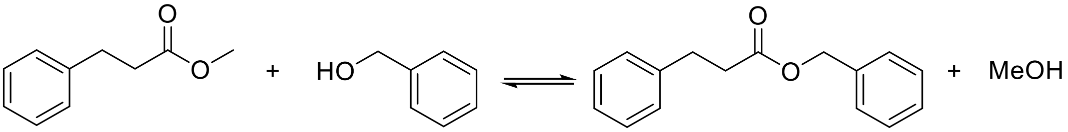
Starting point for the assessment of the catalytic performance of simple salts of Zn(II) has been a previous work dated 2008, that reports a study on the transesterification of various methyl esters, catalyzed by a sophisticated tetranuclear complex of Zn(II) (scheme 3.7). The reactions were conducted at reflux for 18h in di-isopropyl ether and in a controlled atmosphere of Ar.[55]



Scheme 3.7 – Tetranuclear zinc (II) catalyst for transesterification reaction

A critical evaluation of this process discloses that it is still far from being economic and of easy applicability, and that still much can be done to improve the reaction in terms of efficiency and compatibility. Therefore, in order to simplify both catalytic system and reaction conditions, while maintaining acceptable conversions, a comparative systematic study has been undertaken in this thesis.

To relate the results with those existing in literature,[53] conversion of hydrocinnamic methyl ester (methyl 3-phenylpropanoate) into the corresponding benzyl ester was selected as model reaction (scheme 3.8).



Scheme 3.8 – Transesterification of methyl 3-phenylpropanoate with benzyl alcohol

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[55] Iwasaki, T.; Maegawa, Y.; Hayashi, Y.; Ohshima, T.; Mashima, K. *J. Org. Chem.*, **2008**, 73, *13*, 5147–5150.

A preliminary screening using zinc acetate was carried out in order to optimize the reaction conditions, Refluxing toluene was identified as the most promising solvent, and a reaction of time of 18 hours was selected to ensure convenient conversions. Then, several simple Zn(II) salts were tested in the same reaction (table 3.2).

Entry	**Zn(II) salt**	***Conversion*, (%)**
1	none	<1
2	$ZnCl_2$	37
3	$ZnBr_2$	<5
4	ZnI_2	<5
5	Zn(triflate)$_2$	6
6	ZnO	29
7	$Zn(OAc)_2$	72
8	$Zn(BF_4)_2 \cdot 6H_2O$	8
9	$Zn(ClO_4)_2 \cdot 6H_2O$	6
10	$Zn(OAc)_2 \cdot 2H_2O$	86
11	$Zn(O_2CCF_3)_2 \cdot H_2O$	93
12	$Zn(NO_3)_2 \cdot 6H_2O$	93

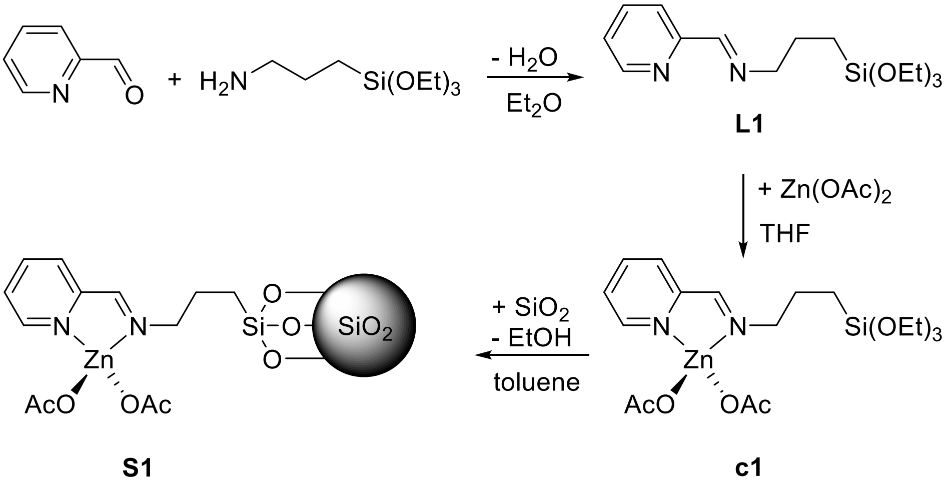
Reaction conditions: 18 h, refluxing toluene (1.7 mL),
substrate/benzyl alcohol = 1 mmol/1.2 mmol, substrate/catalyst = 100/1.

Table 3.2 – Salts of zinc (II) screening

These results clearly demonstrate that some simple zinc(II) salts are eligible transesterification catalysts. Higher activities were obtained with zinc acetate dihydrate, zinc trifluoroacetate hydrate and zinc nitrate hexahydrate (entry 10, 11 and 12). However, zinc acetate dihydrate was preferred due to its handling, which easily allows to weigh small amounts. On the other hand, both $Zn(NO_3)_2 \cdot 6H_2O$ and $Zn(O_2CCF_3)_2 \cdot H_2O$ display a certain level of hygroscopicity, which does not consent their use in moist air. Surprisingly zinc acetate dihydrate did not performed well in biodiesel synthesis, probably due to its poor solubility in the reaction medium.[56] The efforts were aimed, therefore, produce a supported catalyst to disengage from problem of solubility and also unify the activity of the molecular species with the ability to recover it.

3.2.2 – Supported homogeneous catalyst

On the basis of the previous results, zinc acetate was selected as candidate for producing a supported homogeneous catalyst. The dry form was preferred to the hydrate one only for synthetic reasons. In fact, the synthesis (scheme 3.9) proceeds through an imination between pyridin-2-carbaldehyde and 3-(triethoxysilyl)propan-1-amine to produce ligand **L1**. Then, coordination to the metal in dry THF affords complex **c1**. Next step is the anchorage to the support through Si-O-Si bond formation, in refluxing toluene and nitrogen atmosphere, employing the silyl ether functionality of the ligand. The supported homogeneous catalyst **S1** is isolated as a light brown powder. The last step is water sensitive (the silyl functionalization may hydrolize in these conditions) and therefore it is better to avoid any water content in the zinc salt.



Scheme 3.9 – Zinc(II) supported catalyst synthesis

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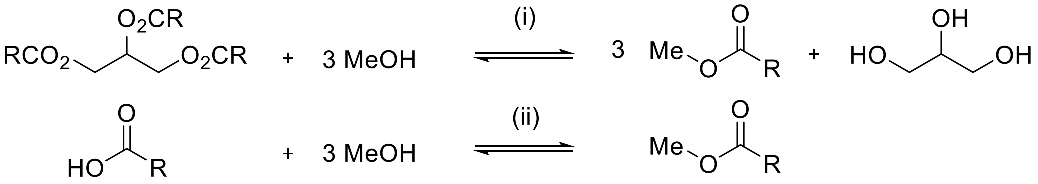
[56] Di Serio, M. et al. *J. Mol. Cat. A*, **2012**, *353– 354,* 106– 110.

Exhaustive washing with dichloromethane in a Soxhlet apparatus ensured complete removal of any unreacted complex. The content of Zn in **S1** (2.4% w/w) was found to be constant in any subsequent preparation. The percentage of nitrogen, equal to 1.05% w/w, confirmed that all the zinc was coordinated to the bidentate ligand anchored on silica. TGA analysis disclosed that the catalyst is stable up to 718 K when decomposition starts.

Catalyst **S1** was used in biodiesel synthesis from different types of acid feedstocks, in order to assess its ability to promote both transesterification (*i* in scheme 3.10) and esterification (*ii*) reactions.



Scheme 3.10 – Transesterification and esterification of acid waste oils

Two oils were obtained by adding oleic acid to soybean oil (entry 1 and 2 in table 3.3); other two substrates are real matrices, respectively, *lampante* olive oil (in US is called *U.S. Virgin Olive Oil Not Fit For Human Consumption Without Further Processing*) and olive pomace oil (*olio di sansa* in Italian, also known as *orujo* or *residue olive oil*) (entry 3 and four). The transesterifications were conducted in a 210 mL batch jacketed Parr reactor in stainless steel capable of reaching 528 K and 69 bar of pressure with an inlet gas line and an outer valve for sampling (figure 3.3).

Figure 3.3 – Parr reactor

The temperature was monitored with two NI thermocouple type K. Temperature data were collected with a homemade software on a personal computer and remotely controlled in real time.

The conversion was evaluated via ^{1}HNMR comparing the integral of the terminal methyl (-OCH_3) at 3.67 ppm and the integral of the methylene group vicinal to the carboxylic group (-CH_2COOR) at 2.30 ppm in $CDCl_3$ (figure 3.4). Residual acidity was measured through titration.

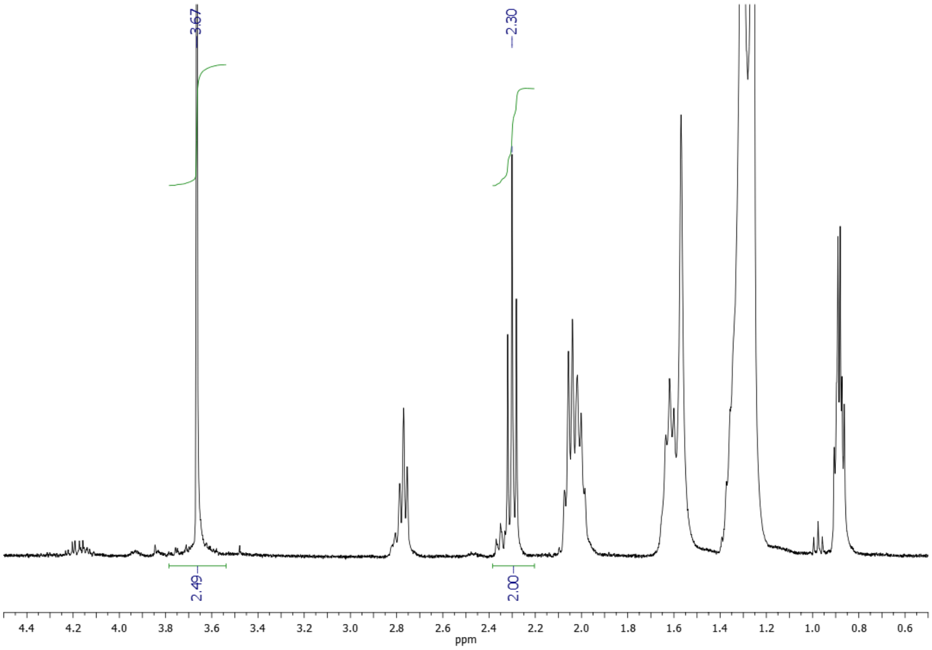


Figure 3.4 – ^{1}HNMR spectrum of a reaction mixture of soybean oil transesterification

In line with the expectations, **S1** is capable to promote contemporary both esterification and transesterification, revealing high activity in the different waste oils, even with a different degree of starting acidity (table 3.3).

Entry	**Vegetable Oil**	**Starting Acidity (mg/g)**	**FAME *Yield* (%)**	**Final Acidity (mg/g)**
1	Acid Soybean Oil 1	18.0	94 ± 2	1.6 ± 0.1
2	Acid Soybean Oil 2	40.0	93 ± 2	1.8 ± 0.1
3	*Lampante* Olive Oil	40.8	90 ± 2	2.9 ± 0.2
4	Crude Olive Pomace Oil	22.3	91 ± 2	3.6 ± 0.4

Reaction condition : T = 433 K; t = 2 h, n_{Zn} = 0.21 mmol, m_{MeOH} = 20g, m_{oil} = 11.2g

Table 3.3 – Biodiesel (FAME) synthesis from waste vegetable oils

Furthermore, after the reaction, the catalyst could be easily separated from the reaction mixture by simple decantation. This made possible its immediate recycling by adding fresh oil and methanol to the reaction vessel. As shown in table 3.4 and in table 3.5 for two types of oils, the catalyst activity remains high and constant. Notably, this is even true with crude olive pomace oil, which represents a real residue matrix.

Run	**Vegetable oil**	**FAME *Yield* (%)**	**Final Acidity (mg/g)**
1	Crude Olive Pomace Oil (starting acidity of 22.3 mg/g)	91 ± 2	3.6 ± 0.4
2		90 ± 2	3.8 ± 0.2
3		87 ± 2	3.5 ± 0.2
4		90 ± 2	2.7 ± 0.2
5		88 ± 2	3.2 ± 0.2

Reaction condition : T = 433 K; t = 2 h, n_{Zn} = 0.21 mmol, m_{MeOH} = 20g, m_{oil} = 11.2g

Table 3.4 – Recycles of the catalyst in crude olive pomace oil conversion

Run	**Vegetable Oil**	**FAME *Yield* (%)**	**Final Acidity (mg/g)**
1	Acid Soybean Oil 1 (Starting Acidity of 18.0 mg/g)	94 ± 2	1.6 ± 0.1
2		94 ± 2	2.2 ± 0.1
3		94 ± 2	2.6 ± 0.2

Reaction condition : T = 433 K; t = 2 h, n_{Zn} = 0.21 mmol, m_{MeOH} = 20g, m_{oil} = 11.2g

Table 3.5 – Recycles of the catalyst in soybean oil conversion

After the recycles the molar ratio between N and Zn in the catalyst was found essentially identical to the initial value. Reusing tests were performed by following the kinetics at lower reaction times in order to disclose any deactivation process in the first runs.

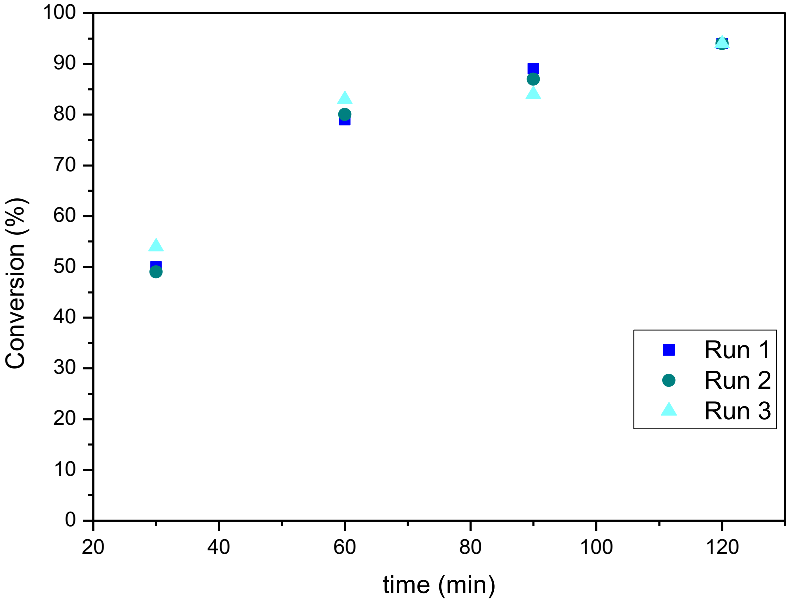


Figure 3.5 - Catalyst **S1** reuses kinetics with acid soybean oil.

The results revealed high constancy and reproducibility, as shown in figure 3.5. Accordingly, leaching of metal is also not important as demonstrated by the quite same activity of the blank run (in the range of experimental error) displayed by the sole methanol pretreated for two hours with the catalyst under the same reaction. These results underscore that the catalyst active species is precisely the supported metal.

3.3 – Materials and methods

General

All solvents and reagents were purchased by Sigma-Aldrich and were used without further purification.

Protonic NMR spectra have been recorded in $CDCl_3$, DMSO ($CDCl_3$, δ 7.26ppm; CD_3SOCD_3, δ 2.50ppm;), at 400MHz spectrometer (Bruker Avance 400), the chemical shift value refers to solvent. The following abbreviations have been used for describing NMR multiplicities: s, singlet; d, doublet; dd, double doublet; t, triplet; dt, double triplet; m, multiplet; app t, apparent triplet; quin, quintuplet; sex, sextuplet.

In order to carry out more reactions simultaneously, it has used the Carousel 6 Reaction Station by Radleys with six positions occupied by flask (10 mL).

The silica, used to support the complex **c1**, AEROLIST (surface area, 150 m2/g) in pellets was activated by heating in oven at 573 K for 5 h.

The Zn content in the supported catalyst was determined by ICP (inductively coupled plasma) analysis on Aurora M90 Bruker spectrometer. TGA analysis were performed with Perkin Elmer ST6000, heating the sample from 298 K to 1173 K, at 10 K min^{-1} in N_2 stream (20 mL/min). Elemental analysis have been carried out in a LECO CHN analyzer, operated up to 1123 K under O_2/He flow.

General procedure for screening of zinc salts in transesterification reaction

A solution of the appropriate quatity of a zinc salt (0,01 mmol), methyl-3-phenylpropanoate (156 µL, 1 mmol), benzyl alcohol (124 µL, 1,2 mmol), and toluene (1,7 mL) was prepared. The mixture, containing [benzyl alcohol]= 0.6M and [methyl ester]= 0.5M, was refluxed for 18h. After each run the reaction mixtures were dried under vacuum, and the crude product was subjected to ^{1}H-NMR analysis.

*Synthesis of ligand **L1***

The ligand was prepared by mixing 10.7 g (0.100 mol) of pyridine-2-carboxaldehyde and 22.1 g (0.100 mol) of 3-(triethoxysilyl)propane-1-amine in 200 mL of diethyl ether. After 18 h of stirring, the solution was dried over sodium sulfate and then filtered. The product was obtained in quantitatively by removing the solvent under vacuum.

1H NMR (dmso-d6) d: 8.59 (d, 3J = 5.8 Hz, 1H), 8.30 (s, 1H), 7.95 (d, 3J = 7.2 Hz, 1H), 7.80 (app t, 3J = 7.2 Hz, 1H), 7.38 (dd, 3J = 7.2 Hz, 3 J = 5.8 Hz, 1H), 3.70 (q, 3J = 6.9 Hz, 6H), 3.59 (t, 3J = 6.3 Hz, 2H), 1.70 (m, 3J = 6.3 Hz, 2H), 1.10 (t, 3J = 6.9 Hz, 9H), 0.57 (m, 3J = 6.3 Hz, 2H).

*Synthesis of complex **c1***

The complex was prepared by mixing 31.0 g (0.100 mol) of **L1** and 18.3 g (0.100 mol) of zinc acetate in 200 mL of dry THF. After one hour of stirring, the volume of the solution was reduced at 50 mL under vacuum. The complex was crystallized by addition of 200 mL of hexane. The yellow product was collected by filtration, washed three time with 50 mL of hexane and dried under vacuum (yield: 45 g, 91%). The compound was stored in a dessiccator.

1H NMR (dmso-d6) d: 8.69 (d, 3J = 5.5 Hz, 1H), 8.64 (s, 1H), 8.21 (app t, 3J = 7.9 Hz, 1H), 8.01 (d, 3J = 7.9 Hz, 1H), 7.78 (dd, 3J = 7.9 Hz, 3J = 5.5 Hz, 1H), 3.75 (q, 3J = 6.7 Hz, 6H), 3.57 (t, 3J = 6.3 Hz, 2H), 1.80 (s, 6H), 1.72 (m, 3J = 6.3 Hz, 2H), 1.14 (t, 3J = 6.7 Hz, 9H), 0.57 (m, 3J = 6.3 Hz, 2H).

*Synthesis of supported catalyst **S1***

The commercial silica was pre-treated at 573 K for 5 h, obtaining a silica with a specific area of 163 m^2/g and pores volume of 0.81 cm^3/g (B.E.T.). The catalyst was prepared by adding the silica (80 g) to a solution of 24.7 g (0.0500 mol) of complex **c1** in 1.0 L of dry toluene. The mixture was refluxed 20 h under stirring. The solid was filtered, washed with dichloromethane for 16 h in a Soxhlet apparatus, and then dried under vacuum (88 g).

General procedure for biodiesel synthesis

Oil (11.2 g), methanol (20.0 g) and **S1** (0.560 g, 0.21 mmol of Zn) were stirred (rate 500 rpm) in a Parr Instrument steel reactor. The temperature was increased from room temperature to 433 K in 35 min. After 2 h the reactor was cooled and the reaction mixture separated from the catalyst and analyzed. Fresh oil and methanol were added to the residual catalyst for successive runs.

The FAME yields were determined by NMR spectroscopy and the residual FFA concentration by titration.

3.4 – Conclusions

In conclusion, it is described a novel homogeneous supported catalyst for esterification and transesterification of vegetable oils.

The proposed system is advantageously placed within the scenario of current literature for the many benefits it offers:

- ease of synthesis on large scale starting from inexpensive and available reagents;

- high activity toward different types of oil;

- robustness allowing immediate recovery (there is no need to regenerate the catalyst) and efficient recycling.

Furthermore, this is a promising route to solve a major challenge for catalytic scientists: to find solid materials capable of simultaneous free fatty acids esterification and triglycerides transesterification under mild conditions.

Results of paragraph 3.2.3 were published as: *A novel and robust homogeneous supported catalyst for biodiesel production* Benessere, V.; Cucciolito, M. E.; Esposito, R.; Lega, M.; Turco, R.; Ruffo, F.; Di Serio, M. *Fuel*, 171, **2016**, 1.

Chapter 4

Glycerol

4.1 – Glycerol: from byproduct to resource

As stated before, the main byproduct of biodiesel synthesis is glycerol. Consequently, the push to increase biodiesel production also caused a market invasion of glycerol. It is estimated that its global production will reach 41.9 billion liters in 2020.[57]

The major manufacturers refine and use this product in different fields, especially in the pharmaceutical, food, cosmetic and polymer industries,[58] exploiting its unique physical and chemical properties: the presence of three hydroxyl groups makes it completely miscible with water and light alcohols, while making it insoluble in hydrocarbons. In addition, intermolecular and intramolecular hydrogen bonds raise the boiling point at 563 K (at atmospheric pressure) and give it high viscosity, equal to 1,412 $Pa \cdot s$ at room temperature.[59] Smaller producers, however, cannot justify the cost of purification and therefore prefer to pay for its disposal.

The current price of glycerol is about 20 cents per kilogram. It is expected that, in the future, increasing production will result in further price reductions.

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[57] a) Johnson, D. T.; Taconi, K. A. *Environ. Prog.* **2007**, *26*, 338. b) Organization for Economic Co-operation and Development (OECD) and the Food and Agriculture Organization (FAO) of the United Nations; 2011–2020.

[58] a) Callam, C. S.; Singer, S. J.; Lowary, T. L.; Hadad, C. M. *J Am Chem Soc* **2001**, *123*, 11743. b) Da Silva, G. P.; de Lima, C. J. B.; Contiero, J. *Catal Today* **2015**, *257*, 259. c) Zhou, C.-H. C.; Beltramini, J. N.; Fan, Y.-X.; Lu, G. Q. M. *Chem Soc Rev* **2008**, 37, 527.

[59] Pagliaro, M.; Ciriminna, R.; Kimura, H.; Rossi, M.; Della Pina C. *Angew Chem In Ed* **2007**, *46*, 4434.

Therefore, it is now a priority to make full use of glycerol to ensure the sustainability of biodiesel industry.

This molecule is, indeed, a very interesting starting material because it is:

- a highly functionalized molecule
- a very versatile precursor of a variety of compounds
- an easy available raw material (as a byproduct of a growing industrial process)
- a renewable resource

Transformations can be very different such as acetalization, ketalization, dehydration, etherification, esterification, hydrogenolysis and oxidation,[60] which afford high added value products such as propandiols, acrolein, dihydroxyacetone, glyceric acid, tartronic acid, epichlorhydrin, hydrogen, syngas, ethers, esters and many others (scheme 4.1).[61] In this sense glycerol can be considered as an excellent chemical platform.[55b, 56, 62]

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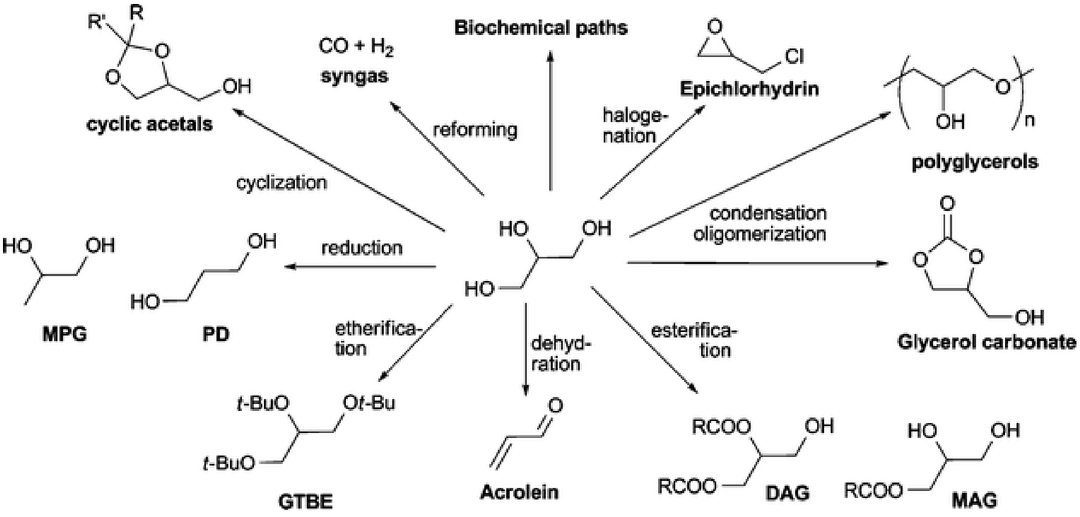
[60] a) Agirre, I.; Garcia, I.; Requies, J.; Barrio, V. L.; GuemeZ, M. B.; Cambra, J. F.; Arias, P. L. *Biomass Bioenergy* **2011**, *35*, 3636; b) Royon, D.; Locatelli, S.; Gonzo, E. E. *J Supercrit Fluids* **2011**, *58*, 88; c) Reddy, P. S.; Sudarsanam, P.; Mallesham, B.; Raju, G.; Reddy, B.M. *J Ind Eng Chem* **2011**, *17*, 377; d) Suriyaprapadilok, N.; Kitiyanan, B. *Energy Procedia* **2011**, *9*, 63; e) Li, L.; Koranyi, T. I.; Sels, B. F.; Pescarmona, P. P. *Green Chem* **2012**, *14*, 1611; f) Menezes, F. D. L.; Guimaraes, M. D. O.; Da Silva, M. J. *Ind Eng Chem Res* **2013**, *52*, 16709.

[61] a) Zhu, S.; Gao, X.; Zhu, Y.; Zheng, H.; Li, Y. *J Catal* **2013**, *303*, 70; b) Chen, L.; Liang, J.; Lin, H.; Weng, W.; Wan, H.; Védrine, *J C Appl Catal A* **2005**, *293*, 49; c) Hirai, T.; Ikenaga, N.; Miyake, T.; Suzuki, T. *Energy Fuels* **2005**, *19*, 1761; d) Cassel, S.; Debaig, C.; Benvegnu, T.; Chaimbault, P.; Lafosse, M.; Plusquellec, D. et al. *Eur J Org Chem* **2001**, *5*, 875; e) Kenar, *J A Lipid Technol* **2007**, *19*, 249; f) Len, C.; Luque, R. Sustain *Chem Process* **2014**, *2*, 1; g) Rastegari, H.; Ghaziaskar, H. S. *J Ind Eng Chem* **2015**, *21*, 856.

[62] Zheng, Y.; Chen, X.; Shen, Y. *Chem Rev* **2008**, *108*, 5253.



Scheme 4.1 – Glycerol transformations

4.1.2 – *Solketal*

Within this context and among the several routes that transform glycerol into useful products, the cyclization with carbonyl compounds to give cyclic acetals is particularly interesting for different reasons:

- functionalization of glycerol may need the protection of two hydroxyl groups leaving a third available for further reactions. The protection of diols with acetals is today an open research field.

- cyclic glycerol acetals are themselves valuable chemicals: they can be used as solvents, surfactants,[63] as flavors in food and cosmetic industries[64] and as diesel fuel additive.[65]

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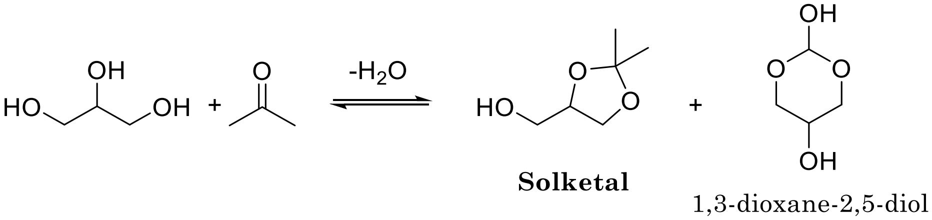
[63] Piasecki, A.; Sokolowski, A.; Burczyk, B.; Kotlewska, U. *J Am Oil Chem Soc* **1997**, *74*, 33.

[64] a) Climent, M. J.; Corma, A.; Veltry, A. *Appl Catal A* **2004**, *263*, 155; b) Climent, M. J.; Veltry, A.; Corma, A. *Green Chem* **2002**, *4*, 565.

[65] a) Fr. Pat. 2 833 607 A1, **2003**; b) Int. Pat. 2005/093 015 A1, **2005**.

- the reaction is typically acid catalyzed, a field in which the experience gained within this thesis can be applied.

One of the simplest cyclic acetals that can be synthetized is *rac*-(2,2-dimethyl-1,3-dioxolan-4-yl)methanol, also commonly known as *solketal* (scheme 4.2).



Scheme 4.2 – Solketal synthesis

The reaction is often accompanied by the formation of the six-member cyclic acetal byproduct (1,3-dioxane-2,5-diol), though the selectivity is in most of the cases greatly unbalanced in favor of solketal (typical distribution is 98 : 2 respectively five-member to six-member).

This molecule mainly finds applications as solvent and as a fuel additive in gasoline, diesel and biodiesel to improve octane number and reduce gum formation.[66]

Not surprisingly, new catalytic systems for the sustainable conversion of glycerol into solketal are constantly proposed. Most of them are heterogeneous, and generally imply the use of solid acid catalysts such as Amberlyst,[67] heteropolyacids supported on silica,[68] Zr- and Sn-mesoporous substituted silicates,[69] carbon functionalized with

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[66] Mota, C. J. A. et al. *Energy Fuels* **2010**, *24*, 2733.

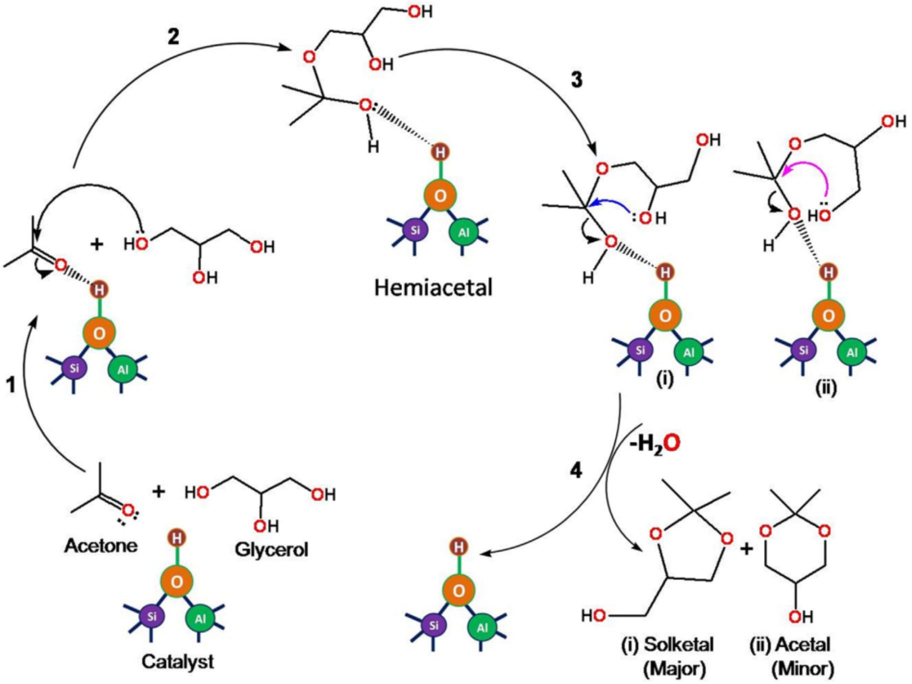
[67] a) Deutsch, J.; Martin, A.; Lieske, H. *J. Catal.* **2007,** *245*, 428; b) da Silva, C. X. A.; Gonçalves, V. L.C.; Mota, C. J. A. *Green Chem.* **2009**, *11*, 38; c) Vicente, G.; Melero, J. A.; Morales, G.; Paniagua, M.; Martín, E. *Green Chem.* **2010**, *12*, 899; d) Nanda, M. R et al. *Fuel* **2014**, *117*, 470; e) Nanda, M. R. et al., *Fuel* **2014**, *128*, 113.

[68] Ferreira, P.; et al. *Appl. Catal. B Environ.* **2010**, *98*, 94.

[69] Li, L.; Korányi, T. I.; Sels, B. F.; Pescarmona, P. P. *Green Chem.* **2012**, *14*, 1611.

Brønsted acid groups,[70] zeolites,[71] metal aluminum phosphates M-AlPO4/xAlPO$_4$ (x =Zn, Cu, Ni, or Co),[72] mixed Al/Nb oxides,[73] and montmorillonite.[74]

A widely accepted reaction mechanism for acetalization over acid surfaces is presented in scheme 4.3 taken from Manjunathan, P. et al. *J. Mol. Catal. A Chem.* **2015**.



Scheme 4.3 – Acetalization mechanism with a heterogeneous acid catalyst

Acetone is activated by the acidic sites on the catalyst (**1**). Then it undergoes a nucleophilic attack by a glycerol hydroxyl (**2**). Finally, a second glycerol hydroxyl attacks the carbon 2 of acetone (**3**) and a water molecule is eliminated (**4**) to obtain the cyclic acetal.

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[70] a) Rodrigues, R.; Gonçalves, M.; Mandelli, D.; Pescarmona, P. P.; Carvalho, W. A. *Cat. Sci. Technol.* **2014**, *4*, 2293; b) Gonçalves, M.; Rodrigues, R.; Galhardo, T. S.; Carvalho, W. A. *Fuel* **2016**, *181*, 46.

[71] a) Manjunathan, P. et al. *J. Mol. Catal. A Chem.* **2015**, *396*, 47; b) Rossa, V. et al. *Ind. Eng. Chem. Res.* **2017**, *56*, 479.

[72] Zhang, S.; Zhao, Z.; Ao, Y. *Appl. Catal. A Gen.* **2015**, *496*, 32.

[73] Rodrigues, R.; Mandelli, D.; Gonçalves, N.; S.; Pescarmona, P. P.; Carvalho, W. A. *J. Mol. Catal. A Chem.* **2016**, *422*, 122.

[74] Timofeeva, M. N.; Panchenko, V. N.; Krupskaya, V. V.; Gil, A.; Vicente, M. A. *Catal. Commun.* **2017**, *90*, 65.

In these cases, complete conversion of glycerol is rarely achieved,[75] and a substantial amount of solid catalyst is generally required (5–40%).

By far less investigated are homogeneous catalysts, despite they commonly warrant mild reaction conditions, high efficiency, better control of the reactive sites, and an easier understanding of the reaction mechanism. In the face of these advantages, the difficult separation from the product often limits their application. The homogenous catalysts so far described for the production of solketal are both Brønsted[73, 76] and Lewis acids, such as $SnCl_2$[77] and iridium complexes,[78] either used at considerable concentrations (1%) and in the presence of additional solvents, or based on an extremely expensive metal. Very recently, a catalyst based on a Brønsted acid ionic liquid has been proposed,[79] which combines the benefits of homogenous and heterogeneous catalysis, thanks to its possible reuse. In this case, the obstacle to a large-scale application seems to be the high cost of the reaction medium. Therefore, it seems that a fully convincing catalytic system to produce solketal has not yet been optimized.

4.2 – Iron(III) catalysis

In this thesis, a catalytic system for a sustainable synthesis of solketal was developed and a reaction mechanism along with DFT calculation were proposed. The attention was focused on iron(III) because of the low toxicity profile, great availability, geographical distribution and low cost of this metal and its salts. Furthermore, despite of its great performance in Lewis acid catalysis (e.g. Friedel-Craft acylation), it does not appear in the literature mentioned so far.

Simple salts along with a new class of complexes containing pyridine-2-imine ligands (figure 4.1) were screened in this reaction.

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[75] Nanda, M. R.; Zhang, Y.; Yuan, Z.; Qin, W.; Ghaziaskar, H. S.; Xu, C. C. *Renew. Sust. Energ. Rev.* **2016**, *56*, 1022.

[76] N. Suriyaprapadilok, B. Kitiyanan, *Energy Procedia* **2011**, *9*, 63.

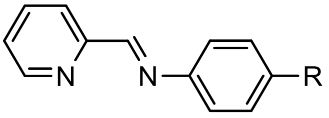
[77] Menezes, F. D. L.; Guimaraes, M. D. O.; da Silva, M. J. *Ind. Eng. Chem. Res.* **2013**, *52*, 16709.

[78] C. Crotti, E. Farnetti, N. Guidolin, *Green Chem.* **2010**, *12*, 2225.

[79] Gui, Z.; Zahrtmann, N.; Saravanamurugan, S.; Reyero, I.; Qi, Z.; Bañares, M. A.; Riisager, A.; Garcia-Suarez, E. J. *Chemistry Select* **2016**, *1*, 5869.

[$FeCl_3$(**1-R**)]

1-H: R=H
1-OMe: R= OMe
1-CF_3: R= CF_3
1-NO_2: R= NO_2

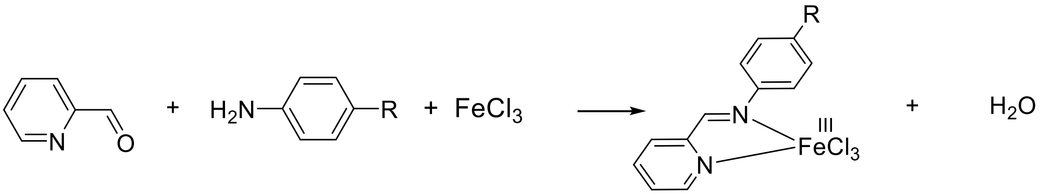


1-R

Figure 4.1 – Pyridine-2-imine iron (III) complexes.

The latter ones were selected aiming to discover any beneficial effect arising from the presence of the modular ancillary ligands **1-R**. Furthermore, unlike many simple salts of iron(III), they are not hygroscopic and can be easily handled in air, which greatly facilitates the experimental manipulations.

The procedure for the preparation of the iron(III) complexes is reported in scheme 4.4:



1-H (R = H)
1-OMe (R = OMe)
1-CF_3 (R = CF_3)
1-NO_2 (R = NO_2)

Scheme 4.4 – Synthesis of complexes of iron(III)

The catalysts [$FeCl_3$(**1-R**)][80] were prepared in ether through a simple template procedure[81] involving the *in situ* reaction between pyridine-2-carboxyaldehyde and the appropriate aniline in the presence of $FeCl_3$. Immediate precipitation of the yellow-

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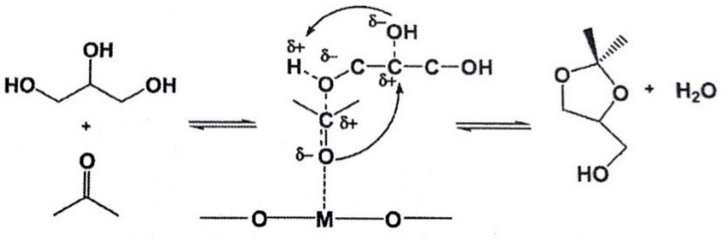
[80] a) Capitan, F.; Salinas, F.; Capitan-Vallvey, L. F. *Anales de Quimica* **1978**, *74*, 276; b) Marjani, K.; Mousavi, M.; Hughes, D. L. *Transition Met Chem* **2009**, *34*, 85.

[81] Olivo, G.; Lanzalunga, O.; Di Stefano, S. *Adv Synth Catal* **2016**, *358*, 843.

orange complexes was observed. UV[82] and IR[83] spectroscopy confirmed the presence of C = N bonds.

4.2.1 – Reaction mechanism

Literature[67] proposes a reaction mechanism for the acetalization catalyzed by Lewis acids, although without any theoretical confirmation (scheme 4.5).



Scheme 4.5 – Mechanism proposed in literature

According to this mechanism, the carbonyl is activated by coordinating the metal. Then, the carbonyl carbon is attacked by a hydroxyl group of glycerol while the carbonyl oxygen closes the cycle contemporary to the elimination of water.

Starting from this assumption, it is herein proposed a reaction mechanism (scheme 4.6) that separates the process in more detailed steps, along with a preliminary DFT calculation for all of them.

The choice of the active catalytic species, the iron(III) aqua-ion, is due to the experimental evidence that several iron salts are able to catalyze this reaction with high TOF, irrespective of the nature of the counterions and the number of coordinated water molecules (see results in next paragraph).

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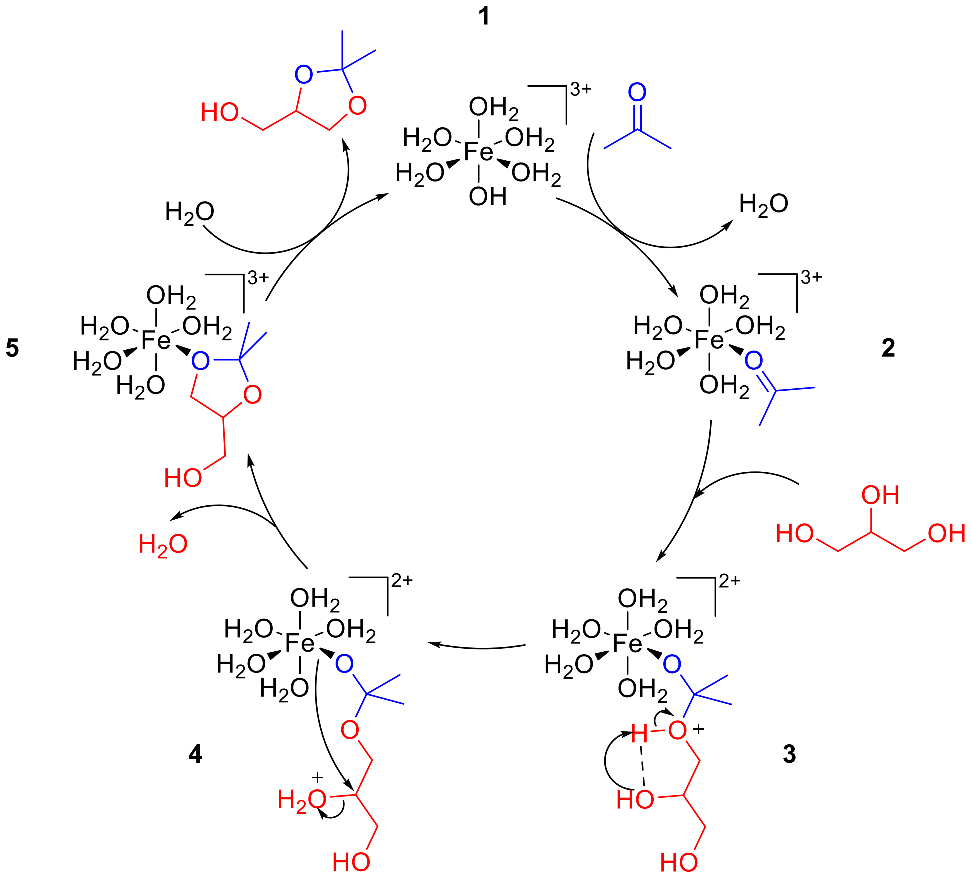
[82] Olivo, G.; Nardi, M.; Vìdal, D.; Barbieri, A.; Lapi, A.; Gómez, L.; Lanzalunga, O.; Costas, M.; Di Stefano, S. *Inorg Chem* **2015**, *54*, 10141.

[83] Taghi Goldani, M.; Mohammadi, A.; Sandaroos, R. *J Chem Sci* **2014**, *126*, 801.



Scheme 4.6 – Proposed reaction mechanism based on a generic Iron(III) aqua-ion

Coordination of the carbonyl to the metal center gives the adduct **2**; rate limiting step is a nucleophilic attack by a glycerol hydroxyl group to the carbonyl carbon yielding the adduct **3** that undergoes an intramolecular proton transfer to give **4**. This transfer occurs on the secondary alcohol group for geometrical reasons. Exit of water is the driving force for an intramolecular rearrangement where the coordinated oxygen closes the ring attacking the central carbon atom to give adduct **5** that rapidly dissociates and the regain of a water molecule restores the catalytic species.

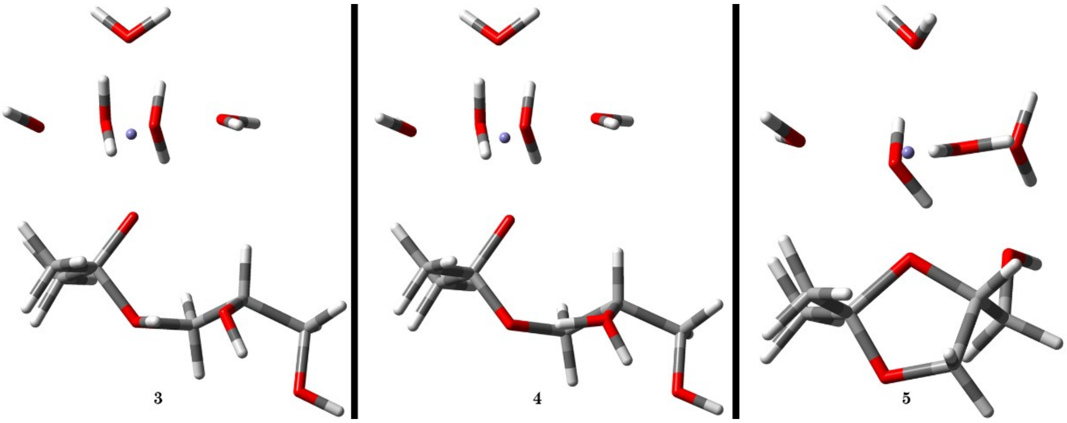
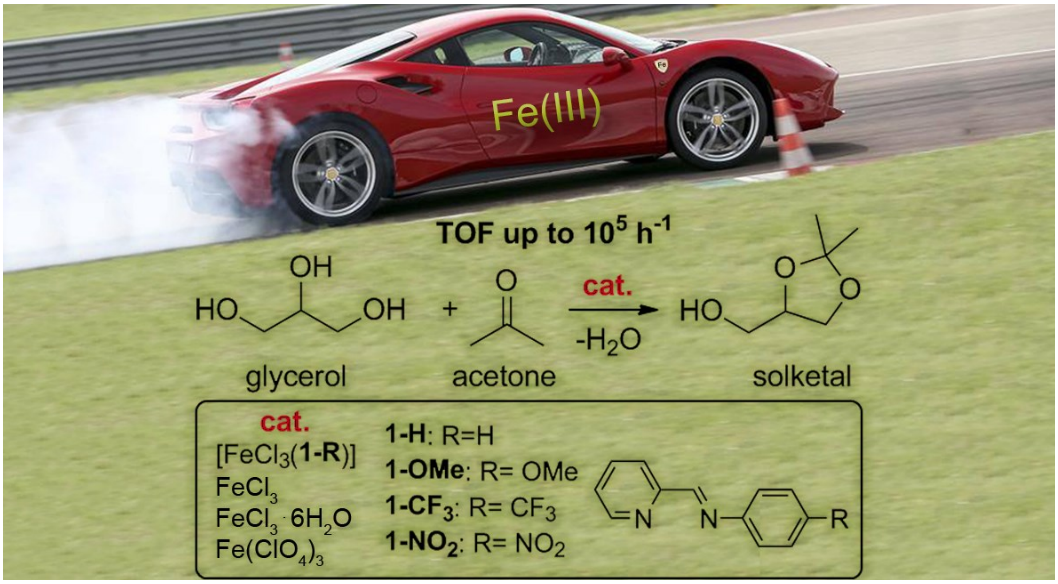


Figure 4.2 – Intermediates **3**, **4** and **5** structures optimized at DFT level

This generic mechanism can also explain why formation of the five-member ring is favorite respect to the six-member one.

4.2.2 – Results

The iron(III) species tested in ketalization of glycerol with acetone were complexes [FeCl$_3$(**1-R**)], dry FeCl$_3$, FeCl$_3$ · 6H$_2$O and Fe(ClO$_4$)$_3$ (Scheme 4.7).



Scheme 4.7 – Catalysts used in ketalization of glycerol

In this reaction, the removal of water is a crucial step to shift the equilibrium towards the products. Therefore, tests were conducted under reflux conditions with an acetone:glycerol ratio 4:1 for 90 minutes, by passing the vapors through a column filled with molecular sieves 3Å, placed upstream of the condenser (figure 4.3).

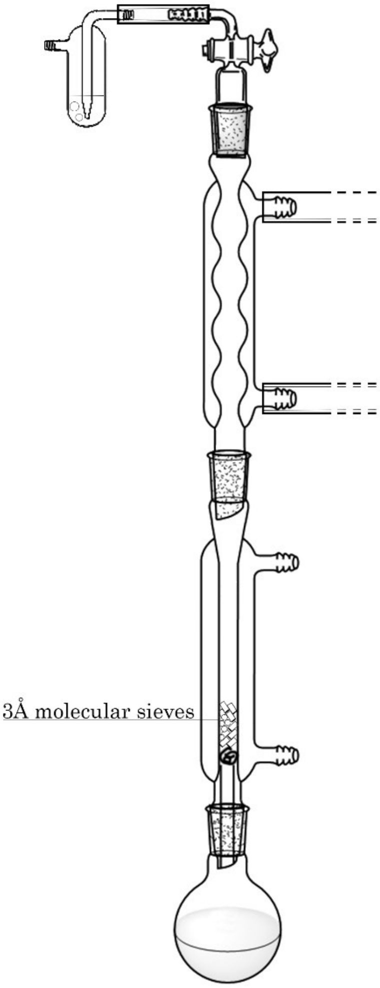


Figure 4.3 – Reaction system

Initially, the reaction mixture is biphasic due to the poor miscibility of glycerol with acetone. As the reaction proceeds, the system becomes homogeneous because the presence of the solketal improves the reciprocal miscibility of the components.

The reaction mixture was analyzed directly through ^{1}H NMR spectroscopy, and conversion and selectivity were evaluated by integrating appropriate spectrum regions (figure 4.4).

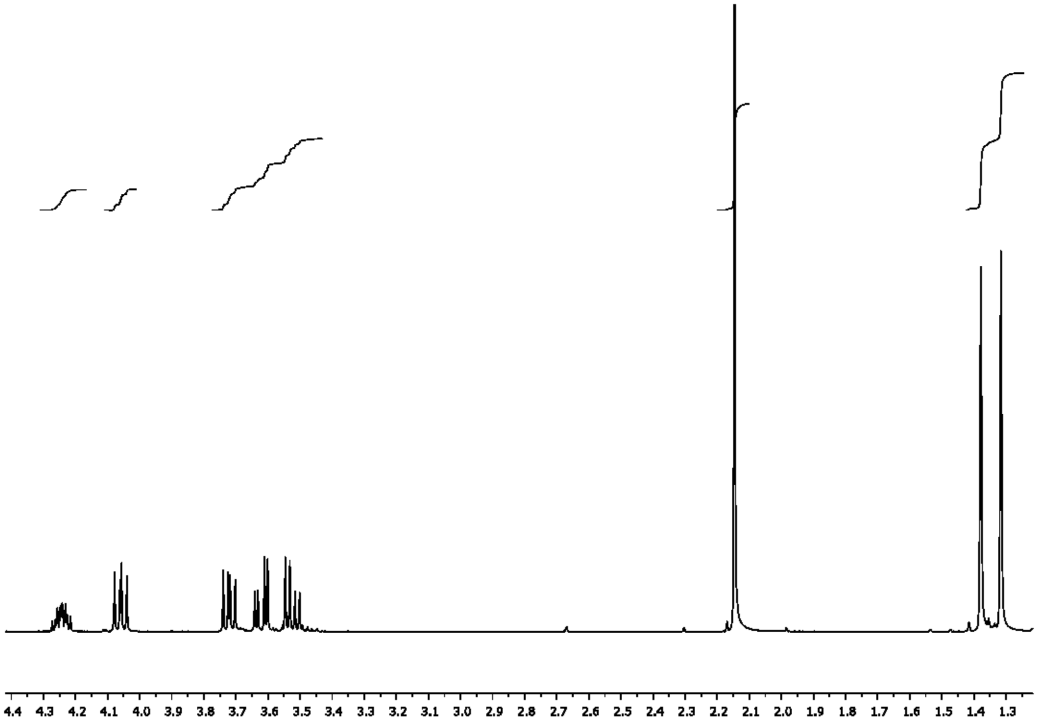


Figure 4.4 – ^{1}H NMR spectrum of a high conversion reaction mixture in D_2O.

Results of catalysts screening are reported in table 4.1:

Entry[a]	**Catalyst**	**Catalyst loading, % (mol/mol)**[b]	***Conversion*, %**[c]
1	-	-	<20
2	$FeCl_3$	0.050	>99
3	$FeCl_3$	0.0050	>99
4	$FeCl_3$	0.0010	93 ± 1
5	$FeCl_3$	0.00050	92 ± 1
6	[$FeCl_3$(**1-NO$_2$**)]	0.050	>99
7	[$FeCl_3$(**1-NO$_2$**)]	0.0050	>99
8	[$FeCl_3$(**1-NO$_2$**)]	0.0010	94 ± 1
9	[$FeCl_3$(**1-NO$_2$**)]	0.00050	78 ± 1
10	$FeCl_3{\cdot}6H_2O$	0.00050	84 ± 1
11	$Fe(ClO_4)_3$	0.00050	87 ± 1
12	[$FeCl_3$(**1-H**)]	0.00050	45 ± 1
13	[$FeCl_3$(**1-OMe**)]	0.00050	46 ± 1
14	[$FeCl_3$(**1-CF$_3$**)]	0.00050	74 ± 1

[a] Reaction conditions: (0.92 g, 10 mmol) glycerol purity grade 99.5% (0.92 g, 10 mmol); acetone purity grade 99.8% (2.3 g, 40 mmol); reflux temperature; 1.5 h reaction time.

[b] Respect to glycerol.

[c] Selectivity ≥ 98%.

Table 4.1 – Catalysts screening

In the absence of a catalyst (entry 1 in table 4.1), the conversion is poor: the system appears to be biphasic at the end of 90 minutes of reflux, indicating the presence of substantial amounts of unreacted glycerol.

In the range of 0.050-0.0010 % mol/mol respect to alcohol, $FeCl_3$ and [$FeCl_3$(**1-NO$_2$**) show high and comparable conversions (entries 2-4 vs. 6-8).

Even at low concentrations (0.00050 mol/mol), the same catalysts show significant and satisfactory activities (5 and 9). It is important to note that TOF values (up to 10^5 h^{-1} for experiment 5) are much higher than those reported so far for this reaction: about 500 h^{-1} for the expensive iridium catalyst[76] and about 50 h^{-1} for SnCl$_2$ and common Brønsted acids, such as sulfuric acid or p-toluenesulfonic acid.[58f]

The same loading (0.00050%) was adopted for comparing the other selected iron(III) compounds (entries 10–14). The screening of the entire panel revealed that the simple salts along with [FeCl$_3$(**1–CF3**)] and [FeCl$_3$(**1–NO2**)] are considerably active. These results also point out that the likely mitigation of acidity due to the presence of the nitrogen donors is largely compensated by the electron-withdrawing substituents.

Therefore, successive experiments (table 4.2) were carried out using [FeCl$_3$(**1–NO$_2$**)] because of its excellent activity even at low concentrations and its insensitivity to air and moisture.

Entry	**[FeCl$_3$(1-NO$_2$)], % (mol/mol)[b]**	**acetone/glycerol (mol/mol)**	**Conversion, %[c]**
1	0.0010	6 : 1	78 ± 1
2	0.0010	4 : 1	94 ± 1
3	0.0010	3 : 1	88 ± 1
4	0.0010	2 : 1	72 ± 1
5	0.0020	6 : 1	79 ± 1
6	0.0020	4 : 1	95 ± 1
7	0.0020	3 : 1	97 ± 1
8	0.0020	2 : 1	65 ± 1

[a] Reaction conditions: acetone purity grade 99.8% (2.3 g, 40 mmol); reflux temperature; 1.5 h reaction time.

[b] Respect to glycerol.

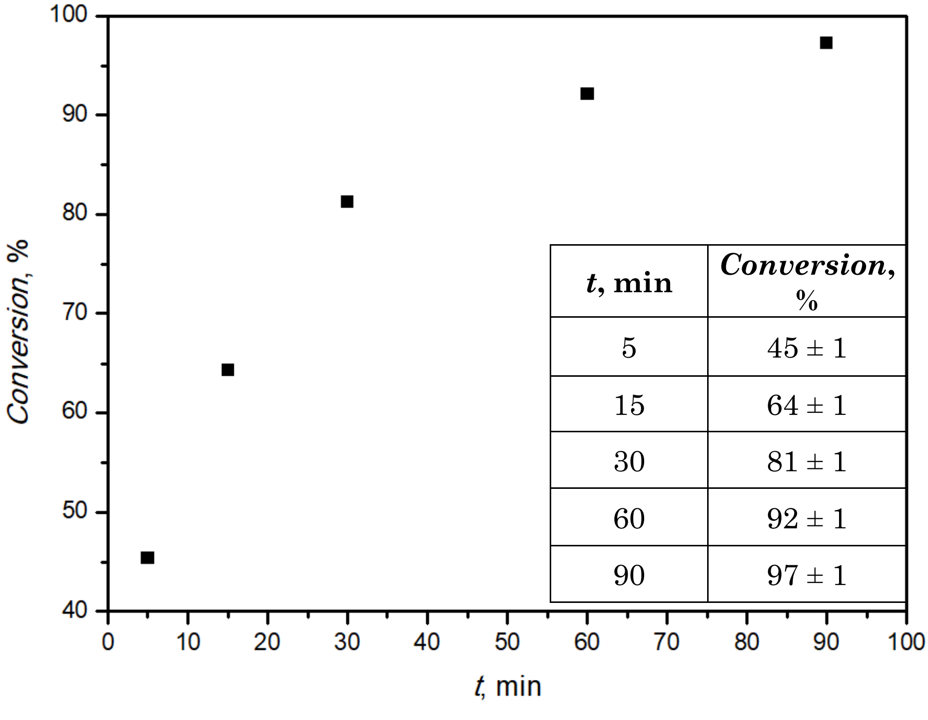
[c] Selectivity ≥ 98%.

Table 4.2 – Acetone/glycerol ratio screening

These further experiments were carried out varying the acetone/glycerol ratio while keeping the catalyst loading between 0.0010 and 0.0020% mol/mol. It is clear that the ratio acetone/glycerol plays a fundamental role. In fact, a high value (6 : 1, entries 1 and 5 of table 4.2) depresses the conversion, probably due to the consequent dilution of the catalyst. Instead a low ratio (2 : 1, entries 4 and 8) does not give satisfactory results, perhaps given the lower availability of the reagent. Therefore, the best outcomes were observed with intermediate ratios of 3 : 1 and 4 : 1.

On this basis, the reaction mixture of entry 7 was treated aiming at isolating solketal. After the catalytic run, excess acetone was recovered by flash distillation. This simple work-up, which did not require any additional solvents or severe conditions, returned solketal with an iron content below 10 ppm, *i.e.* a purity grade compatible with bulk applications.

In the same reaction conditions (entry 7) a kinetic curve was also drawn (figure 4.5), where it can be appreciated that conversion reaches 45% in only five minutes.



***t*, min**	***Conversion*, %**
5	45 ± 1
15	64 ± 1
30	81 ± 1
60	92 ± 1
90	97 ± 1

Figure 4.5 – Catalysis kinetic at 0.0020% mol of catalyst [$FeCl_3$(1-NO_2)]

As final remark, it is interesting to know that a preliminary test also successfully verified the compatibility of the catalysts with crude glycerol from biodiesel production through the catalytic systems of the chapter 2 (supported homogeneus catalyst based on zinc(II) named **S1**).

4.3 – Materials and methods

General

All solvents and reagents were purchased from Sigma-Aldrich and were used without further purification. IR and UV-vis spectra were recorded using either the JASCO FT/IR-430 spectrophotometer and the UV/VIS JASCO V-530 spectrophotometer respectively. NMR spectra were recorded using a Bruker Ascend 400 MHz or a Varian 500 MHz spectrometer using D_2O as solvent.

*Synthesis of [$FeCl_3$(**1-R**)] complexes*

The synthesis of [$FeCl_3$(**1-R**)] complexes was carried out in a single step. In a round bottom flask 5 mmol (0.535 g) of pyridine-2-carboxaldehyde, 5 mmol (0.811 g) of anhydrous $FeCl_3$ and 5 mmol of the appropriate para-substituted aniline (**1-H** = 0.466 g; **1-OMe** = 0.616 g; **1-CF3** = 0.806 g; **1-NO2** = 0.691 g) and 50 ml ethyl ether were mixed. Then the mixture was stirred at room temperature for 30 min. The complexes precipitated in the form of yellow-orange solids. The latter were filtered, washed with ethyl ether and dried in vacuo. (yield: 80-90%).

IR (nujol on KBr, imine stretching):

- $FeCl_3$(**1-H**) 1626 cm^{-1};
- $FeCl_3$(**1-OMe**) 1623 cm^{-1};
- $FeCl_3$(**1-CF$_3$**) 1635 cm^{-1};
- $FeCl_3$(**1-NO$_2$**) 1634 cm^{-1}.

UV-vis: (in acetone, λ_{max}):

- $FeCl_3$(**1-H**) 360 nm;
- $FeCl_3$(**1-OMe**) 360 nm;
- $FeCl_3$(**1-CF$_3$**) 360 nm;
- $FeCl_3$(**1-NO$_2$**) 363 nm.

Catalytic runs

The catalysts were placed in the desired percentages together with 10 mmol of glycerol and 40 mmol of acetone. The reactions were conducted under magnetic stirring for 90 minutes at reflux temperature of acetone, placing a column, before the condenser, containing 2.54 g of molecular sieves 3Å, activated in hoven at 423 K. At the end of reaction time, at the mixture is added D_2O to evantually dissolve unreacted glycerol. Then the mixture was characterized by ^{1}H NMR in D_2O.

Example of a spectrum of a catalytic test performed to complete glycerol conversion: ^{1}H NMR (500 MHz, D_2O) δ 4.33 (dd, *J* = 7.6, 4.3 Hz, 1H), 4.15 (t, *J* = 7.7 Hz, 1H), 3.81 (t, *J* = 7.4 Hz, 1H), 3.75 – 3.69 (m, 1H), 3.62 (dd, *J* = 12.1, 5.7 Hz, 1H), 1.47 (s, 3H), 1.41 (s, 3H).

4.4 – Conclusions

These results demonstrate that simple iron(III) compounds promote the formation of solketal from acetone and glycerol with unprecedented TOFs values. Complete conversion of glycerol was achieved. The easy procedure allows the production of pure solketal with low iron content. The possibility to use complexes with modular nitrogen ligands is particularly attractive for their stability and handling, and also because their tunability makes the methodology transferable to other carbonyl compounds wherein simple iron salts may not be soluble.

Furthermore, the introduction of chiral ligands opens towards the enantioselective synthesis of chiral acetals, which are important synthons for high value-added compounds.

These results were published as: Esposito, R.; Cucciolito M. E.; D'Amora, A.; Di Guida, R.; Montagnaro, F.; Ruffo, F. *Fuel Process. Technol.* **2017**, *167*, 670.

Chapter 5

Conclusions

To the future!

In this thesis three new catalytic system to convert vegetable oils into valuable product were presented.

A catalytic system based on tungsten to oxidize oleic acid: Benessere, V.; Cucciolito, M. E.; De Santis, A.; Di Serio, M.; Esposito, R.; Ruffo, F.; Turco, R. *J. Am. Oil Chem Soc*, **2015**, *92*, 1701.

A homogeneous supported catalyst for the production of biodiesel: Benessere, V.; Cucciolito, M. E.; Esposito, R.; Lega, M.; Turco, R.; Ruffo, F.; Di Serio, M. *Fuel*, **2016**, *171*, 1.

A catalytic system to give added value to the byproduct of biodiesel, glycerol, transforming it in solketal: Esposito, R.; Cucciolito M. E.; D'Amora, A.; Di Guida, R.; Montagnaro, F.; Ruffo, F. *Fuel Process. Technol.* **2017**, *167*, 670.

They were developed trying to be as much as possible in line with the twelve principles of green chemistry in which the research group, where this three-year thesis has been developed, strongly believes. Nevertheless, there is no pretension to have found definitive green solutions to some chemical problems. On the contrary, in more general meanings, there is the full knowledge and humility to know that mankind is still far to fully understand the chemistry, the nature and the universe. This thesis is a minute step in a direction. However, it is clearly oriented in that direction. Direction of sustainability. Sustainability or "green" must be not only an empty word, a trend of the moment or the key word to easier obtain funds.

In the introduction there is a strong sentence: "In the only possible future in which the mankind still survives, this ethical chemistry" (the green chemistry) "would be the only way to do chemistry". It wants to be not a catastrophic claim, but often we forget that we are strictly bond to that planet. Even chemists, scientists sometimes are skeptics on arguments like global warming, resources overconsumption and pollution. Doubt is the base of science and scientific method, so, it's legitimate to be skeptic. At the same time however, a good scientist has to look at facts and data, think what can be possible and do not exclude any path *a priori*. And, also, must look at the literature, to the past, to try to foresee the results of an experiment.

Many[84] warnings suggest that something is changing the equilibria of our planet. Rationally, we have to contemplate all the consequences that this implies, first off all that it is our fault. Temperatures are raising (figure 5.1)[85] and CO_2 concentration in air has reached 400 ppm, a number that this planet has not seen in the last 4 million years (figure 5.2).[86]

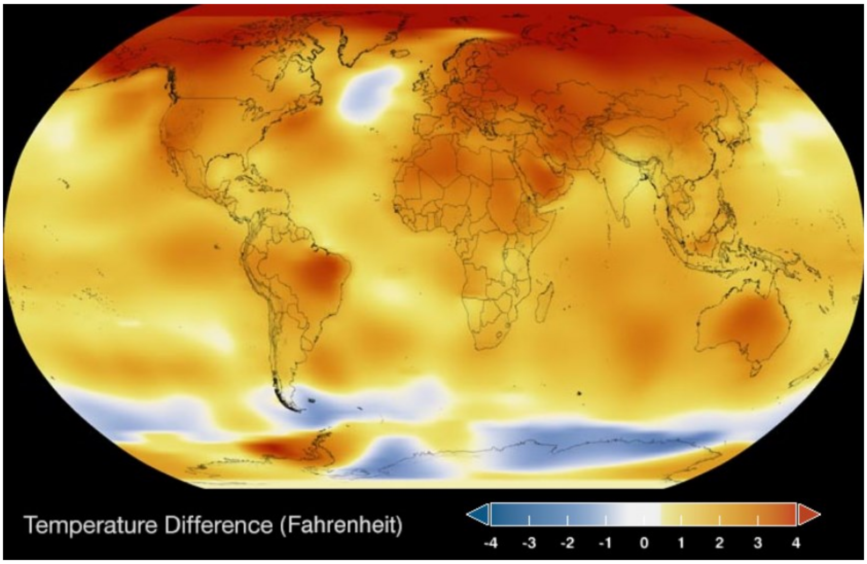


Figure 5.1 – Change in global surface temperature relative to 1951-1980 average temperatures

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[84] a) Intergovernal Panel on Climate Change (IPCC), *Climate Change* ***2014*** *– Impacts, Adaptation and Vulnerability: Regional Aspects* b) Parry, M.; Canziani, O. F.; Palutikof, J.; van der Linden, P.; Hanson, C. *Climate change* ***2007****: impacts, adaptation, and vulnerability* c) McCarthy, J. J.; Canziani, O. F.; Leary, N. A.; Dokken, D. J.; White K. S. *Climate change* ***2001****: impacts, adaptation, and vulnerability* d) United Nations Climate Change Conference, Paris **2015**; d) Monastersky, R. *Nature* **2013**, *497*, 13.

[85] https://climate.nasa.gov/vital-signs/global-temperature/

[86] https://climate.nasa.gov/climate_resources/7/

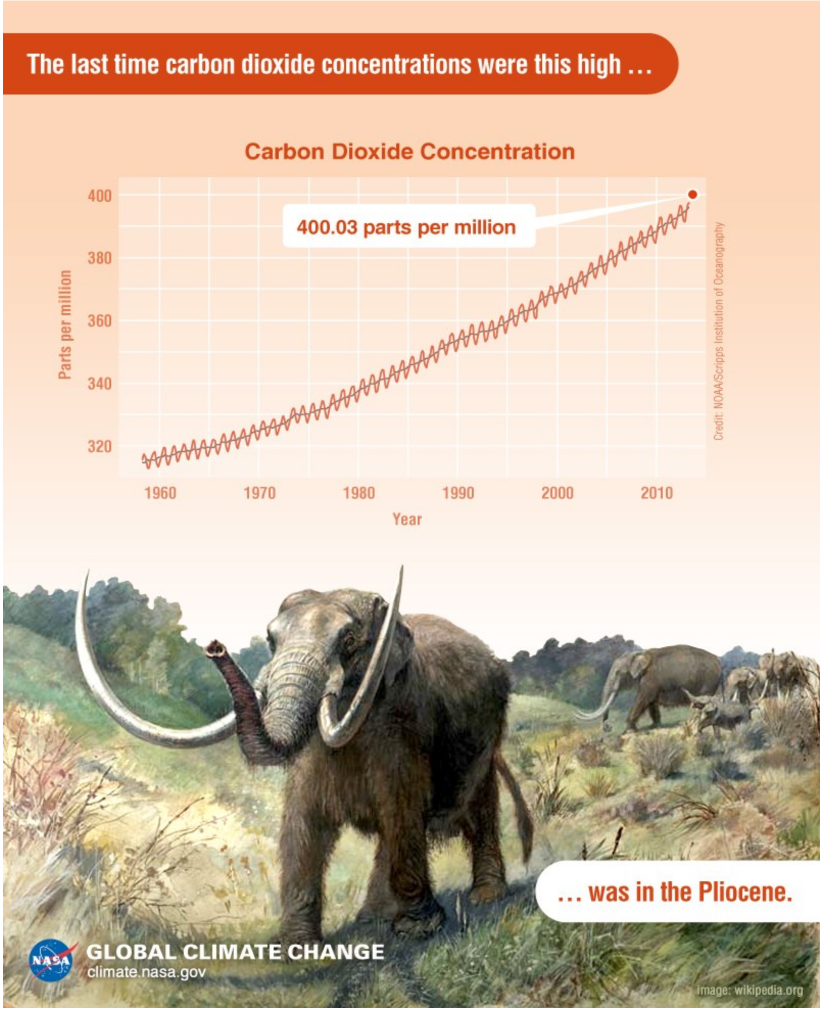

Figure 5.2 – CO_2 concentration in atmosphere

Extinction (in a long or short time period) is another possibility, the more pessimistic, that we have to consider. In a recent paper,[87] a new interesting evolution theory has been presented. The theory hypothesizes that because random genetic mutations can be described as an oscillatory phenomenon and environmental changes oscillates as well, the evolution can be described as a resonance phenomenon. Consequently, evolutions or extinctions can occur in a very short time (contrary to what the classical Darwinism claims). With this in mind we have to consider that the changes that we are causing are happening faster than how we can adapt to it.

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[87] Damasco, A.; Giuliani, A. *Physica A* **2017**, *471*, 750.

Localized examples of human extinction are many. Easter Island (Rapa Nui) is a significant example of extinction of a population due to artificial environmental changes. The island was populated since 300~600 AD. The agricultural technology improvement pushed population to grow and to expand the land use around 1400 AD. In that years the population reached probably 15-30,000 people. Consequent deforestation changed the microclimatic environment. Erosion of the terrain and extinction of the palm trees caused lack of resources that brought a developed civilization to a slow decline transforming the people into few cannibalistic tribes with the population dropped to 2-3,000 people. That was the situation when in 1722 AD Europeans explorers discovered it.[88]

Anthropocene, our era, distinguishes itself because human activity can drastically change the environmental conditions. The best weapon we have to fight this dystopia, waiting for us around the corner, is science. Scientific method and global knowledge brought us further than a single mind could ever have done. Scientific discoveries let us imagine a brighter future. A utopic future where mankind survives itself finding sustainable solutions to the main problems of our times.

Some of these solutions are not so far as someone could think. The primary source of CO_2 is electrical power production.[89]

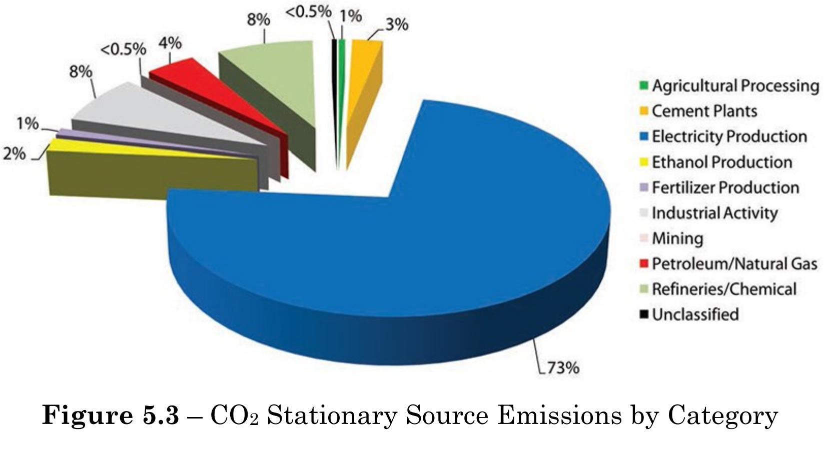

Figure 5.3 – CO_2 Stationary Source Emissions by Category

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[88] a) Peiser, B. *Energy Environ*. **2005**, *16*, 513; b) Mieth, A.; Bork, H. R.; Feeser, I. *Rapa Nui Juoirnal* **2002**, 16, 89.

[89] https://www.netl.doe.gov/research/coal/carbon-storage/carbon-storage-faqs/what-are-the-primary-sources-of-co2

Science just gave some sustainable alternatives in energy production with technology like solar and wind that are still technologically improving. But maybe the definitive solution could come from the combination of these with another technology we are developing. ITER is a 35 nations collaboration to build an operative nuclear fusion plant.[90] A first power plant that demonstrates the feasibility of magnetic confining of fusion plasma was built in France. The next step is the building of DEMO, two demonstrative plants that will produce net energy (the first experiment is set to 500 MW per 500 seconds for the European plant and 1500 MW for the Japanese plant, that is comparable to a modern fission plant). They should be operative in 2040s.[91]

Science let us dream a far future in which mankind understands universe a bit more, even at the point to break the light speed limit. In 1994 a physicist, Miguel Alcubierre, theoretically demonstrated how, travelling faster than light is possible, curving time-space.[92] Some other physicists, at the NASA, took it very seriously and started to work on experimental demonstrations of that theory.[93]

So, we can dream a future where mankind learns how to develop progress without damaging its habitat, its planet, and flies bringing its knowledge, its heritage, around the universe.

This far remote utopic future conflicts with the present and the nearest problems that we have to face.

Today, chemistry plays a gigantic role. Even more in this era where most of human activities are so strictly related to chemicals and chemical industries. Thanks to chemistry, men can produce drugs that saves lives, that give longer life expectation and a better quality of life. Every daily object passed through some plants that use chemistry and formulations of chemical knowledge, in a certain moment of its life. Therefore, as chemists, in our hands we have one of the greater tool ever created by men. And we have to learn and teach how to use this tool in the most rational way. As an Hippocratic Oath we should embrace principles of green chemistry, we should incorporate them in our discipline as a tacit guide.

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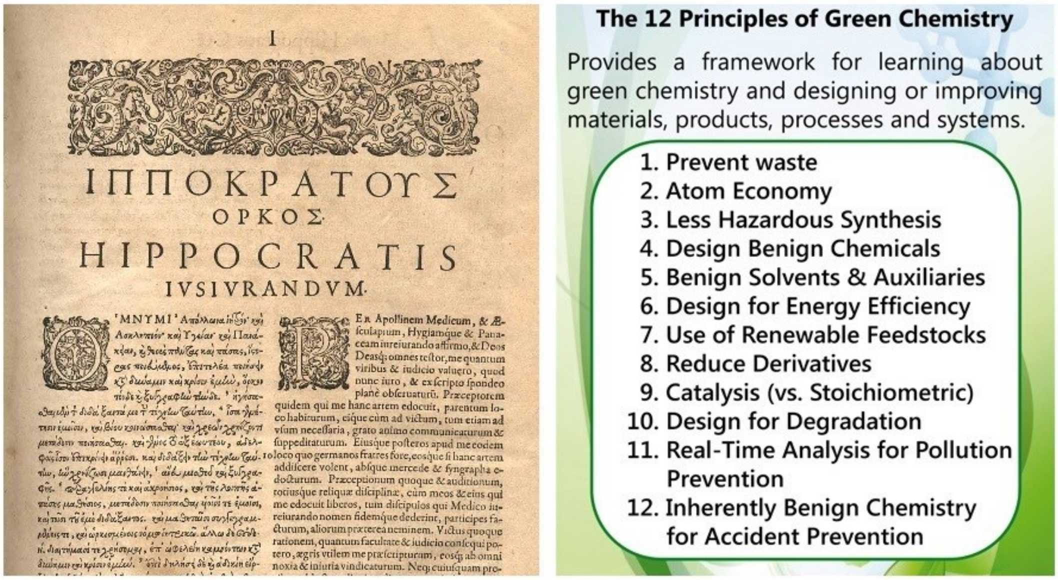
[90] https://www.iter.org/proj/inafewlines

[91] https://www.iter.org/mag/3/22

[92] Alcubierre, M. *Class. Quantum Grav.* **1994**, *11*, L73.

[93] https://ntrs.nasa.gov/archive/nasa/casi.ntrs.nasa.gov/20110015936.pdf



I

ΙΠΠΟΚΡΑΤΟΥΣ
ΟΡΚΟΣ.
HIPPOCRATIS
IVSIVRANDVM.

PEr Apollinem Medicum, & Æſculapium, Hygiamq́ue & Panaceam iureiurando affirmo, & Deos Deasq; omnes teſtor, me quantum viribus & iudicio valuero, quod nunc iuro, & ex ſcripto ſpondeo planè obſeruaturū. Præceptorem quidem qui me hanc artem edocuit, parentum loco habiturum, eiq́ue cùm ad victum, tum etiam ad vſum neceſſaria, grato animo communicaturum & ſuppeditaturum. Eiusq́ue poſteros apud me eodem loco quo germanos fratres fore, eosq́ue ſi hanc artem addiſcere volent, abſque mercede & ſyngrapha edocturum. Præceptionum quoque & auditionum, totiusq́ue reliquæ diſciplinæ, cùm meos & eius qui me edocuit liberos, tum diſcipulos qui Medico iureiurando nomen fidemq́ue dederint, participes facturum, aliorum præterea neminem. Victus quoque rationem, quantum facultate & iudicio conſequi potero, ægris vtilem me præſcripturum, eosq; ab omni noxia & iniuria vindicaturum. Neq; cuiuſquam pro-

The 12 Principles of Green Chemistry

Provides a framework for learning about green chemistry and designing or improving materials, products, processes and systems.

1. Prevent waste
2. Atom Economy
3. Less Hazardous Synthesis
4. Design Benign Chemicals
5. Benign Solvents & Auxiliaries
6. Design for Energy Efficiency
7. Use of Renewable Feedstocks
8. Reduce Derivatives
9. Catalysis (vs. Stoichiometric)
10. Design for Degradation
11. Real-Time Analysis for Pollution Prevention
12. Inherently Benign Chemistry for Accident Prevention

Figure 5.4 – Hippocratic Oath (left) and Green Chemistry principles (right)

Chemistry and, more in general, science can guide the world, and change it. They did it greatly in the past and can do it again. What we can do now is to keep consciousness of this, to hand down our oath and teach sustainability concepts to the future generations hoping that their leading class will rule with this in mind.

PhD Course Activity Summary

Candidate: Roberto Esposito

Tutor: Prof. Francesco Ruffo

1) **Attended Courses (6 minimum, 8 hours each):**

- Chimica Fisica dei Nanosistemi – Prof. Paduano, L.
- Glicoscienza – Prof. Parrilli, M; Prof. Bedini, E.
- Le tecniche di estrazione solido-liquido impiegate nella preparazione del campione per l'analisi chimica e nella produzione di estratti per usi industriali – Prof. Naviglio, D.
- Prof.ssa Montesarchio, D.
- Corso Avanzato di Spettrometria di Massa – Prof. Pucci, P.
- Selective Organometallic Catalysis: systems and advanced techniques – Prof. Budzelaar, P. H. M.

2) **Attended Seminars:**

Title	Speaker	Date	Place
Le fitotossine un'avventura lunga 40 anni.	Evidente, A.	10/12/2014	Napoli, Dipartimento di Scienze Chimiche
New chiral catalysts derived from Fe(II) and Bi(III) for asymmetric synthesis.	Ollevier, T.	15/12/2014	Napoli, Dipartimento di Scienze Chimiche

Enhanced sampling techniques aimed at characterizing protein-ligand binding for design application.	Rocchia, W.	22/12/2014	Napoli, Dipartimento di Scienze Chimiche
Multiscale modelling of Soft Matter: atoms, beads and fields.	Milano, G.	19/02/2015	Napoli, Dipartimento di Scienze Chimiche
Pharmaceutical companies: external manufacturing and quality assurance.	Demasi, D.	25/05/2015	Napoli, Dipartimento di Scienze Chimiche
Effect of reduced graphene oxide in disentangled polyethylene and LLDPE.	Ronca, S.	17/07/2015	Napoli, Dipartimento di Scienze Chimiche
Progettazione, risk assessment e controllo qualità del packaging alimentare: il ruolo inatteso del consulente chimico.	Benessere, V.	17/03/2016	Napoli, Dipartimento di Scienze Chimiche

The importance of catalysis I the synthesis of active pharmaceutical ingredients.	Scalone, M.	25/11/2016	Napoli, Dipartimento di Scienze Chimiche
La chimica tra le tecnologie e la bioeconomia.	Bellofiore, P.	10/04/2017	Napoli, Dipartimento di Scienze Chimiche
CO_2 Switchable Surfaces and Coatings.	Jessop, P.	23/05/2017	Napoli, Dipartimento di Scienze Chimiche
Bond Shift Isomers.	Wentrup, C.	16/06/2017	Napoli, Dipartimento di Scienze Chimiche

3) **Publications (include submitted and in preparation):**
    - Calvanese, L.; Cucciolito, M. E.; D'amora, A.; D'Auria, G.; Esposito, A.; Esposito, R.; Falcigno, L.; Ruffo, F. *Eur. J. Inorg. Chem.* **2015**, 4068.
    - Benessere, V.; Cucciolito, M. E.; De Santis, A.; Di Serio, M.; Esposito, R.; Ruffo, F.; Turco, R. *J. Am. Oil Chem. Soc.* **2015**, *92,* 1701.
    - Benessere, V.; Cucciolito, M. E.; Esposito, R.; Lega, M.; Turco, R.; Ruffo, F.; Di Serio, M. *Fuel* **2016**, *171*, 1.
    - Esposito, R.; Calvanese, C.; Cucciolito, M. E.; D'Auria G.; Falcigno L.; Fiorini,V.; Pezzella, P.; Roviello, G.; Stagni, S.; Talarico, G.; Ruffo, F. *Organometallics* **2017**, *36*, 384.
    - Esposito, R.; Cucciolito M. E.; D'Amora, A.; Di Guida, R.; Montagnaro, F.; Ruffo, F. *Fuel Process. Technol.* **2017**, *167*, 670.
    - Which is the atomic number *Z* of the element that inaugurates a given electronic sublevel *l*? Esposito, R.; Ruffo, F. *in preparation.*

4) **Attended congresses/workshops/summer schools:**
    - **10th International School of Organometallic Chemistry - Camerino 2015 (PhD school)**
    - 3° Workshop Nazionale Gruppo Interdivisionale Green Chemistry – Chimica Sostenibile – 12 Giugno 2015
    - XIX Congresso Nazionale Divisione di Chimica Industriale della SCI - Salerno 2015
    - Advanced Training Course on Emerging Biotechnologies for Sustainable Waste Menagement and Biorefinery Development - Napoli 2016
    - XII Congresso del Gruppo Interdivisionale di Chimica Organometallica della SCI – XII COGICO, Genova 2016

- 6th EuCheMS Chemistry Congress - Siviglia 2016
- **International Summer School 2016 – Bio-Leaching and Metal Extraction Processes for Urban Mining: From Fundamental Principles to Practical Applications - Dresda (PhD school)**
- SPRING Meeting - Bertinoro 2017
- CIRCC XIV PhD day – Bari, 30 March 2017
- **11th International School of Organometallic Chemistry - San Benetto del Tronto 2017 (PhD school)**
- Congresso Nazionale della SCI – Paestum 2017 – As SCI Staff Member

5) **Other Activities:**
   - Progetto Lauree Scientifiche 2015 – Staff Member
   - Progetto Lauree Scientifiche 2016 – Staff Member
   - Progetto Lauree Scientifiche 2017 – Staff Member
   - Inorganic Chemistry Quiz Writer for *Giochi Nazionali della chimica Regionali* 2016/2017
   - Inorganic Chemistry Quiz Writer for *Giochi Nazionali della chimica Nazionali* - Roma 2017