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A new eco-friendly one-pot tandem synthesis of cyclic carbonates from oleochemicals

Supervisor
Ch. Prof. Alvise Perosa

Assistant supervisor
Ch. Prof. Maurizio Selva

Graduand
Nicola Sargentoni
877616

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LIST OF ABBREVIATIONS

AA	Azelaic Acid
CMO	Carbonated Methyl Oleate
DMC	Dimethyl Carbonate
EMO	Epoxidized Methyl Oleate
FA	Fatty Acids
FAE	Fatty Acids Esters
FAME	Fatty Acids Methyl Esters
GHG	Green House Gas
IL	Ionic Liquid
MO	Methyl Oleate
MSW	Municipal Solid Waste
OA	Oleic Acid
PA	Pelargonic Acid
PEG	Polyethylene Glycol
POM	Polyoxometalate
PPOM	Peroxopolyoxometalate
PTC	Phase-Transfer Catalyst
QAS	Quaternary Ammonium Salt
QPS	Quaternary Phosphonium Salt
RE	Renewable Energy
TBAB	Tetrabutylammonium bromide
TG	Triglyceride
TILC	Tungstate-based Ionic Liquid Catalyst
TOA	Trioctylamine
TOP	Trioctylphosphine
UFA	Unsaturated Fatty Acids

CHAPTER I

INTRODUCTION

1.1 The World We Live in

The conception of the world, as a planet of endless wealth, has changed sharply over the last decades, demonstrating the cultural heritage's impracticability the human population is following. A new way must be embraced to start living seamlessly in and with the world.

Despite the industrialization process has constituted an essential milestone in terms of life's quality and economic evolution, the Earth experienced an increased pollution and all the natural, non-renewable resources started to be used without any control.[1]

The consciousness and concern about the ecological problems grew slowly along the years. First concerns began to emerge since 1949, when the United Nations Scientific Conference on the Conservation and Use of Resources (UNSCCUR) was attended in Lake Success (USA); moreover, in 1962, Rachel Carlson published the book "Silent Spring" which stated the negative impacts of an improper usage of pesticides and insecticides and prompted national actions to regulate them.[2] In 1968 the ecological issues were highlighted during the Intergovernmental Conference of Experts on the Scientific Bases for Rational Use and Conservation of Biosphere Resources, known as the Biosphere Conference.[3]

Two more years later, the 22th of April 1970 became the first anniversary of the "Earth Day" as well as the birth of the modern environmental movement (Figure 1.1).[4,5]

"All the News
That's Fit to Print"

The New York Times

LATE CITY EDITION

Weather: Cloudy, rain likely today and tonight. Partly sunny tomorrow. Temp. range: today 64-50; Wed. 67-46. Full U.S. report on Page 73.

VOL. CXIX ... No. 40,997 © 1970 The New York Times Company. NEW YORK, THURSDAY, APRIL 23, 1970 10 CENTS

PRICES CLIMB 0.4% BUT RATE OF RISE APPEARS TO SLOW

Gain in the Consumer Index for March Lags Behind the 4 Previous Months

INCREASE IS STEEP HERE

Medical Care and Mortgage Interest Are the Major Elements in Changes

By EDWIN L. DALE Jr.
Special to The New York Times

WASHINGTON, April 22—Consumer prices rose strongly again in March but there were signs that the pace of inflation was slowing, the Labor Department reported today.

After adjustment of the data to reflect normal seasonal changes, the Consumer Price Index rose four-tenths of 1 per cent in March, less than the five-tenths rise in February and the six-tenths rate of the three months before that.

What is more, one-quarter of the entire March increase in the index was accounted for by a somewhat artificial recording of an increase in Veterans Administration mortgage interest rates. The ceiling on these rates was recently raised by

Millions Join Earth Day Observances Across the Nation

The New York Times (by Patrick A. Burns)

Throngs jamming Fifth Avenue yesterday in response to a call for the regeneration of a polluted environment. View is north from 43d Street, with Central Park in background.

CAMBODIAN CRISIS GROWS AS TROOPS SEEM TO FALTER

With Reds Near, Pnompenh Is Gloomy Over Limited Response to Aid Pleas

CIVIL AVIATION CURBED

Aide Declines to State How Long Army Can Hold Out With the Arms It Has

By HENRY KAMM
Special to The New York Times

PNOMPENH, Cambodia, April 22—An atmosphere of heightening national emergency is overtaking Cambodia.

It is due to evidence that the Cambodian Army is unable to turn back the Vietnamese Communist forces, which at one point are within 15 miles of the capital, and to the limited response to Premier Lon Nol's appeal to all nations for arms aid.

The military authorities closed the Pnompenh airport this evening to all civilian traffic. According to military sources, it is to remain closed until tomorrow in connection with an important military operation. The operation is presumably intended to dislodge the North Vietnamese

U.S. CONCERN SUED WITH 2 IN JAPAN

Mood Is Joyful as City Gives

Activity Ranges From Oratory

BACKERS OF ROJAS THREATEN REVOLT

U.S. Plane Flies In Arms As Trinidad Fights Mutiny

Figure 1.1: New York Times' Front-Page announcing the first "Earth Day"

To complete this roundup of meaningful events, in 1972 the book “The Limits to Growth” was published by Donella H. Meadows, on commission by The Club of Rome, a no-profit and non-governmental organization founded by Aurelio Peccei. Based on the simulation of a computer,[6] the conclusions reached can be summarized as follow:

1. If the present world population, pollution and resource depletion continue to grow unchanged, the limits to growth on this planet will be reached within the next century;
2. It’s still possible to change these growth trends and create an economic and environmental stability that is sustainable into the future. A new way must be designed so that each person on Earth is satisfied and has equal chances to realize his potential;
3. The sooner the world population starts working for the previous outcome, the better will be for the Earth.[7]

In the same year the Stockholm Conferenced claimed the Action Plan for the Human Environment and the Stockholm Declaration was adopted.[8a] The Action Plan (composed by three main categories, then expanded in 109 recommendations) identified those environmental issues that require global awareness and launched *Earthwatch*, the global environmental assessment program. The Action Plan’s recommendations and negotiations led to the development of international agreements.[8c]

The Stockholm Declaration, as well as the Biosphere Conference, placed environmental issues on the top of international concerns[8a-b] with its 26 principles: for instance, it emphasized the importance to protect the environment for future generations (Principle 1), to conserve natural resources (Principles 2) and to prevent pollution and the discharge of toxic substances (Principles 6, 7). Despite the Stockholm Declaration placed primary responsibility for environmental protection on national governments, it also defined the environment as an area that requires international actions, underscoring the imperative of a global cooperation. Although the term is not present anywhere in the document, the Stockholm Declaration helped to establish the basis for the “sustainable development”.[8c]

1.1.1 Sustainable Development

After about ten years of the proposed actions at the Stockholm Conference, in December 1983 the United Nations Assembly decided to establish the World Commission of Environment and Development (WCED).[9] The WCED introduced the term "Sustainable Development" in "Our Common Future", known as "Brundtland Report", a document published in 1987.

The definition of sustainable development meets the needs of the present without compromising the future generations' possibilities to meet their own needs, so "the strategy aims to promote harmony among human beings and between humanity and nature".[10]

The main idea is to give everyone the equal possibility of a social and economic growth, preserving the whole ecosystem for future generations, as resumed in the Venn's diagram of sustainability (Figure 1.2),[11] defined as the three pillars of sustainability. To achieve a real sustainable development, economic, social and environmental factors need to be balanced. They can be defined as follow: *Environmental sustainability* means that people are living within the capability of the natural resources. An *economic sustainability* requires that a business or country uses its resources efficiently and responsibly. Finally, *social sustainability* is the ability of society, or any social system, to achieve a good wellness. Only through balancing these three pillars, a sustainable development and a circular economy can be achieved.[12]

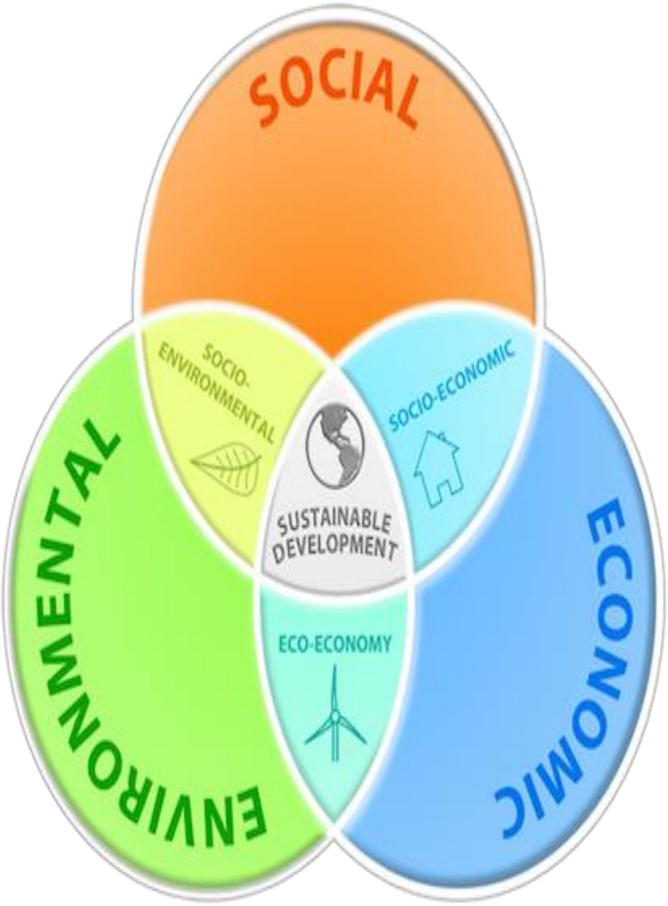


Figure 1.2: Venn's diagram of sustainability

1.1.2. Green Chemistry

The idea of green chemistry arose as a response to the Pollution Prevent Act of 1990, which suggested to decrease pollution by improving design instead of treatment and disposal.[13]

In 1999, the Royal Society of Chemistry founded its journal: *Green Chemistry*.[13]

Green Chemistry constitutes both an innovative approach to the synthesis, processing and use of chemicals that reduce risks to human, and a fundamental tool to accomplish the pollution prevention.[14] The twelve principles of green chemistry, edited by Paul Anastas and John Warner in 1998, as shown in Figure 1.3, are: [15]

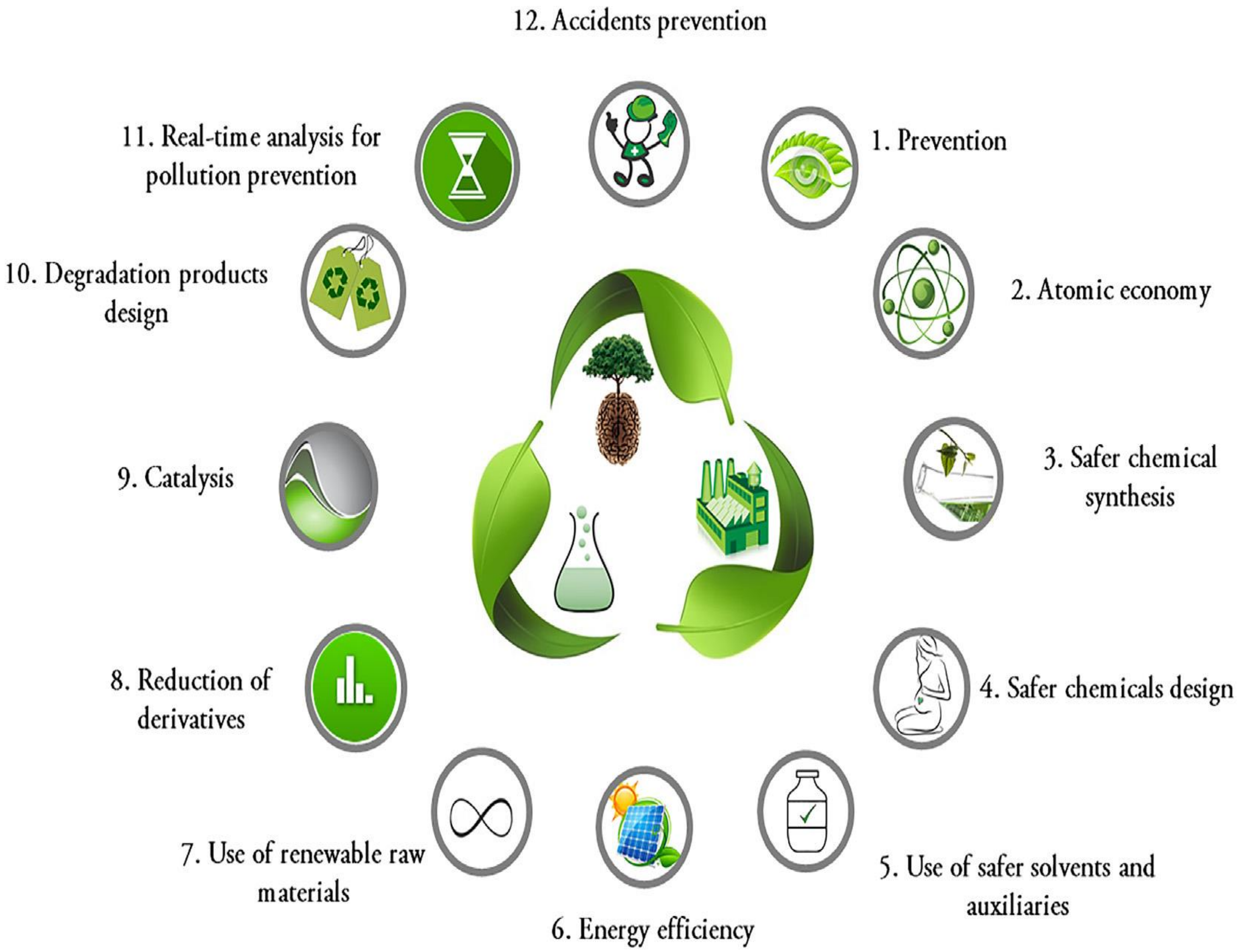


Figure 1.3: A simplified version of the twelve principles proposed by Anastas and Warner

1. *Prevention*: Avoiding wastes' production is better than to treat or clean up them;
2. *Atomic Economy*: All materials should be incorporated into the final product and synthetic methods must be designed to achieve this goal;
3. *Safer Chemical Synthesis*: Non-toxic or low toxic substances should be adopted and exploited in the synthesis and new methods must be designed;
4. *Safer Chemical Design*: Chemical products should be designed to affect their desired function while minimizing their toxicity;
5. *Safer Solvents and Auxiliaries*: Auxiliary substances should be unnecessary wherever possible and innocuous when used;
6. *Energy Efficiency*: Chemical processes should be minimized in terms of energy requirements and recognized for their environmental and economic impacts;
7. *Use of Renewable Feedstocks*: A raw material or feedstock should be renewable;
8. *Reduced Derivatives*: Unnecessary derivatization (use of blocking groups, protection/ deprotection, etc..) should be minimized or avoided if possible;
9. *Catalysis*: Catalytic reagents should be used instead of stoichiometric reagents and new systems must be designed to achieve this purpose;
10. *Design for Degradation*: Chemical products should break down into innocuous degradation products once they end their primary function;
11. *Real-time analysis for Pollution Prevention:* Analytical methodologies need to be further developed to allow real-time monitoring the pollution;
12. *Accident Prevention:* Chemical accidents must be minimized by choosing safer substances.

These principles are based on prevention and a careful selection of what chemicals to use and the deployment of non-toxic materials, as well as chemicals easily degradable without wastes. In simple words, the principles push towards products whose synthesis, analysis and destination after their use have low environmental and human risks. If, on one hand, these basic tasks represent the strength and innovation of green chemistry, one the other hand these goals are also its biggest frailty. More specifically, moving from an old and conventional process to a new one, submitted to the green chemistry's principles, requires a lot of time, design and it is often difficult and expensive.[16] As Theodore Roosvelt once quoted: “Nothing in the world is worth having or worth doing unless it means effort, pain, difficulty”.

1.2 Where to start: Biomass

Fossil feedstocks are the major sources employed in the industrial sector. Although they account for about 80% of the world's energy demand,[17] they are non-renewable resources: as their reserves are growing much slower than their actual deployment, they will surely run out. Moreover, the exploitation of fossil sources leads to the emission of greenhouse gases (GHG). The Scientific community has demonstrated that these emissions are amongst the main cause for the global warming, as well as the world climate change.[18] As a response to these concerns, joint policies of different Countries have been adopted to reduce emissions, highlighting the renewable resources as ideal and eco-friendly substitutes.[19]

Among all the "renewable energy" (RE), that derive directly or indirectly form the sun, biomass is acquiring ever-greater relevance and it is the most investigated, both by geographical distribution (Figure 1.4) and by number of publications, with 56% of publications on renewable energy, from 1979 to 2009, regarding biomass (Figure 1.5).[20]

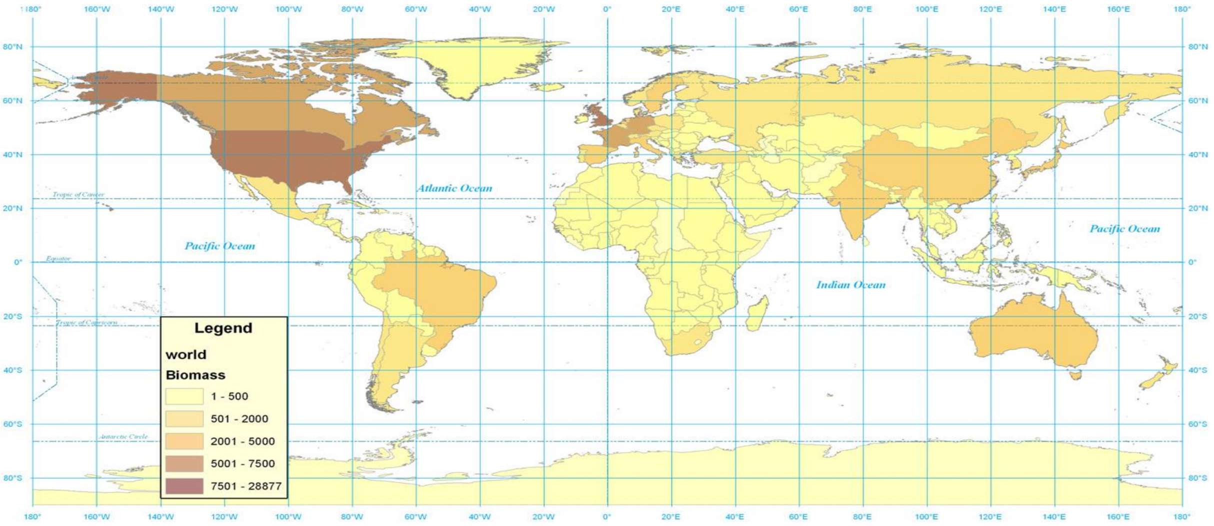


Figure 1.4: World map of the number of scientific publications on biomass in the period 1979–2009

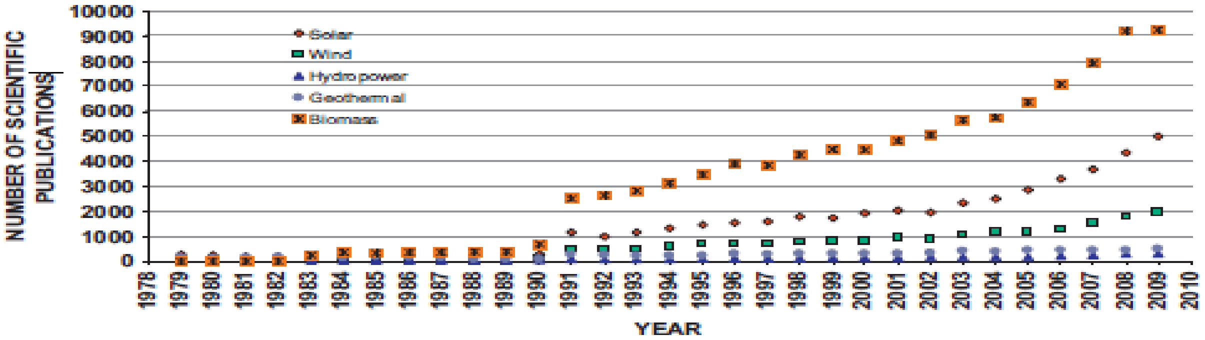


Figure 1.5: Evolution of scientific publication on biomass from 1979 to 2009

1.2.1 Compostion and Classification

Any terrestrial or marine organic matter of plant or animal origin, produced directly or indirectly through the process of photosynthesis in a spontaneous way or cultivated by humans can be defined as biomass.[21] The most important biomass sources are shown in Figure 1.6.[22] Industrial waste represents one of the main concerns to the environment, since they may contain highly polluting chemicals, metals or drugs.[23] Municipal solid waste (MSW) includes mixed commercial and residential garbage, such as paper, plastics or rubber and can be considered as resources if correctly separated; forestry biomass is composed both by residues left after logging and by whole-tree collected explicitly for energy production; agricultural residues can be defined as those wastes available without interfering with the production of food.[24]

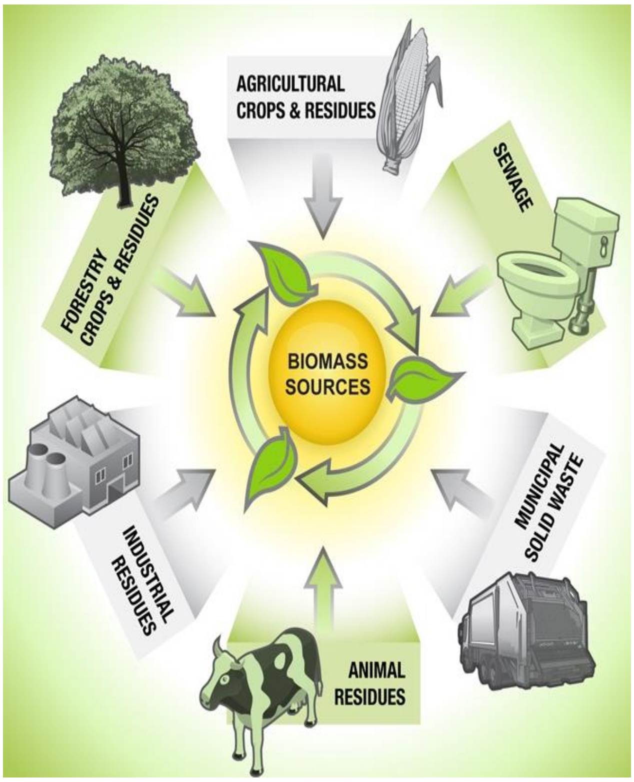


Figure 1.6: The most important biomass sources

Only biomass of plant origin and, specifically, agricultural and forestry residues and wastes are considered in this Thesis, as they are the main sources for the production of biofuel and biomaterials. Due to substantial differences in term of variety and quantity and their different compositional characteristics, there is no univocal way of classification.[25]

Based on their chemical composition, agricultural and forestry sources can be classified into four main categories:

A) Lignocellulosic biomass;

B) Starch-Based Plants;

C) Terpenes and Rubber-Plants;

D) Triglycerides producing-plants and Microalgae.

A) Lignocellulosic Biomass

Lignocellulose is composed mostly of carbohydrate polymers (cellulose and hemicellulose) and lignin, in relative amounts from 30-60 wt%, 10-40 wt% and 20-30 wt% respectively. Cellulose is the most common polysaccharide consisting of D-glucopyranose monomers conjuncted with β-1,4 bonds.[26] Hemicellulose is a copolymer constituted of five different monomer sugars. Lignin is a phenolic polymer and provides structural rigidity to plants binding together cellulose and hemicellulose. Lignin is the only known renewable source of aromatic compounds.

B) Starch-Based Plants

Starch-based plants are made up of about 75 wt% of sugar polymers.[27] Glucose polymers, namely starches, are particularly abundant in agricultural crops. These polymers are obtained via α-glycoside bonds of glucose which produce amorphous structures easily hydrolysable to their major components: amylose and amylopectin. Starches, along with cellulose and hemicellulose, are exploited to obtain biofuels and chemicals.

C) Terpenes and Rubber-Plants

Plants belonging to *Euphorbiaceae* family and others, as *Guayule* or *Hevea Brasiliensis* transform carbohydrates into terpenes, which are hydrocarbons with a carbon skeleton derived from isoprene. Terpene feedstocks are a natural supply of building blocks for the fine chemical industry. They are an important source of intermediates and ingredients for flavors and fragrances[28] but their current production is quite low compared to other biomass.

D) Triglycerides producing-plants and Microalgae

Triglycerides can be found in different kinds of plants as palm, soybeans or sunflower. Triglycerides are the main components of natural oils and animal fats: both oils and fats are attractive for the industrial sector because of their competitive cost, large availability and functionality. Their peculiar structure makes both oils and fats high-energy density materials: beyond their common uses as lubricants and raw materials for detergents and chemicals, natural oils and fats find applications also in the biofuels sector.

Triglycerides, in particular natural oils, will be exhaustively discussed in the next paragraphs.

Microalgae are primitive organisms with a simple cellular structure and a large surface to volume body ratio. They are fast growing and convert efficiently CO_2 into a high-density liquid that can be used as biodiesel through the exploitation of solar energy.[29] Their exploitation, however, is limited due to investment costs for treatment of algal feedstocks.[30]

The different chemical classification of agricultural and forestry biomass is summarized in Figure 1.7.[21]

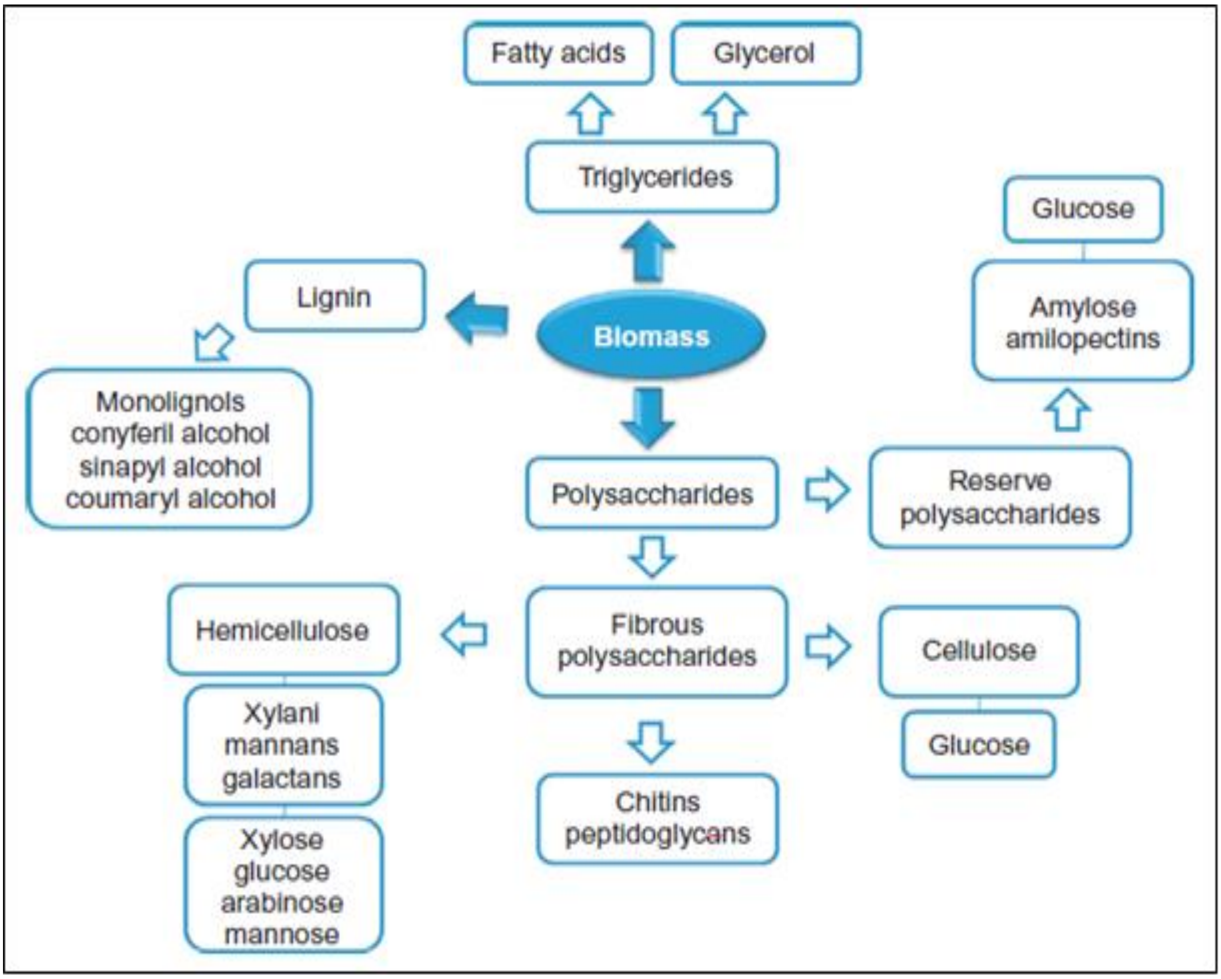


Figure 1.7: Agricultural and Forestry Biomass primary substances

1.2.2 Energy production and Bioproducts

Biomass consitutes one of the first energy source used by human population with tidal and eolic energy: direct combustion to produce heat was the most common method for converting biomass and, lately, for generating electricity. Biomass can also be converted in other energy carriers, for example trasportation fuels or bio-products.

There are some physicochemical characteristics of biomass playing a crucial role in directing the available feedstock into the biofules or the electricity/heat domain: caloric value, proportions of fixed carbon and volatile substances, ash content, alkali metal content, moisture content and cellulose/lignin ratio. The first five properties mostly influence the conversion processes of dry biomass, while the last two are essential for the conversion processes of wet biomass.[31]

Biomass (especially lignocellulosic material) undergoes pretreatment processes in order to be more easily convererted into transportation fuels and value-added co-products.[32] Indeed, pretreatment permits to simultaneously decrease the crystallinity index of cellulose and to increase its available surface area by removing layers of lignin.[33] Pretreatment methods used for lignocellulosic materials are classified into mechanical, chemical, chemical/mechanical, and biological methods. Some of the most famous pretreatment processes are shown in Table 1.1.[25]

Pretreatment Process	**Type**	**Short Description**
Mechanical	Milling	Use of mechanical devices to reduce the size
	Ultrasonic	Use of ultrasonic to obtain smaller molecules
Chemical	Alkaline hydrolysis	Calcium (or sodium) hydroxide and ammonia are used to reduce lignin and hemicellulose
	Organosolv	Organic solvent are used to remove lignin
Chemical/Mechanical	Steam Explosion	Biomass is filled with an high pressure steam and, then, decompressed to break down lignin
	CO_2	Steam Explosion using CO_2 as steam gas
Biological	Hydrolysis	Microorganisms are used to degrade hemicellulose and lignin

Table 1.1: Some of the most important pretreatment process

The main processes to convert biomass into energy are shown in Figure 1.8[21] and can be classified in three main categories:

A) *Thermo-chemical conversions*: in which heat and/or chemicals are used (*i.e.* gasification, liquefaction, pyrolysis and combustion);

B) *Biochemical conversions:* in these processes, *i.e.* fermentation and anaerobic digestion, biomass is decomposed to available carbohydrates, convertable into liquid fuels and biogas, as well as different types of bio-products by using biological agents as bacteria or enzymes;[34]

C) *Physico-chemical conversions.* biomass is mainly converted to high-density biofuels. More specifically, vegetable oil ad animal fats are converted into biodiesel via transesterification reactions.[35]

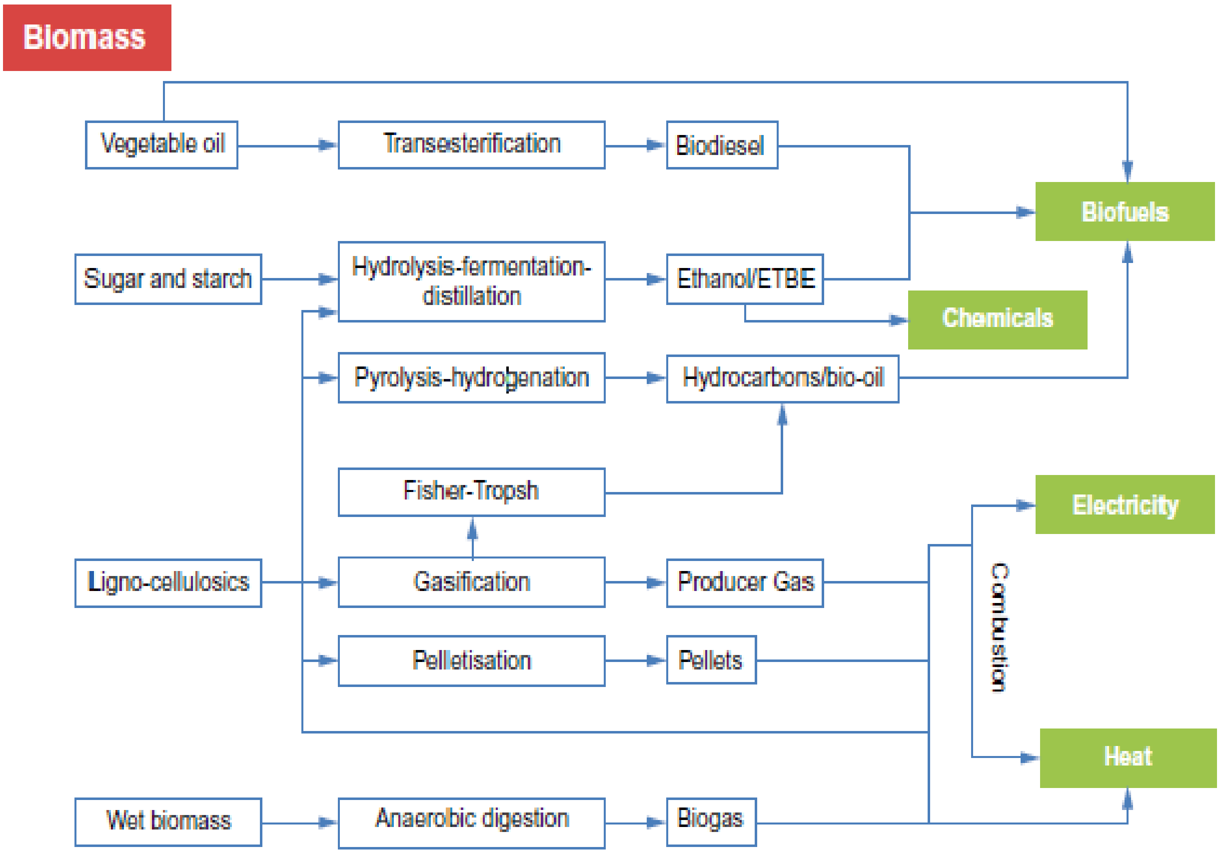


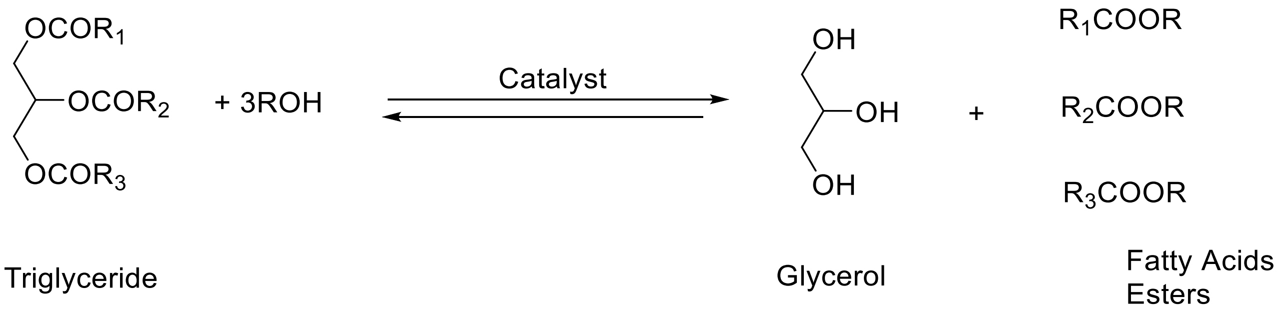
Figure 1.8: Scheme of different process for conversion of biomass

Biomass continues to be the main source of renewable energy in Europe. To give some examples: the world energy request in 2010 was 5.5 x 10^{20} J and it's predicted to increase to 8.6 x 10^{20} J within the 2050,[36] while the annual terrestrial primary production adds approximately 120 x 10^{12} kg of dry vegetative biomass, storing almost 2.2 x 10^{21} J of energy in plant materials.[37] From 1990 to 2010 bioenergy supply has increased from 38 to 52 x 10^{18} J as a result of growing energy demand and the World Energy Council predicted that bioenergy consumption would increase three-fold to 2050 relative to the 2010 level.[38] The global consumption of bioenergy will clearly continue to increase: lignocellulosic bioethanol and biogas will be the most prosperous bioenergy with highest growing potential in close future.[39]

1.3 Triglycerides

Triglycerides (or triacylglycerols, TGs) are tri-ester obtained by an esterification process of glycerol with three molecules of fatty acids, not necessarily the same ones. Triacylglycerols are the main constituents of vegetable oils, as well as human and animal fats: different kinds of plants are excellent sources of triglycerides (*e.g.*, palm or soybean). TGs are also a major component of human skin oils and can be found in the blood: triglycerides are a component of apolipoproteins with cholesterol.[40]

Triglycerides do not represent exploitable fuel: the crude vegetable oil must be transformed to avoid problems such as incomplete combustion and consequential accumulation of residues. TGs must undergo a transesterification reaction (catalyzed by acids or alkaline catalysts) to break apart the triglycerides' molecules into their constituents, namely fatty acids esters (FAE) and glycerol, as shown in Scheme 1.1.[41]



Scheme 1.1: Transesterification of triglycerides to produce fatty acid esters and glycerol

As an equilibrium reaction, the balance can be shifted towards products by using an excess of alcohol or by removing a reaction product; usually, glycerol is separated by centrifugation or decantation.

1.4 Fatty Acids and Fatty Acids Esters

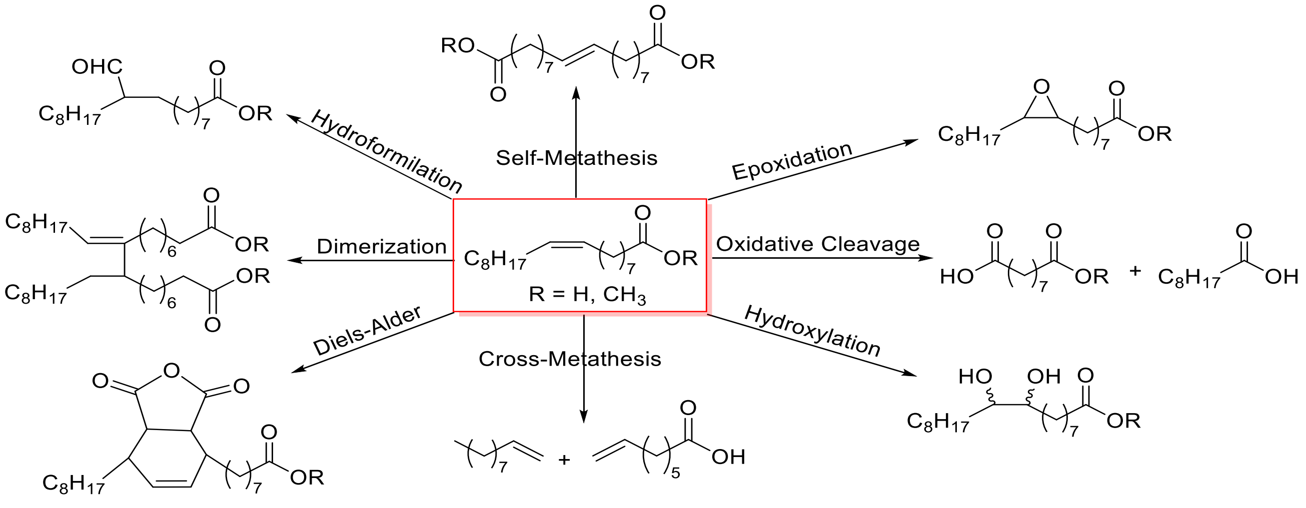
Fatty acids (FA) are carboxylic acids with a long saturated or unsaturated aliphatic chain: many naturally occurring fatty acids have 4–28 carbon atoms chain. Fatty acids and relative esters are obtained from triglycerides or from phospholipids, both by hydrolysis. As already seen in Scheme 1.1, fatty acids esters are also achieved by transesterification. Some of the most common fatty acids, their composition and main sources, are shown in Table 1.2.

Fatty Acids Name	**IUPAC Name**	**Carbons**	**Type of Fatty Acids**	**Common Sources**
Palmitic Acid	Hexadecanoic acid	16	Saturated	Palm Oil
Stearic Acid	Octadecanoic acid	18	Saturated	Animal Oil
Oleic Acid	Octadec-9-enoic acid	18	Monounsaturated	Olive/Sunflower Oil
Linoleic Acid	Octadeca-9,12-dienoic acid	18	Polyunsaturated	Safflower Oil

Table 1.2: List of common fatty acids: carbon atoms chain, type and common sources

Among all the fatty acids, monounsaturated are particularly attractive for the chemical industry, due to their low price and worldwide availability: these are the main reasons why a plethora of studies have been devoted to the conversion of fats into fuel and other useful products in recent years.[42] Indeed, the total consumption of fats and oils has increased from 41 million tons in 1970 to 200 million tons in 2014.[43]

Among monounsaturated fatty acids, oleic acid (OA) and its methyl ester, methyl oleate (MO), represent an interesting and innovative building blocks for the chemical industry.[44] Many reactions have been studied to exploit the C_9-C_{10} double bond, as shown in Scheme 1.2.[43]



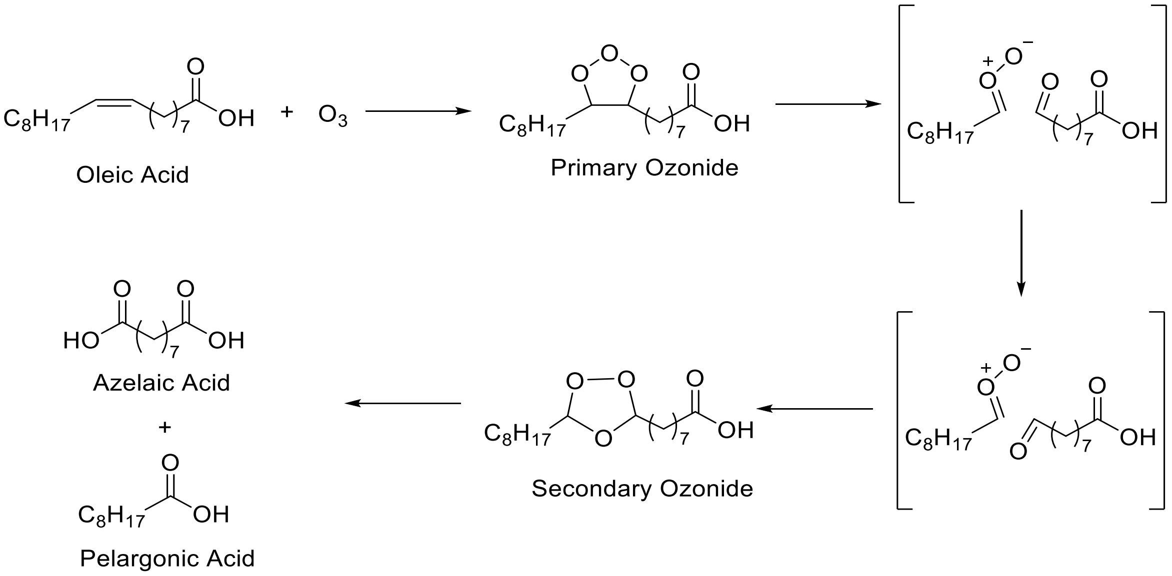
Scheme 1.2: Most common transformation of double bond of OA or MO

In accordance with the purposes of this Thesis, the attention will be focused only to the oxidative cleavage and to the epoxidation process.

Oxidative Cleavage

The oxidative cleavage of oleic acid involves scission of the carbon-carbon double bond with incorporation of oxygen into the two fragments. The oxidative scission is very attractive as it provides pelargonic (PA, a C_9 mono-acid) and azelaic acid (AA, a C_9 di-acid).[46] These acids can be exploited as starting materials for the preparation of numerous bio-based products: azelaic acid, along with pelargonic acid, is converted into different esters for the production of plasticizers, biodegradable lubricants, adhesives and, in addition, AA can be also converted into solvents, polymers and as agent for cosmetics. [44,46,47]

Traditionally, the cleavage is performed by ozonolysis, a metal-free process with ozone as oxidant,[48,49,50,51] whose mechanism is proposed in Scheme 1.3.[52] However, due to its instability, use of ozone at high temperatures represents a serious drawback of this process.[53]



Scheme 1.3: Proposed mechanism for the ozonolysis of oleic acid

In order to avoid direct ozonolysis, different catalytic system have been tested. The main pathways are the direct cleavage of the double bond, as shown in Scheme 1.3, or the two or three-step processes through epoxides, diols or keto-carboxylic acids: both routes have been described using various oxidants,[52] especially hydrogen peroxide (H_2O_2) constitutes a valid alternative since its oxidizing ability, great atom economy, formation of water as only by-product and low safety and environmental concerns.[54]

Epoxidation

The traditional process of epoxidation is carried out using peracids formed *in-situ*, by a reaction of some carboxylic acid with concentrated hydrogen peroxide. [55] In recent works,[56,57,58] oxidation is catalyzed by liquid inorganic acids, as HCl, H_2SO_4 or H_3PO_4. This process must face several issues: the selectivity to epoxidized products is relatively low due to acid catalyzed ring-opening, the separation of acidic by-products is not easy and highly concentrated hydrogen peroxide, along with strong acids, cause corrosion problems.[59]

During the last years, aqueous H_2O_2-based epoxidation has received much attention due to economic accessibility and low environmental impact[60], hence soluble transition metal-based catalysts have been developed in the place of inorganic acids. In literature, various papers have been published regarding the use of tungsten catalyst and hydrogen peroxide as oxidant for the epoxidation of crude or purified vegetable oils. In 1959, Payne and Williams firstly proposed the epoxidation of α,β-unsaturated acids using sodium tungstate as catalyst with hydrogen peroxide.[61] As the addition of aqueous H_2O_2 to olefinic substrates forms two-phase mixtures, different phase-transfer catalysts (PTC) have been studied,[62,63,64] for instance: crown ethers, quaternary phosphonium salts (QPS), quaternary (or heterocyclic) ammonium salts (QAS) and polyethylene glycol (PEG).[64]

Since then, many two-phase epoxidation processes have been investigated using hydrogen peroxide, as primary oxidant, and metal-based polyoxometalates (POM) as catalysts. In addition, POMs are transformed to peroxopolyoxometalates (PPOMs) by excess of H_2O_2 in solution: PPOMs have been suggested to be the active intermediates in epoxidation reaction with hydrogen peroxide. Transition metal peroxopolyoxo complexes can be considered as inorganic catalytic analogues of peracids.[65] Moreover, peroxopolyoxo-anions have high stability in water and organic media. For two-phase liquid-liquid systems, peroxopolyoxo-anion complexes can be coupled with a cation with phase-transfer properties when the substrate and hydrogen peroxide are present in different phases.[66] Thus, quaternary ammonium or phosphonium salts, have been largely studied as potential phase-transfer catalyst. It was found that the organic structure of the cation not only influences its ability to transport an anion from aqueous to organic phase but also strongly affects the rate of the organic phase reaction.[67] In Figure 1.9[68] and Figure 1.10[69] some tungsten-based POMs structures (left) and PPOMs structures (right) are shown.

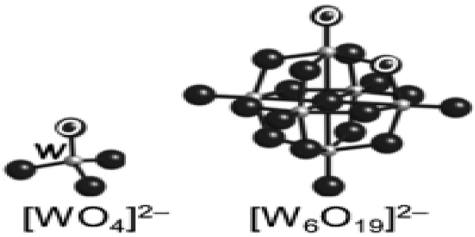


Figure 1.9: Structures of some tungstate POMs

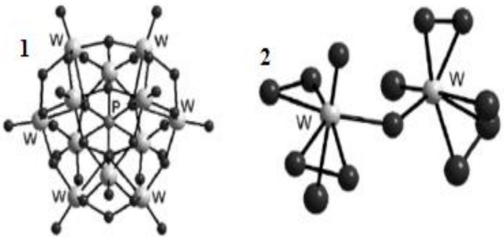
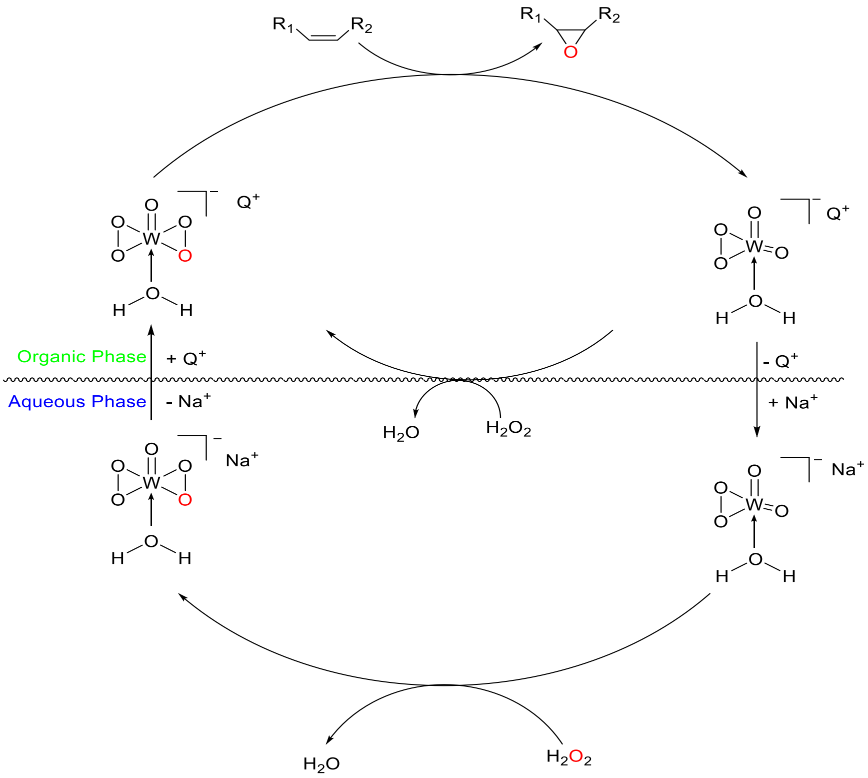


Figure 1.10: Schematic structure of PPOM anions: (1) $[PW_{12}O_{40}]^{3-}$; (2) $[W_2O_3(O_2)_4H_2O_2]^{2-}$

There are plenty of results reported on epoxidation with these complexes as catalysts, for example the famous Ishii's anion ($[PW_{12}O_{40}]^{3-}$)[70a-c] or Venturello's anion ($\{PO_4[(WO(O_2)_2]_4\}^{3-}$)[71a-c], whose catalysts are used for the selective epoxidation of alkenes, as well as vegetable oils and their derivatives. However, the main drawbacks for industrial application of Venturello-Ishii catalytic systems are the use of chlorinated hydrocarbons as solvents[72] and the use of phase-transfer catalysts with halide counterions.[73]

To resume, in a conventional epoxidation a tungsten complex is formed *in situ* in the aqueous phase. It is then stabilized by QAS or QPS cation on the interface and transferred to the organic phase; interactions of the catalyst with substrate allow the epoxidation of the substrate in the organic phase. At last, regeneration of the catalyst occurs with H_2O_2 in the aqueous phase (Scheme 1.4).[54]

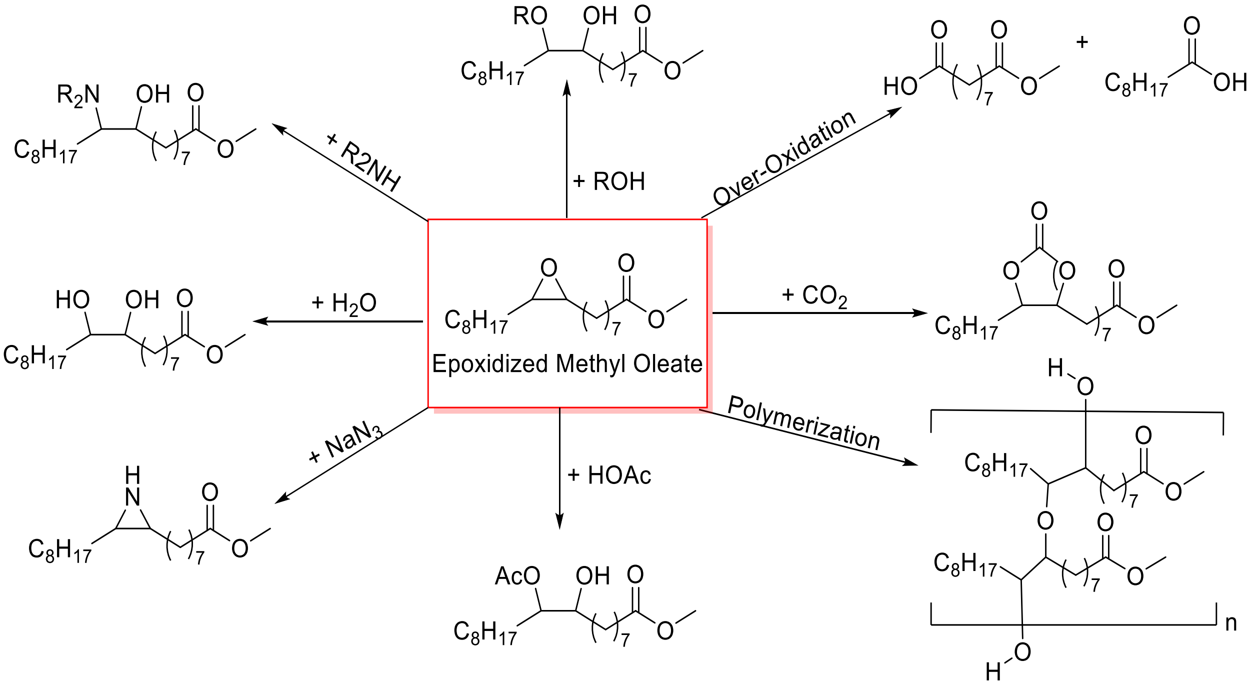


Scheme 1.4: Catalytic cycle of epoxidation. Q+ = Quaternary Ammonium Salts

These catalytic systems are extremely promising for the selective epoxidation of unsaturated fatty acids (UFAs) and fatty acids methyl esters (FAMEs), due to their high selectivity toward the epoxidation and the possibility to perform the epoxidation without solvents.[74]

Since esters are a class of general interest as plasticizers, many studies have been done to carry out the potential value of epoxy fatty acids esters as vinyl plasticizers;[75] indeed, epoxy fatty acid esters are employed, either alone or in combination, in plasticizer compositions.[76]

On the other side, epoxidized fatty acids esters are handy intermediates able to be converted to azelaic and pelargonic acid, by over-oxidation, or to cyclic carbonates, by CO_2 insertion, or polymers as well. [77] The epoxy group can also undergo various subsequent reactions that lead to ring opening: diols are formed with water, ethers with alcohols, amino alcohols with secondary amines and hydroxyacetates with acetic acid. Other reactions of the epoxy group occur while retaining the three-membered ring structure (*i.e.*, conversion to aziridines with sodium azide). The most common syntheses from epoxidized methyl oleate (EMO) are summarized in Scheme 1.5.[43]

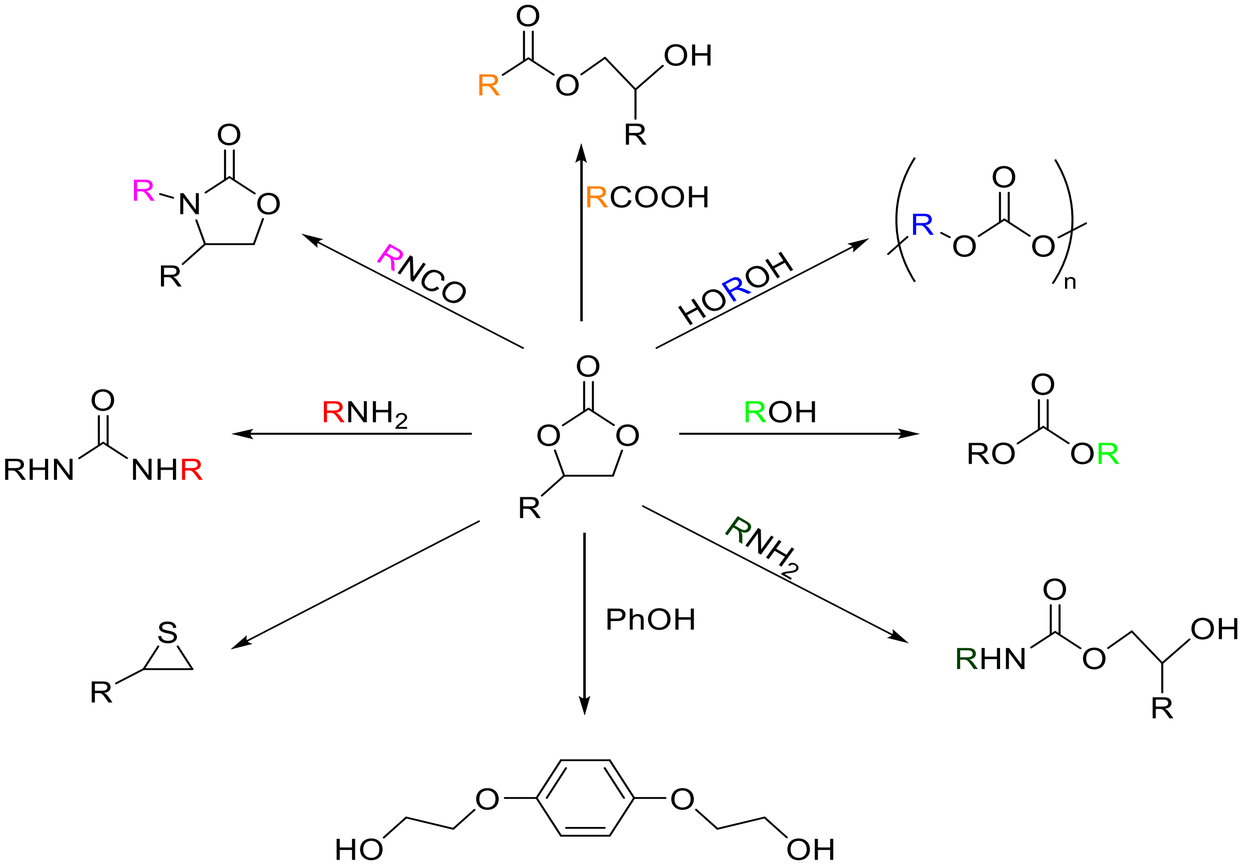


Scheme 1.5: Possible products obtainable from epoxidized oleic acid

Among the different obtainable products, the attention will be mainly focused on cyclic carbonates, in order to follow the purposes of this Thesis.

1.5 Fatty Esters Cyclic Carbonates

Internal cyclic carbonates are attainable products obtained from epoxidized fatty acids by carbon dioxide fixation. These carbonates have been used as emollients,[78] fuel additives,[79] polymer precursors,[80] lubricants and chemical solvents,[79] as well as plasticizers [81] and biomedical products.[82] In Scheme 1.6[83b] some applications are shown.

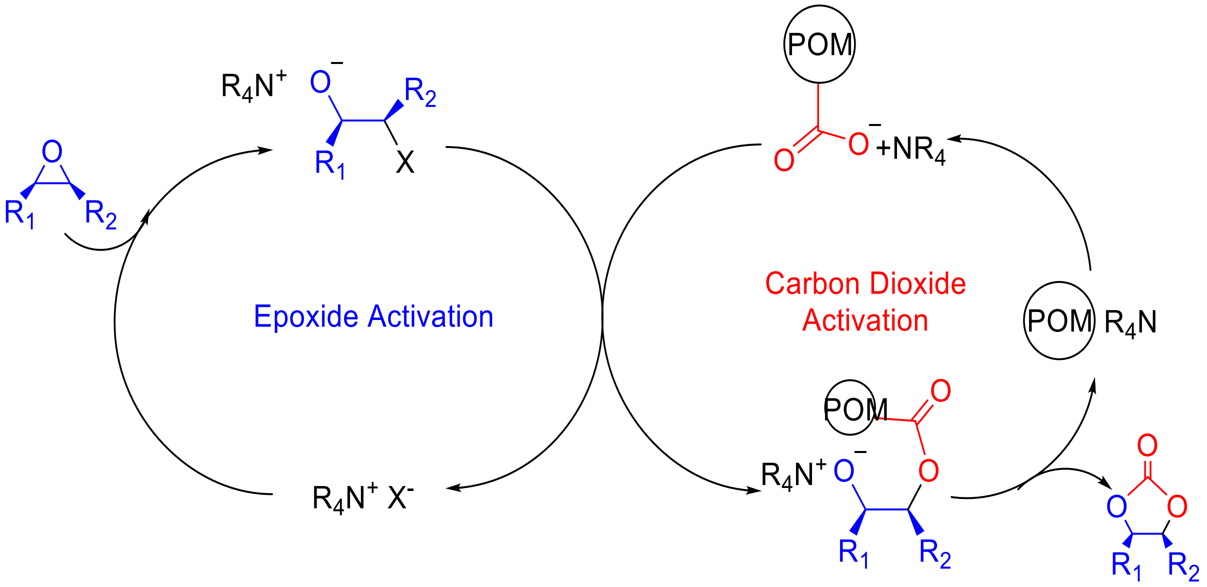


Scheme 1.6: Some avaialable applications of cyclic carbonates

As the rise of CO_2 emissions represents an issue of global reach, the possibility to employ carbon dioxide as a renewable C_1 building block is a very attractive option, demonstrating that wasted CO_2 can be an alternative, cheap and abundant carbon feedstock for chemical production in future.[84] Despite the thermodynamic stability and kinetic inertia of CO_2, a large variety of catalysts is known to facilitate the CO_2 insertion into epoxides,[85] such as: ionic liquid based systems[83a], halides[86] and quaternary salts.[87] In particular, QAS or QPS with different halides as counterions have been largely employed as effective catalysts in the carbon dioxide fixation. Carbonated oleo compounds were usually obtained from the corresponding epoxides and CO_2 using tetra-n-butylammonium bromide as catalyst.[80,85] Moreover, the catalytic role of this system is well established: the epoxy ring is opened by forming a halo-alkoxide intermediate that attacks CO_2 with subsequent formation of cyclic carbonate.[83c,86,88]

Recently, polyoxometalate-based systems have shown a selective catalytic activity toward this reaction.[89,90,91] Coordination of CO_2 to polyoxometalates has been reported to result in stable complexes. In particular, interactions between ammonium salts with certain tungstate polyoxometalate and CO_2 have been shown to lead to activation of CO_2 via a η^1-C coordination mode at the substituted transition metal.[92]

Thus, various systems have been developed exploiting organic halides and polyoxometalates as catalytic systems for the insertion of carbon dioxide into epoxides.[80,84,89] A synergistic effect is considered to play a fundamental role in the mechanism: while the negatively charged metal-based polyoxometalates interacts with CO_2, the onium salt opens the epoxy ring by forming a halo-alkoxide intermediate. The combination of these two modes leads to the cooperative effect by increasing the rate of both SN_2 type steps in the overall reaction (Scheme 1.7).[84]



Scheme 1.7: Proposed pathway for the catalytic system

At present, the catalytic systems constituted by ionic liquids of QAS with POMs have been investigated[92] and seems to be the most promising pathway for the synthesis of cyclic carbonated methyl oleate. The possibility to incorporate CO_2 into epoxidized fatty acids esters and the great interest of our research group, especially about ionic liquids, as well as CO_2 fixation,[93,94] are the groundworks on which this Thesis has been built.

1.6 One-Pot Tandem Reactions

The "one-pot" tandem methodology is known to subsequently execute multiple chemical reactions in the same reactor vessel without intermediate purification steps. This strategy has been recognized as a promising archetype in both industry and pharmaceuticals due to its potential in scale-up production, saving costs, time and wastes formation,[95] thereby fitting superbly into the principles of green chemistry. One-pot processes can be classified based on the nature of the catalysts and on the mechanisms (Figure 1.11):[96]

- Cascade (or domino) reactions are two (or more) one-pot reactions that take place with the same catalytic system and by the same mechanism (red box);[97]
- Tandem reactions are one-pot transformation in which two (or more) sequential mechanistically distinct processes occur (green box);[96]
- Auto tandem catalysis (AuTC) occurs when a single reagent catalyzes multiple, mechanistically distinct processes of a chemical reaction (yellow box);[98]
- Assisted tandem catalysis (AsTC) occurs when a single catalyst is present but some sort of input (such as changing pressure and/or temperature or adding a reagent, solvent or co-catalyst) is required after that the first catalytic cycle (pink box);[97]
- Orthogonal tandem catalysis (OTC) occurs when two different catalysts operate together to perform two sequential catalytic cycles (blue box).[97]

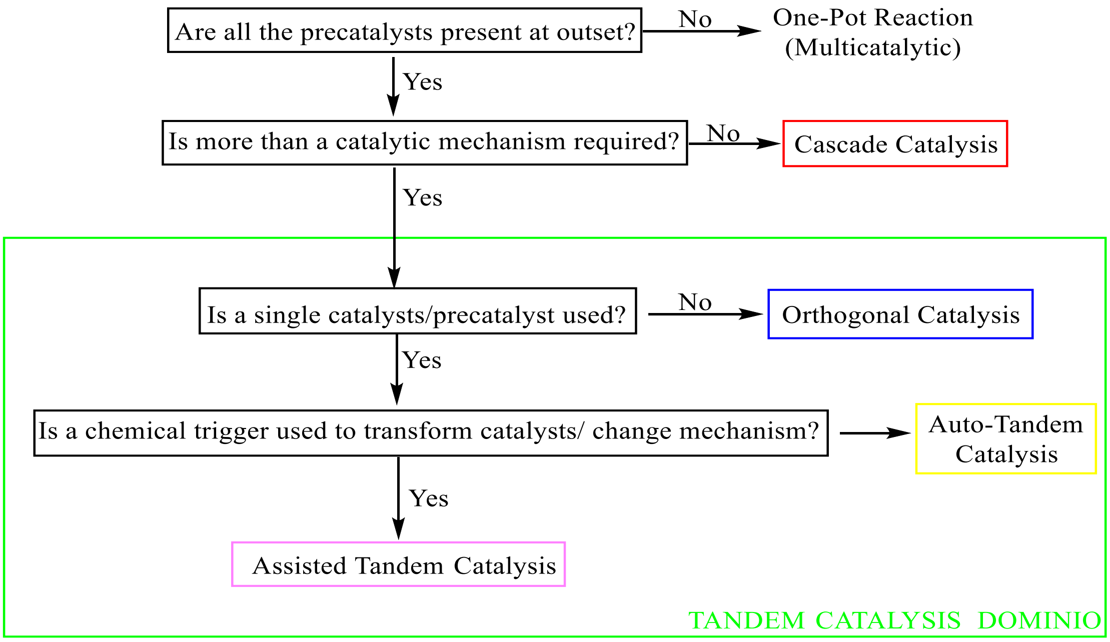
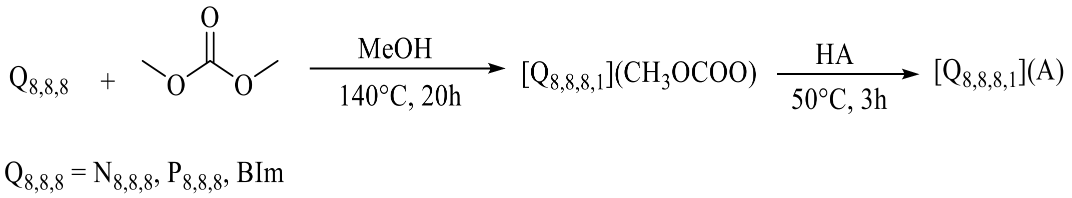


Figure 1.11: Flowchart for classification of one-pot processes involving sequential elaboration [96]

1.7 Aim and Summary of the Thesis

One-pot multistep reactions containing transition-metal catalysts are attractive in terms of both efficiency and selectivity.[99a] Several well-established one-pot tandem reactions involving metal catalysts, or enzymes as well, has been investigated and developed[99b,100]. This methodology has never been applied for the production of cyclic carbonates using oleochemicals as starting materials

The purpose of this Thesis is to develop a new one-pot tandem strategy for the formation of internal cyclic carbonates fatty esters exploiting tungstate-based ionic liquids as phase-transfer catalysts. Thus, the attention was initially focused on the synthesis and characterization of tungstate-based ionic liquids catalysts (TILCs). This methodology is established on a procedure developed in previous works by our research group:[101] methylcarbonate-onium ionic liquids were synthetized starting from trioctylamine (TOA), trioctylphosphine (TOP) and 1-butylimidazole (BIm) (*e.g.*, Scheme 1.8); then, the methyl carbonate anion has been changed with tungstate counter ions, especially WO_4^{2-} and $PW_{12}O_{40}^{3-}$. Through this route, trioctylmethylammonium-tungstate ($[N_{8,8,8,1}]_2$-WO_4, **2a**), phospotungstate ($[N_{8,8,8,1}]_3$-$PW_{12}O_{40}$ **2b**), trioctylmethylphosponium-tungstate ($[P_{8,8,8,1}]_2$-WO_4 **2c**) and 1-butyl-3-methyl-imidazolium tungstate ($[BMIM]_2$-WO_4, **2d**) were synthetized and fully characterized (FT-IR, ^{1}H-NMR, ^{13}C-NMR, ^{31}P-NMR and ^{183}W-NMR).



Scheme 1.8: Overall synthesis of tungstate-based ionic liquids

Once all the TILCs were synthetized and fully characterized, the one-pot tandem methodology was investigated. The overall synthesis provides for an initial epoxidation on the double bond contained in the FAME (by using H_2O_2 as oxidant) and a subsequent CO_2 fixation process.

The Thesis work is so divided into three main steps:

1) Esterification of oleic acid;
2) Optimization of epoxidation and carbonation steps taken individually;
3) Optimization of one-pot tandem reaction.

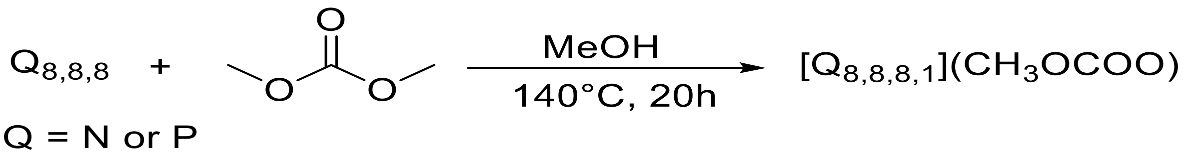
CHAPTER II

RESULTS AND DISCUSSION

2.1 Synthesis of tungstate-based ionic liquids

2.1.1 Halide-free route

For the syntesis of tungstate-based ionic liquids catalysts (TILCs), trioctylamine (TOA, $N_{8,8,8}$), trioctylphospine (TOP, $P_{8,8,8}$) and 1-butylimidazole (BIm) have been used as starting materials. A well-established procedure developed by our research group has been emploied.[101] Initally, the substrates were set to react with dimethyl carbonate (DMC) and methanol, as solvent. Conventionally, TOA (16g, 1equiv) or TOP (16.8g, 1equiv) were set to react with DMC (32.1g, 7.8equiv) and methanol (25.3g, 20equiv) at 140°C for 20h in a sealed steel autoclave (Scheme 2.1).

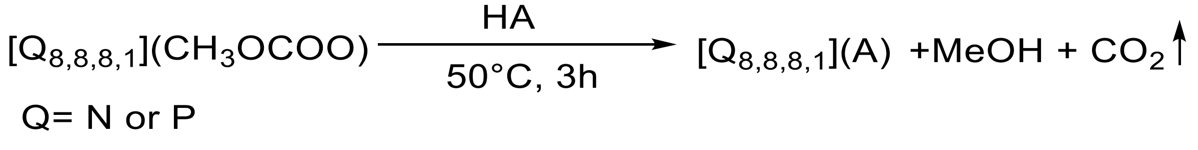


Scheme 2.1: Quaternarization of TOA and TOP with DMC

Both trioctylmethylammonium methyl carbonate ($[N_{8,8,8,1}](CH_3OCOO)$, **1a**) and trioctylmethylphosphonium methyl carbonate ($[P_{8,8,8,1}](CH_3OCOO)$, **1b**) ionic liquids were obtained with an almost quantitative yield, up to 95%.

Methanol and DMC in excess were removed under vacuum to yield the pure onium salt methyl carbonate ionic liquids. **1a** and **1b** were both analyzed by ^{1}H-NMR and ^{13}C-NMR that confirmed their structure and purity.

Then, TILCs were obtained through a simple anion methatesis reaction: methyl carbonate-onium ionic liquids were dissolved in Milli-Q water and pre-heated at 50°C. Thus, the solution was set to react with different Brønsted acids: H_2WO_4 and $H_3PW_{12}O_{40}$ were used (relative molar ratios are shown in Table 2.1). Trioctylmethylammonium tungstate ($[N_{8,8,8,1}]_2(WO_4)$, **2a**), trioctylmethylammonium phospotungstate ($[N_{8,8,8,1}]_3(PW_{12}O_{40})$, **2b**) and trioctylmethylphosponium-tungstate ($[P_{8,8,8,1}]_2(WO_4)$, **2c**) ionic liquids were obtained after 3 hours (Scheme 2.2).



Scheme 2.2: Anion metathesis of methyl carbonate-onium salts by Bronsted acids

This methodology does not require any organohalides for the quaternarization of TOA or TOP because dimethyl carbonate serves both as methylation's agent and as counterion once the quaternarization occurs.

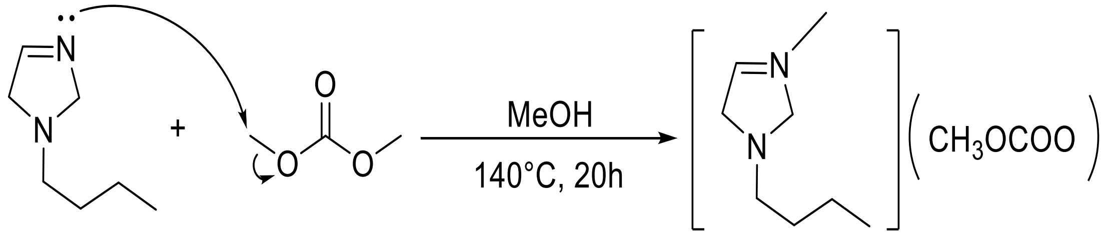
All the produced ionic liquids were isolated and fully characterized with ^{1}H-NMR, ^{13}C-NMR, ^{31}P-NMR, when requested, ^{183}W-NMR and FT-IR. The produced ionic liquids with their Brønsted acid, relative molar ratios and relating yields, are summarized in Table 2.1

	Acids	**Molar Ratio $Q_{8,8,8,1}(CH_3OCOO)$:HA**	**Tungstate Ionic Liquids**	**Yield**
$[N_{8,8,8,1}](CH_3OCOO)$,**1a**	H_2WO_4	0.8 : 2	$[N_{8,8,8,1}]_2(WO_4)$, **2a**	85%
$[N_{8,8,8,1}](CH_3OCOO)$,**1a**	$H_3PW_{12}O_{40}$	0.8 : 3	$[N_{8,8,8,1}]_3(PW_{12}O_{40})$, **2b**	97%
$[P_{8,8,8,1}](CH_3OCOO)$,**1b**	H_2WO_4	0.8 : 2	$[P_{8,8,8,1}]_2(WO_4)$, **2c**	97%

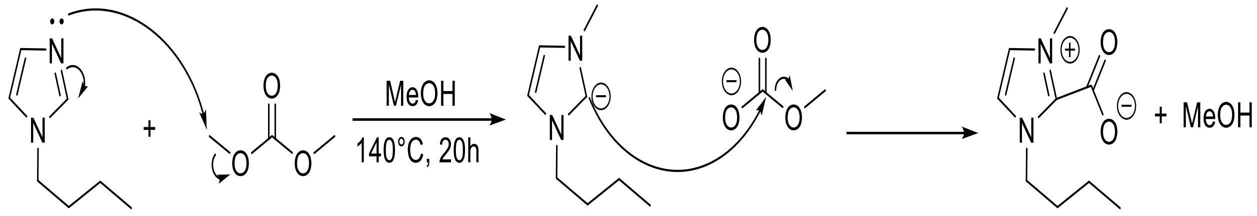
Table 2.1: Composition and yield of produced ionic liquids

2.1.2 The synthesis of butylmethylimidazolium tungstate

While the quaternarization of TOA and TOP led only to predicted ionic liquids, the crude mixture of 1-butylimidazole with DMC, in the same conditions already stated (see Scheme 2.1), showed the presence of two main products: 1-butyl-3-methylimidazolium methyl carbonate, the predicted onium salt methyl carbonate ionic liquid, and 1-butyl-3-methylimidazolium-2-carboxylate, a zwitterion.[103] DMC reacted with 1-butylimidazole in a quaternarization reaction to yield the desired ionic liquid (Scheme 2.3); on the other side, once the methylation has occurred, the highly nucleophilic BMIM's C_2 was able to attack the carboxylic carbon of DMC, hence forming the zwitterion and methanol as by-product (Scheme 2.4). The mixture of ionic liquid and zwitterion (**1c**) was concentrated under vacuum to achieve a 97% isolated mixture. The formation of these two species was proved by ^{1}H-NMR and ^{13}C-NMR analysis of the isolated mixture.

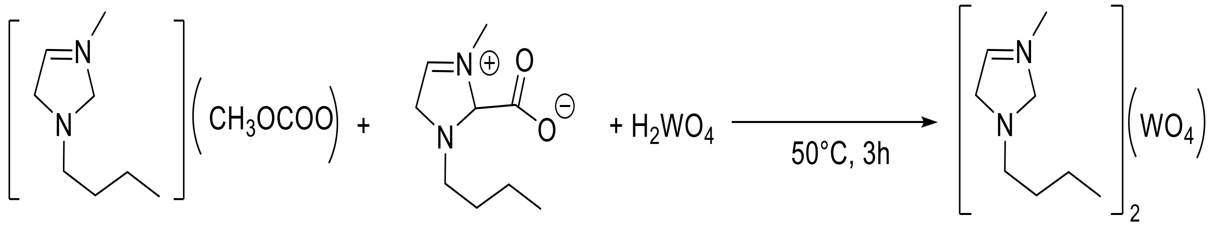


Scheme 2.3: Quaternarization of 1-butylimidazole with DMC



Scheme 2.4: Proposed mechanism for the zwitterion's formation

Despite the presence of two products, metathesis (Scheme 2.5) occurred on both the substrates leading just to the desired 1-butyl-3-methyl-imidazolium-tungstate ($BMIM_2$-WO_4, **2d**) ionic liquid, with almost quantitative yield (95%).



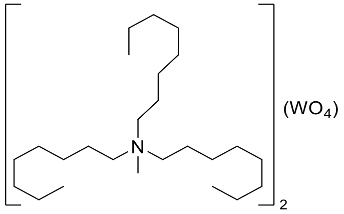
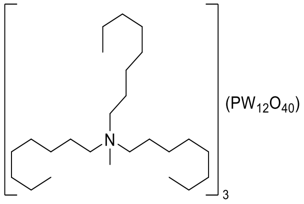
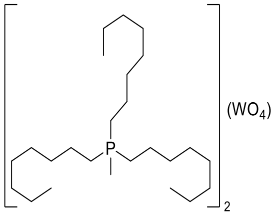
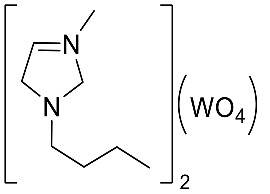
Scheme 2.5: Metathesis of 1-butyl-3-methylimidazolium methyl carbonate and 1-butyl-3-methylimidazolium-2-carboxylate

1-Butyl-3-methyl-imidazolium tungstate (**2d**), along with the former ionic liquids, was fully characterized by ^{1}H-NMR, ^{13}C-NMR, ^{183}W-NMR and FT-IR.

2.1.3 Characterization of tungstate-based ionic liquids

The structures of the tungstate ionic liquids were confirmed by FT-IR, ^{1}H-NMR, ^{13}C-NMR, ^{31}P-NMR (when TILCs characterized from the presence of P were analyzed) and ^{183}W-NMR. Spectra are in the Appendix section. The produced TILCs are summarized in Figure 2.1.

Figure 2.1: Tungstate-based ionic liquids (TILCs) produced via a halide-free pathway

Trioctylmethylammonium tungstate (**2a**)	Trioctylmethylammonium phosphotungstate (**2b**)	Trioctylphosphonium tungstate (**2c**)	Butylmethylimidazolium tungsatate (**2d**)
$[N_{8,8,8,1}]_2(WO_4)$	$[N_{8,8,8,1}]_3(PW_{12}O_{40})$	$[P_{8,8,8,1}]_2(WO_4)$	$[BMIM]_2(WO_4)$
			

All the TILCs **2a-c** showed the bands associated to the cations, in particular the $-CH_2$ symmetric and asymmetric and the $-CH_3$ stretching between 2850 and 3000 cm^{-1}. TILCs **2a-b** (all the ammonium-tungstate ionic liquids) showed the band associated to the $N-CH_3$ stretching between 1200 and 1100 cm^{-1}. Moreover, $[P_{8,8,8,1}]_2(WO_4)$ (**2c**) showed three characteristic peaks associated to the $P-CH_3$ asymmetrical deformation at 1466 cm^{-1}, the $P-CH_3$ symmetric deformation at 1378 cm^{-1} and the $P-CH_3$ rocking at 977 cm^{-1}.

The presence of tungstate species in TILCs was confirmed by the adsorption associated to W-O bond.[104,105] For tetrahedral WO_4^{2-} anion, two active modes are observed at about 927 and 825 cm^{-1}, respectively symmetric and asymmetric stretching.[106]

The ^{1}H- and ^{13}C-NMR spectra of all the TILCs **2a-d** also confirmed the disappearance of the peaks associated to the methanol and the methyl carbonate anion.

^{31}P-NMR of $[N_{8,8,8,1}]_3(PW_{12}O_{40})$ and $[P_{8,8,8,1}]_2(WO_4)$ showed the presence of a single peak, indicating the presence of a single species.

Differences between the ^{1}H-NMR spectra of $[BMIM]_2(WO_4)$ and of its precursors highlighted the formation of the sole tungstate-based ionic liquid. The lower chemical shifts of the three imidazolium protons H_2, H_4, H_5 of $[BMIM]_2(WO_4)$ indicated different hydrogen-bonding and confirmed stronger H-bonding between cation and anion for $[BMIM]_2(WO_4)$. Furthermore, the H_2 chemical shift integrated less than unity, pointing that this proton was largely engaged in H-bonding with WO_4^{2-}, in agreement with the higher basicity of the WO_4^{2-} anion compared to methyl carbonate one.[94]

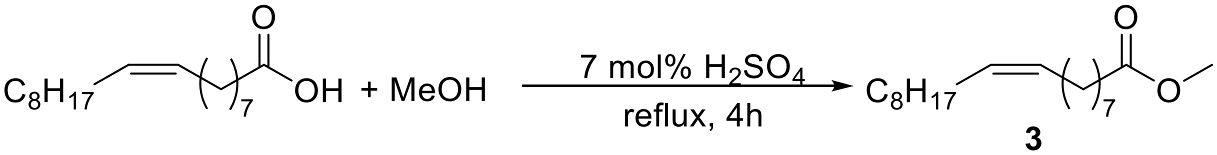
Finally, the ^{183}W-NMR spectra of TILCs **2a**, **2b** and **2d** proved the presence of monomeric tungstate $[WO_4]^{2-}$ as a single resonance was observed in the range +15 – -25 ppm. ^{183}W-NMR spectrum of $[N_{8,8,8,1}]_3(PW_{12}O_{40})$ showed a single resonance at -85ppm: this outcome agrees with what has been demonstrated by Alan M. Bond *et al* for α-$[PW_{12}O_{40}]^{3-}$.[107]

Interactions between ammonium and phosphonium cations (as well as imidazolium cation) and tungstate anion lead to different chemical shifts compared to the sodium tungstate reference.[108]

2.2 Esterification of Oleic Acid

In order to mask the carbonyl group to prevent side reactions and to improve the handling of the molecule, oleic acid was converted into methyl oleate through a simple acid-catalyzed esterification [102]

In a conventional procedure, oleic acid (1.05g, 3.71mmol) and a large excess of methanol (3.96g, 123.6mmol) were pre-heated at 50°C; then, 7% molar of concentrated sulfuric acid (95% v/v) were added and the solution was set to react with magnetic stirring for 4 hours, under reflux (Scheme 2.6).



3

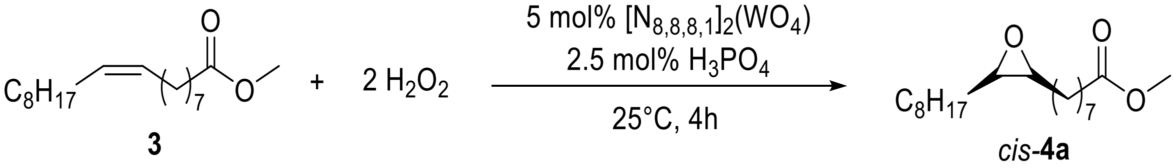
Scheme 2.6: Esterification of oleic acid into methyl oleate (**3**)

The resulting mixture was extracted with ethyl acetate, dried over sodium sulfate and filtered. The unreacted methanol was then evaporated under vacuum. Methyl oleate (**3**) was obtained as highly pure (98% by GC) liquid in 97% isolated yield and was fully characterized by ^{1}H-NMR, ^{13}C-NMR and GC-MS. **3** was selected as model substrate to explore the direct oxidative carboxylation of oleochemicals with hydrogen peroxide as O source and CO_2 as C_1 source.

2.3 Epoxidation of Methyl Oleate with Hydrogen Peroxide

The epoxidation of **3** was conducted in a two-phase system by using H_2O_2 as oxidant. $[N_{8,8,8,1}]_2(WO_4)$ (**2a**) was chosen as the model TILC to investigate the reaction parameters. According to the literature,[71a-c,109a-b] phosphoric acid (H_3PO_4) was initially chosen as co-catalyst due to its ability to boost the activity of tungstate-based catalysts by forming *in-situ* phosphonate-di(peroxo)tungstate species.

In the initial procedure a biphasic solution of **3 (**510mg**,** 1.7 mmol) and H_2O_2 30% (w/w) (358mg, 3.2mmol) with 5% molar of **2a** (0.094g, 0.09mmol) and 2.5% molar of H_3PO_4 (4.2mg, 0.043mmol) was set to react (see Scheme 2.7) at room temperature for 4 hours. No solvents were used. In these conditions the reaction proceeded with a conversion of 41% and the selective formation of *cis*-epoxide was obtained.



Scheme 2.7: Initial procedure for the epoxidation of **3**

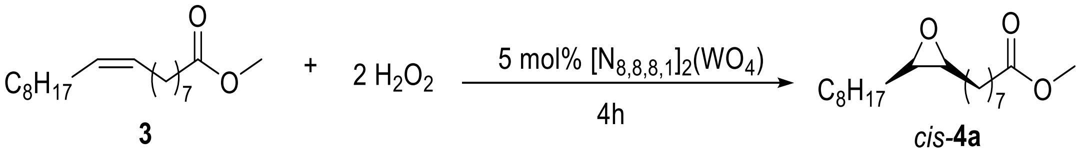
2.3.1. The effects of temperature

Since low conversion at room temperature, temperature was increased to improve the conversion of **3**. Usually, at interval of one hour, samples of reaction were withdrawn and analyzed by ^{1}H-NMR in order to follow the reaction's course: results after 4 hours of reaction are reported in Table 2.2.

Initially, the epoxidation process (eq 1) was adapted at 50°C, with and without phosphoric acid (entry 3 and 4, Table 2.2): in these conditions, 90% of conversion was reached when phosphoric acid was employed (entry 3), lowering to 84% when only **2a** was used (entry 4). This behaviour is probably due to the presence of phosphoric acid that increase the activity of tungstate-based catalysts through the *in-situ* formation of phosphonate-di(peroxo)tungstate complex.[109,110] However, entry 5 demonstrated that a quantitative conversion was reached after 4 hours at 75°C with 5% molar of **2a** (entry 5) without the addition of H_3PO_4 as co-catalyst. From this point on, phosphoric acid was not used any longer.

In addition, increase the temperature did not involve the formation of undesired byproducts, demonstrating the high selectivity of the catalyst toward the epoxidation.

Table 2.2: Epoxidation's yield at different temperatures with or without phosphoric acid



(eq 1)

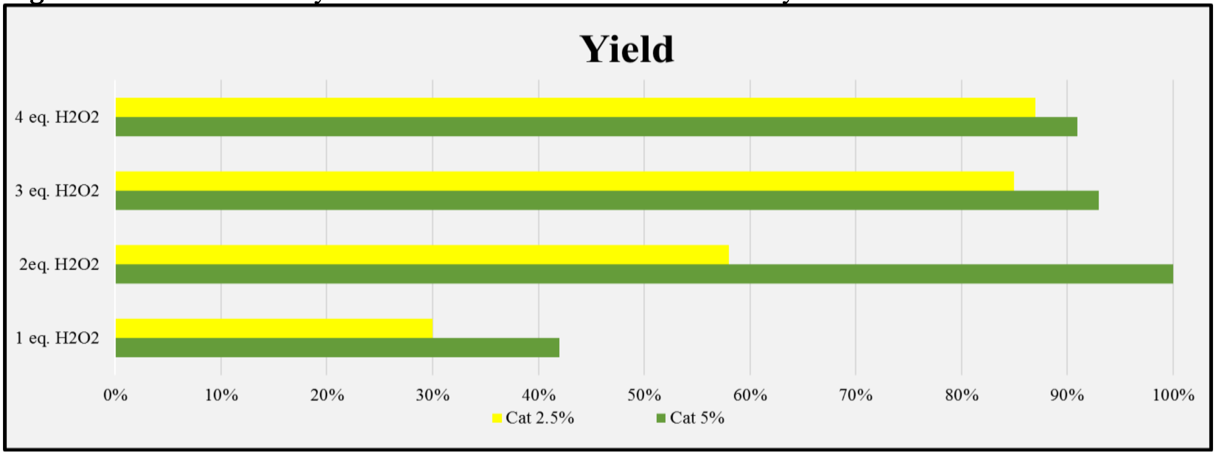
Entry	**Temperature (°C)**	**H_3PO_4 (mol%)**	**Yield (%)**
1[a]	25		5
2	25	2.5	41
3[a]	50		84
4	50	2.5	9
5[a]	75		100

Reaction conditions: **3** (1.7mmol) with H_2O_2 (3.2mmol), 5% mol catalyst (**2a**) and 2.5% mol of co-catalyst (H_3PO_4) T = 25-75°C, t = 4h, solvent-free. Conversion and yield calculated by ^{1}H-NMR. Selectivity was complete (100%) for every reaction. (a)The reaction was conducted for 4 hours in absence of co-catalyst (H_3PO_4).

2.3.2 Effect of the amount of oxidant and catalyst

Once the optimum temperature was found, different amounts of **2a** and hydrogen peroxide were tested. While the catalyst's molar ratio was fixed (5% or 2.5%), the molar ratio of **3** and H_2O_2 was set to change from 1:1 to 1:4. The results are plotted in Figure 2.2 as follow: for every equivalents of hydrogen peroxide, catalyst was loaded with 2.5% molar (yellow profile) or 5% molar (green profile).

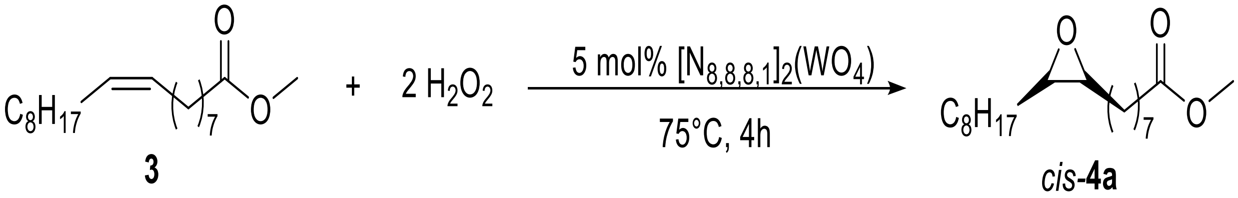
Figure 2.2: Effect of catalyst and oxidant's load on the reaction's yield



Reaction conditions: **3** (1.7mmol) with H_2O_2 (1-4 equiv), 2.5-5% mol catalyst (**2a**), T = 75°C, t = 4h, solvent-free. Conversion and yield calculated by ^{1}H-NMR. Selectivity was complete (100%) for every reaction

As highlighted in Figure 2.2, a linear growth of the reaction yield was observed as increase the equivalents of H_2O_2 with 2.5% molar of 2a (yellow profile), reaching the highest yet not quantitative yield (87%) with 4 equivalents of hydrogen peroxide. On the other side, a quantitative conversion was reached with 5% molar (green profile) of **2a** and an excess of H_2O_2 (*eq*=2). The reaction yield was intriguingly observed to decrease when further hydrogen peroxide was added (*eq* > 2). Two possible answers to this non-linear trend may be: 1) large excess of oxidant may limit the QAS' mass transfer, leading to a reduction of interactions between **2a** and **3** in the organic phase; 2) as different tungstate anions are formed depending on the H_2O_2/W ratio, increasing the ratio may lead to the formation of tungstate species with lower catalytic activity. However, large amounts of hydrogen peroxide do not constitute a favorable condition in order to develop a one-pot tandem reaction: the less H_2O_2 is used, the better will be for the feasibility of the future two-phase system.

The optimized procedure (Scheme 2.8) provided for the reaction of **3** (1.021g, 3.44mmol) was set to react with H_2O_2 (0.75mL, 7.37mmol) and **2a** (0.187g, 0.19mmol), in a 1:2:0.05 molar ratio, at 75°C for 4 hours.



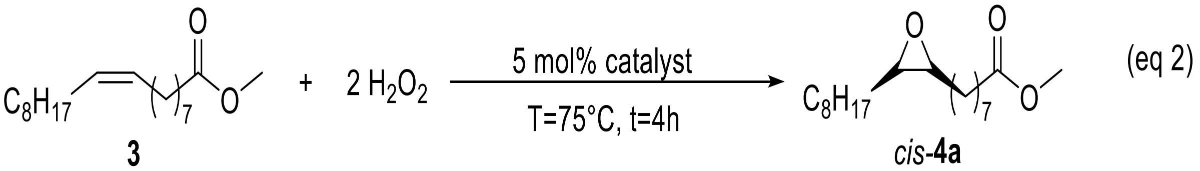
Scheme 2.8: Final procedure for the stereoselective epoxidation of **3**

The reaction mixture was initially filtered through silica in order to remove the catalyst **2a**. The mixture was then extracted with dichloromethane, dried over sodium sulfate and filtered. The organic phase was collected and concentrated under vacuum to achieve the pure product. The conversion of **3** was quantitative (~100%) with complete retention of stereochemistry, only -*cis* epoxide (*cis*-**4a**) was obtained. The product was obtained with high purity (97% by GC). These work-up steps were done to achieve a pure epoxidized methyl oleate (EMO) to exploit as starting material for the CO_2 fixation process.

2.3.3 The feasability of the other tungstate-based catalysts

As already stated, $[N_{8,8,8,1}]_2[WO_4]$ was chosen as the model catalyst to study the epoxidation process into methyl oleate (**3**) to yield epoxidized methyl oleate (*cis*-**4a**) (eq 2). The results obtained by the other TILCs are reported in Table 2.3. None of them showed an adequate catalytic activity toward the epoxidation.

Table 2.3: Epoxidation's yield at different temperatures with or without phosphoric acid



Entry	**Tungsate-based Catalysts**	**Conversion 3 (%)**
1	$[BMIM]_2(WO_4)$, **2d**	0
2	$[N_{8,8,8,1}]_3(PW_{12}O_{40})$ **2b**	11
3	$[P_{8,8,8,1}]_2(WO_4)$ **2c**	69

Reaction conditions: **3** (1.7mmol) with H2O2 (3.2mmol), 5% mol catalyst, T = 75°C, t = 4h, solvent-free. Conversion and yield calculated by 1H-NMR. Selectivity was complete (100%) for every reaction.

The first one to be tested was $[BMIM]_2(WO_4)$ (entry 1) that showed no catalytic activity at all for the epoxidation reaction of C_9-C_{10} double bond of **3**. Due to its low solubility in organic solvents, this catalyst is more likely to stay in the acqueos phase and this may be the reason why $[BMIM]_2(WO_4)$ did not show an adequate phase-transfer activity.

When $[N_{8,8,8,1}]_3(PW_{12}O_{40})$ was tried (entry 2), several issues occurred which influnced the conversion: due to its huge molar mass (3983.3 u.m.a.), great amount of **2b** was requested, making necessary the presence of a dichloromethane as solvent. After 4 hours, the conversion was just of 11%.

The highest conversion percentage (69%) was reached when $[P_{8,8,8,1}]_2(WO_4)$ was used (entry 3). $[P_{8,8,8,1}]_2(WO_4)$ presents a more movable anion than **2a** that can interacts either with the cation head group or with the cation's alkyl chain.[111] Consequently, $[P_{8,8,8,1}]_2(WO_4)$ has an higher basicity and an higher free volume than **2a**. Thus, $[N_{8,8,8,1}]_2(WO_4)$ has a larger charge density on the cationic centre, hence basicity is reduced and electron density is less available for donation, so higher degree of charge-tansfer occurs.[101]

2.3.4 Hydrogen Peroxide Efficency

Hydrogen peroxide is one of the cleanest, eco-friendly and versatile oxidant since water is the only by-product. Decomposition of hydrogen peroxide usually occurs for many oxidation reactions as a side reaction hence significantly decreasing the process efficiency.[112]

Hydrogen peroxide is thermodynamically unstable and decomposes in water and oxygen. The decompostion's rate increases with various parameters as temperature, concentration and pH and type of catalyst.

As already stated in the introduction (*e.g.* paragraph 1.4), hydrogen peroxide readily combines with transition metals such W(VI) to form various peroxopolyoxo species. The monomeric, dimeric or tetrameric tungstate species generated by the reaction of tungstate with hydrogen peroxide catalyze the epoxidation reaction.[113]

In order to calculate the hydrogen peroxide efficiency of the system developed in this Thesis, the amount of unreacted H_2O_2 has been determinated by redox titatrion, based on a protocol powered by Mattler Toledo.[114] In this procedure, a solution of $KMnO_4$ ~0.1M (titrant) has been initially standardized with di-sodium oxalate dissolved in a 5% (v/v) solution of H_2SO_4, accoring to the stechiometry of the reaction in Scheme 2.9.

$$5\ Na_2C_2O_4 + 16H^+ + 2\ KMnO_4 \rightleftarrows 10\ CO_2 + 10Na^+ + 2\ Mn^+ + 8\ H_2O + 2K^+$$

Scheme 2.9: Reaction for titer determination

Since a manual titration has been performed, the equivalence point was reached as soon as the color of the sample solution turns permanently light pink.[114] This titration was repeated three times with different amount of di-sodium oxalate. Results are reported in Table 2.4.

Amount of $Na_2C_2O_4$	**Titration Consumption (VEQ)**	**Molar Concentration**
0.0250 g	0.7 mL	0.107
0.0347 g	1.1 mL	0.095
0.0502 g	1,65 mL	0.084

Table 2.4: Outcomes of the titer determination at different di-sodium oxalate's amount

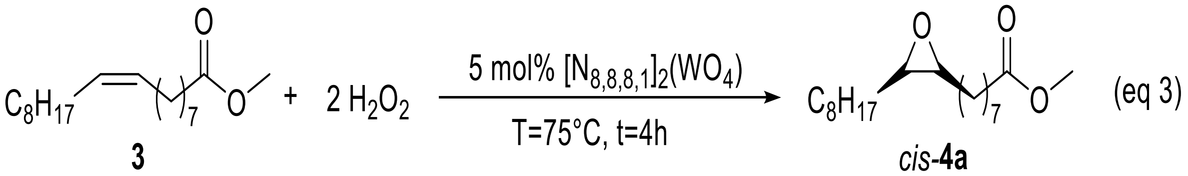
The molar concentration mean of the titran was considered to be 0.095M, with a standard deviation (*s*) of 0.0094 and a relative standard deviation (RSD) of 9.89%.

Once determinated the titer, the standardized solution of $KMnO_4$ was employed to establish the amount of unreacted H_2O_2 of a conventional epoxidation reaction (*e.g.* Scheme 2.8), according to the stechiometry of the reaction in Scheme 2.10.

$$5\ H_2O_2 + 6H^+ + 2\ KMnO_4 \rightleftharpoons 5\ O_2 + 2\ Mn^{2+} + 8H_2O + 2K^+$$

Scheme 2.10: Hydrogen Peroxide content determination reaction

This titration as well was repeated three times; every time, the solution turned permanently light pink after the first drop of titrant. These outcomes highlighted the complete absence of hydrogen peroxide in solution. According to the stechiometry of the epoxidation process into **3** to yield *cis*-**4a** (eq 3), methyl oleate was set to react with H_2O_2 in a 1:2 molar ratio.



The complete absence of hydrogen peroxide in the reaction solution after 4 hours indicated that just an equivalent of hydrogen peroxide exerted its activity as oxidant for the epoxidation; the other equivalent of hydrogen peroxide just thermally decomposed. Hence, the hydrogen efficency of this system is 50%.

2.3.5 Proposed mechanism for the epoxidation

As foretold in the introduction, the initial stage of the epoxidation is the formation of a tungstate peroxopolyoxo complex with H_2O_2 in the aqueous phase. According to the literature, different peroxotungstate species may occur in an aqueous solution depending on pH: at pH>7, $[W(O_2)_4]^{2-}$, $[WO_2(O_2)_2]^{2-}$ and $[WO_3(O_2)]^{2-}$ are formed and their distributions depend on the H_2O_2/W ratio, usally oxo-peroxido $[W(O_2)_4]^{2-}$ **(A)** predominates when H_2O_2/W ratio is 5:1; when 1.3<pH<7, the dimer $[W_2O_3(O_2)_4(H_2O)_2]^{2-}$ **(B)** is the major species.[115] In accordance with the system developed in this Thesis, a monomeric oxobisperoxido tungstate specie **(C)** (Figure 2.3), a Minoum-type specie, is the likeliest to exist. [116]

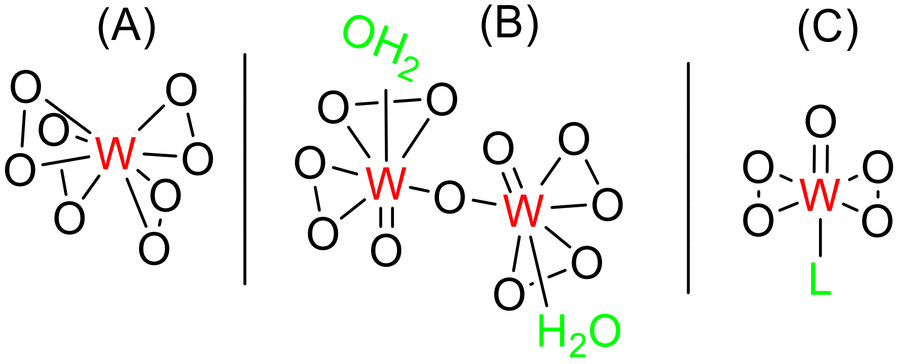
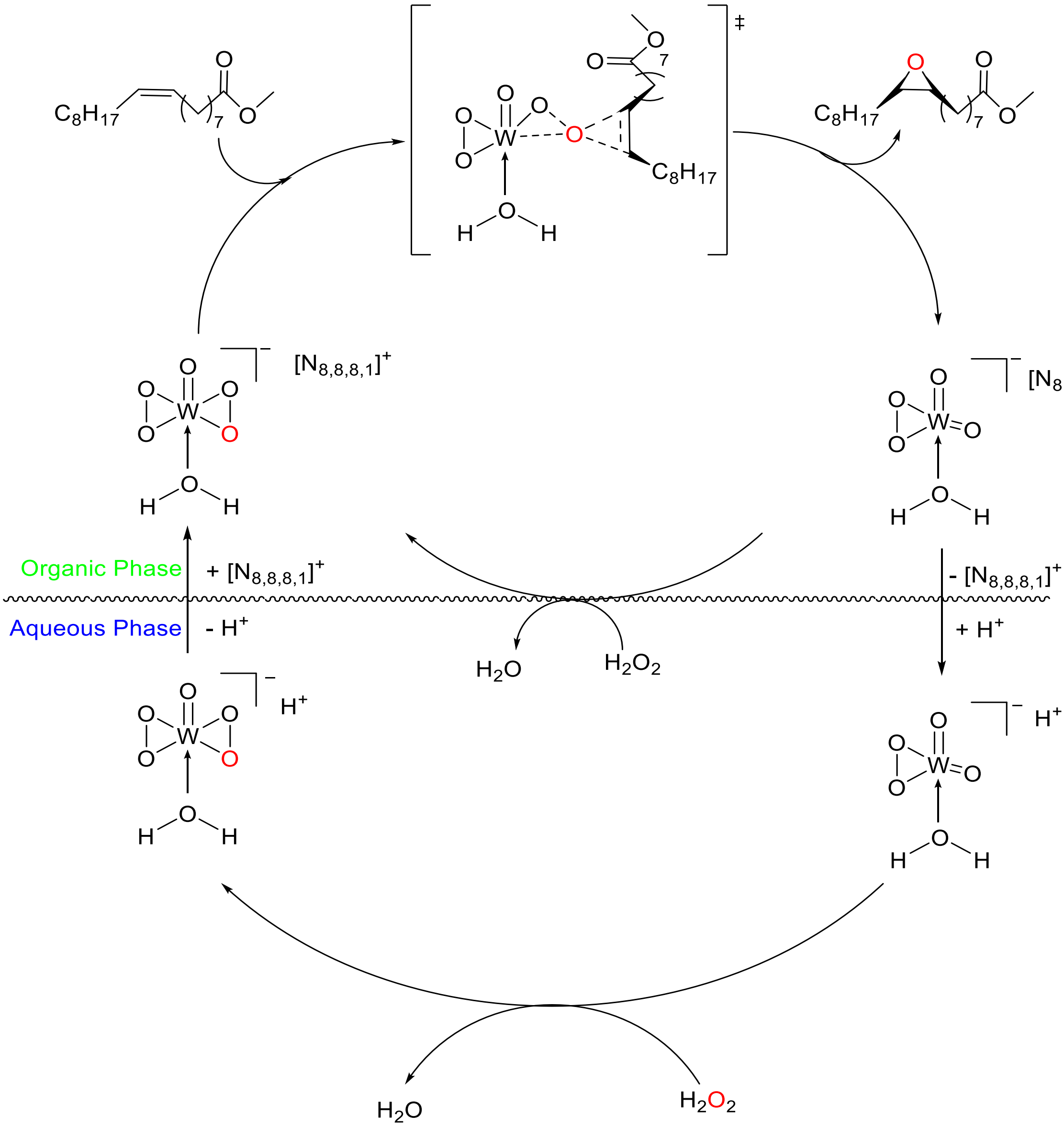


Figure 2.3: Possible obtainable W(VI) oxido-peroxido (**A** or **B**) and oxi-bisoperoxido (**C**) complexes

As the complex is formed in aqueous solution, it can be transferred in the organic phase by QAS cation, specifically trioctylmethylammonium cation. Once in the organic phase, the tungstate oxo-bisperoxido binds the double bond of methyl oleate and allows the O transfer and formation of the epoxide.

Mimoun *et al.* proposed that the first step of the epoxidation mechanism was the coordination of the olefinic moiety to the metal center and, then, a five-membered metallacycle was formed, followed by epoxide's formation.[117a] Further studies demonstrated that a more concerted mechanism occurs where an alkyl hydroperoxide is responsible for the catalytic epoxidation.[117b] As the reaction of this Thesis is completely stereoselective toward the -*cis* epoxide, a concerted mechanism is the most problably to occur (Scheme 2.11).[54]

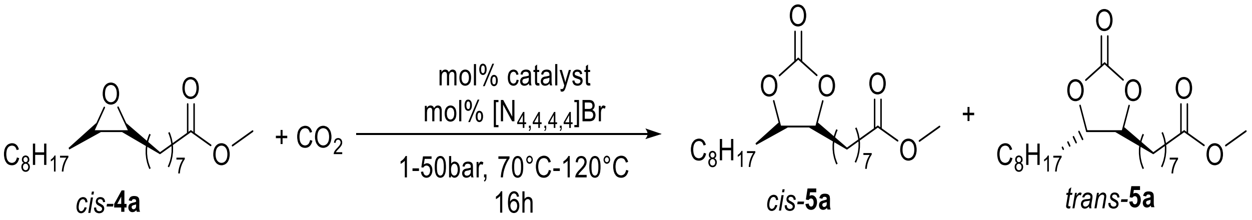


Scheme 2.11: Proposed mechanism for the epoxidation of methyl oleate (**3**)

2.4 Carbonation of Epoxidized Methyl Oleate

The CO_2 fixation process of *cis*-**4a** to reach the corrisponding cyclic carbonates (*cis*-**5a** and *trans*-**5a**) has been developed in accordance with a procedure previously reported by our research group.[94] Tetrabutylammonium bromide ($[N_{4,4,4,4}]Br$) was initally chosen as co-catalysts due to its effective epoxy ring-opening acitivity by forming an halo-alkoxide intermediate and its synergistic effect with polyoxometalates (*e.g.*, Scheme 1.7).[84]

In a conventional procedure, pure epoxidized methyl oleate, along with the catalyst and the co-catalyst, were placed in a round-bottom glass flask which was fitted inside a stainless steel autoclave. The autoclave was sealed, degassed via three vacuum-N_2 cycles and pressurized with CO_2 (1, 10 or 50 bar), then heated at the desired temperature (70°C, 100°C or 120°C) and magnetically stirred for the desired time (16h) (Scheme 2.12).



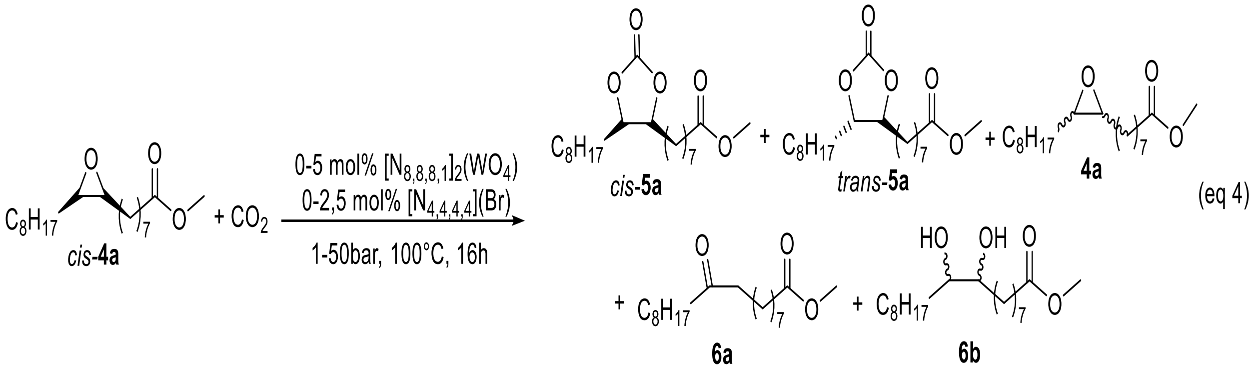
Scheme 2.12: Schematic carbonation of *cis*-**4a** into internal cyclic carbonates.

According to the literature,[94] *cis*-**4a** (0.500g, 1.6mmol) was initially set to react with 5% mol of **2a** and 2.5% mol of tetrabutylammonium bromide ($[N_{4,4,4,4}]Br$, TBABr) for 16 hours at 100°C. Several parameters, as pressure, temperature and co-catalyst's load, were investigated in order to increase both the chemoselectivity and the diastereoselectivity toward the -*cis* carbonate.

2.4.1 The effect of pressure

As already mentioned, $[N_{4,4,4,4}]_2[WO_4]$ and $[N_{4,4,4,4}]Br$ were respectively chosen as the model catalyst and co-catalyst to study the CO_2 fixation reaction into epoxidizied methyl oleate (*cis*-**4a**) to yield carbonated methyl oleate (**5a**) (eq 4). Table 2.5 reports the results obtained by screening a set of different CO_2 pressures (1, 10 and 50 bar) and by exploiting the catalyst and co-catalysts togheter and separated.

Table 2.5: Fixation of CO$_2$ into *cis*-**4a** to yield **5a**



Entry	**CO$_2$ pressure (bar)**	**$[N_{8,8,8,1}]_2(WO_4)$ (mol %)**	**$[N_{4,4,4,4}](Br)$ (mol %)**	**Conversion *cis*-4a (%)**	**Selectivity 5a (%)**	***Cis* : *Trans* Ratio *cis*-5a : *trans*-5a**
1	1	5	2.5	7	20	99 : 1
2[a]	10			0	0	
3[b]	10	5		4	11	99 : 1
4[c]	10		2.5	82	91	56 : 44
5	10	5	2.5	59	77	90 : 10
6[b]	50	5		28	54	99 : 1
7[c]	50		2.5	≈100	≈100	80 : 20
8	50	5	2.5	85	92	99 : 1

Reaction condition: 1.28mmol *cis*-**4a**, 5 mol% catalyst (**2a**), 2.5 mol% co-catalyst ($[N_{4,4,4,4}]Br$), 16h, solvent-free. Conversion, yield and selectivity calculated by ^{1}H-NMR. (a) The reaction was conducted in absence of both catalyst and co-catalyst. (b) The reaction was conducted in absence of co-catalyst. (c) The reaction was conducted in absence of catalyst **2a**.

A preliminary study was done under atmospheric pressure (entry 1) demonstrating that such a low pressure of CO$_2$ was not enough to achieve good results. In these conditions, conversion was extremly low (7%) with large formation of over-oxidation byproducts, in particular ketone (**6a**) and diol (**6b**) were mainly observed.

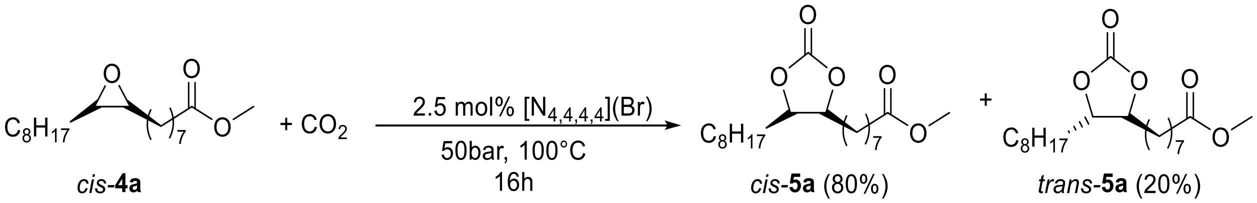
Two higher pressures were tested (10 or 50bar) in the conditions just stated (eq 4).

A initial study was done in the absence of both catalysts and co-catalyst (entry 2). In these conditions, the converion of *cis*-**4a** was 0%, hence auxiliaries are needed in the CO$_2$ fixation process. When **2a** was used alone under 10bar of pressure (entry 3), carbonates were formed with a very poor conversion (4%), despite the reaction was almost completly diastereoselective toward the -*cis* carbonate; in addition, formation of **6b** was observed. The highest conversion was obtained when 2.5% mol of $[N_{4,4,4,4}]$Br were used alone (entry 4) but this negatively affected the selectivity toward carbonates and formation of -*trans* epoxidized methyl oleate (*trans*-**4a**) was observed.[118] Finally, when the catalyst was coupled with $[N_{4,4,4,4}]$Br (entry 5), a 59% conversion with a 77% selectivity toward carbonates and 90:10 *cis:trans* ratio was achieved. Thus, while the catalyst **2a** permits to gain some diastereochemical control on the carbonation at expense of the conversion, the co-catalyst steered the reaction toward the formation of the desired products in terms of conversion and selectivity.

When 50bar of CO_2 pressure were applied, higher conversion and chemoselectivity were achieved. At a first look, applying a major pressure permits to have some chemoselective and diastereoselective control. If we compare the reactions conducted in presence of 50bar of CO_2 (entry 6-8) with the equivalent reactions operating at 10bar of CO_2 (entry 2-4), it is possible to notice that a better conversion, selectivity and diastereoselectivity was always reached. An higher pressure seems to force the reaction toward the desidered products, avoiding possible rearrangments and formation of by-products.[117]

Notwithstanding the low conversion and selectivity when **2a** was used alone (entry 3 and 6), it's important to remark that carbonates were obtained in absence of bromide. Thus, $[N_{8,8,8,1}]_2(WO_4)$ is able to open the epoxy-ring although with poor performances.

As reported in Table 2.5, a quantitative conversion was reached when 50bar of CO_2 pressure was applied with the sole presence of 2.5 mol% of co-catalyst (entry 7), as in Scheme 2.13. Subsequently, a CO_2 pressure of 50bar was choosen as the optimal pressure to adoperate.



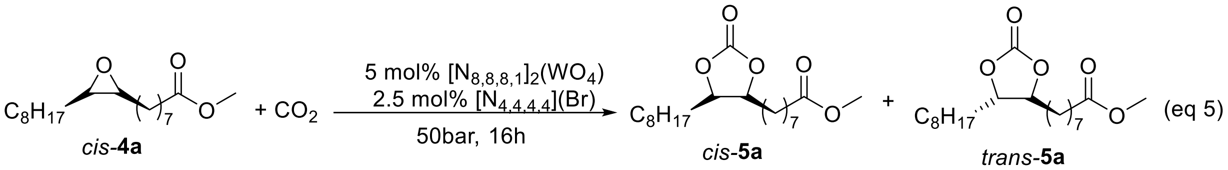
Scheme 2.13: Quantitative conversion of *cis*-**4a** in both -*cis* and -*trans* carbonates

Despite the best outcomes in terms of conversion and chemoselectivity were reached when tetrabutylammonium bromide were adopted alone, the presence of $[N_{8,8,8,1}]_2WO_4$ (**2a**) as catalyst is compulsory for the direct oxidative carboxylation of methyl oleate. Indeed, in order to develop a one-pot tandem methodology, **2a** must be employed for the epoxidation of **3** and has a crucial role for the diastereoselective control of the CO_2 fixation step.

2.4.2 The effect of temperature

In addition to the conventional temperature(100°C), higher (120°C) and lower (70°C) temperatures have been applied to the CO_2 fixation process of epoxidized methyl oleate (*cis*-**4a**) to yield cyclic organic carbonates (**5a**) (eq 5). Results are shown in Table 2.6.

Table 2.6: Outcomes with two different temperature (70°C or 120°C)



Entry	Temperature (°C)	Conversion *cis*-4a (%)	Selectivity 5a (%)	***Cis* : *Trans* Ratio** ***cis*-5a : *trans*-5a**
1	70	10	≈100	99 : 1
2	100	85	92	99 : 1
3	120	50	50	70 : 30

Reaction condition: 1.28mmol *cis*-**4a**, 5 mol% catalyst (**2a**), 2.5 mol% co-catalyst ($[N_{4,4,4,4}]Br$), p(CO_2, 100°C)=50 bar, 16h, solvent-free.

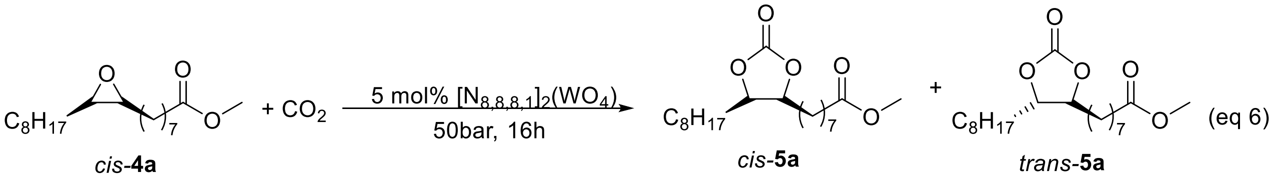
Higher or lower temperatures played a fondumental role over the reaction conversion and selectivity. Lower temperature (entry 1) allowed to eliminate the by-products' formation but a low conversion of 10% was reached, while at higher temperature (120°C, entry 3) the conversion was lower that the reaction conducted at 100°C (entry 2) but also the selectivity towards cyclic organic carbonates and diastereoselectivity concurrently decrease.

2.4.3 The effect of co-catalyst's load

Catalyst and co-catalyst have different effects when employed alone: the catalyst tends to increase the *cis:trans* diastereoselectivity of the process but the selectivity towards cyclic organic carbonates *cis/trans*-**5a** is lower; the co-catalyst leads to higher conversion of *cis*-**4a** and selectivity towards carbonates with decreased diastereoselective control. Thus, different amounts of co-catalyst have been applied to the CO_2 fixation process into *cis*-**4a** (eq 6) to yield carbonates **5a** in order to increase the reaction's performances in terms of chemoselectivity and diastereoselectivity.

As summarised in Table 2.7, the reaction conversion and selectivity toward the carbonates grew linearly as the co-catalyst's amount rise. As already mentioned (*i.e.*, Table 2.5, entry 5), complete selectivity towards **5a** occured when 2.5% mol of [$N_{4,4,4,4}$](Br) were used alone (entry 1) and no formation of diol **5b** or ketone **5a** was observed . The more the molar ratio is shifted in favor of **2a** (from entry 2 to entry 5), the lower the conversion and the larger amount of **6a** and **6b** were formed.

Table 2.7: CO_2 fixation outcomes at different co-catalyst's load



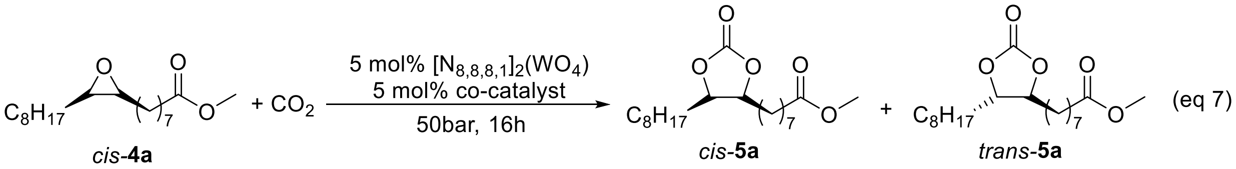
Entry	**[$N_{4,4,4,4}$](Br) (mol%)**	**Conversion *cis*-4a (%)**	**Selectivity 5a (%)**	***Cis : Trans* Ratio *cis*-5a : *trans*-5a**
1[a]	2.5	≈100	≈100	80 : 20
2	5	94	94	99 : 1
3	2.5	87	91	93 : 7
4	1.25	79	87	99 : 1
5[b]		28	54	99 : 1

Reaction conditions: 1.28mmol *cis*-**4a**, 5 mol% catalyst (**2a**), p(CO_2, 100°C)=50 bar, 100°C, 16h, solvent-free. (a) Reaction was conducted in absence of **2a.** (b) Reaction was conducted in absence of co-catalyst ([$N_{4,4,4,4}$]Br).

2.4.3.1 Inorganic salts as possibile co-catalysts

Two other inorganic salts (NaI and NaBr) have been tested to apply in the CO_2 fixation process (eq 7). Results are reported in Table 2.8.

Table 2.8: Outcomes of carbonation with 5 mol% of inorganic salts as co-catalysts



Entry	**Co-catalyst**	**Conversion *cis*-4a (%)**	**Selectivity 5a (%)**	***Cis : Trans* Ratio *cis*-5a : *trans*-5a**
1	NaBr	47%	≈100%	90 : 10
2	NaI	60%	60%	28 : 72

Reaction conditions: 1.28mmol *cis*-**4a**, 5 mol% catalyst (**2a**), 5 mol% co-catalyst, p(CO_2, 100°C)=50 bar, 100°C, 16h, solvent-free.

As evidenced in Table 2.8, both inorgnic salts did not achieve adequate results. Sodium bromide (entry 1) allowed to achieve high chemoselective and diastereoselective control despite the law conversion. In contrast, sodium iodide (entry 2) showed better conversion but selectivity drop to 60% due to large formation of ketone **6a** and *trans*-epoxidized methyl oleate (*trans*-**4a**). Additionaly, sodium iodide led to *cis:trans* ratio shifted toward the -*trans* carbonate. This new outcome highlighted that the carbonation process may follow different routes that can be influenced by different counter ions.

2.4.4 Proposed mechanism of the reaction

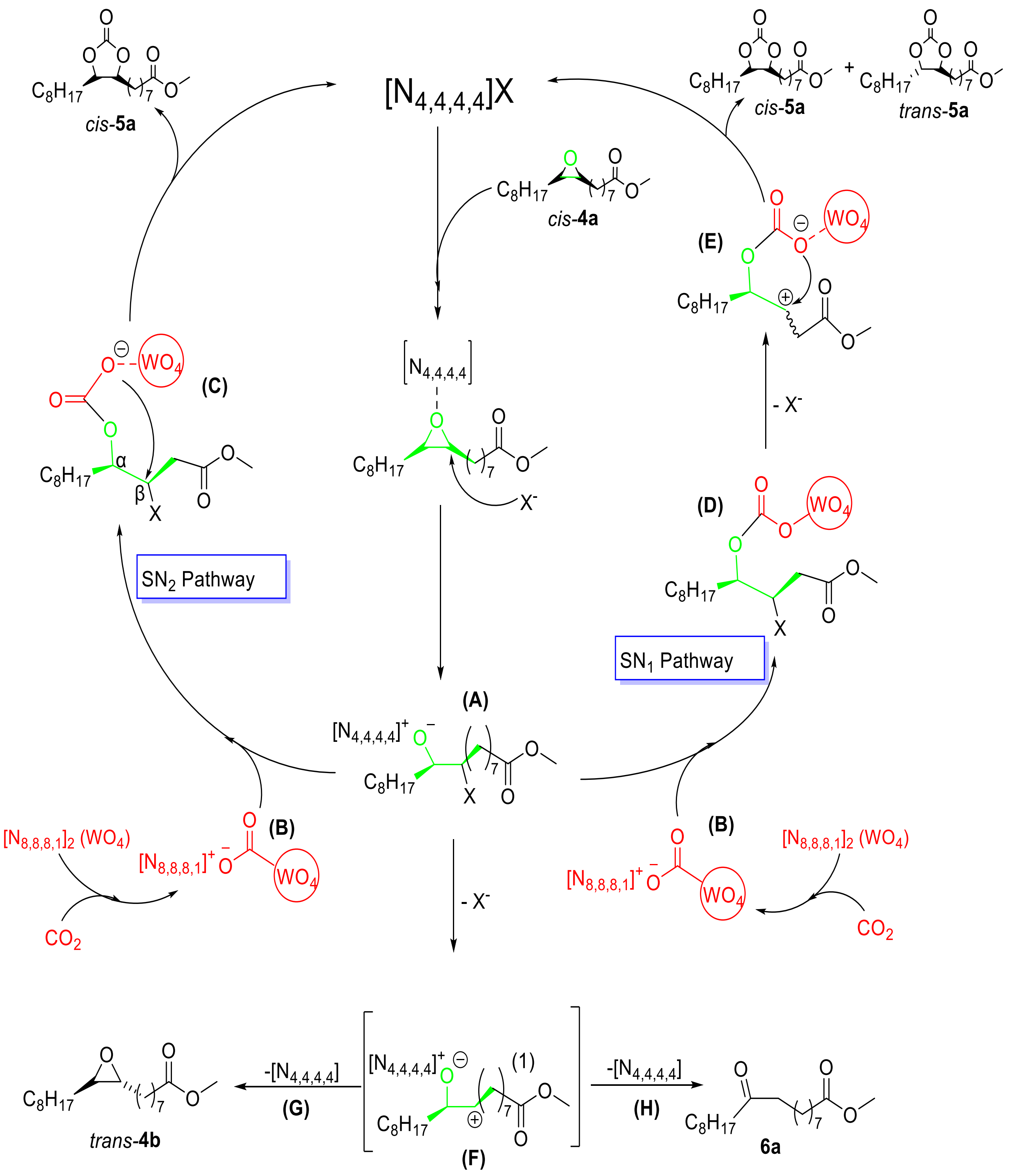
In order to explain the previous outcomes, a mechanism of the carbonation has been proposed, according to the literature.[84,88,92,118] A synergistic effect is considered to play a fundamental role in the reaction mechanism (Scheme 2.14).[84] While it is generally recongized the epoxy ring-opening acitivity of the co-catalyst that promps the formation of an halo-alkoxide intermediate, the negative charged tungstate may interacts with CO_2. So, while a nucleophilic reaction with bromide ion forms an alcoholate which results in an inversion of the configuration at the respective carbon atom (**A**), tungstate has the possibility to activate the CO_2 (**B**).[118]

It is reasonable to contemplate both types of nucleophilic substitutions (SN_1 and SN_2) as both diastereoisomers *cis*-**5a** and *trans*-**5a** were produced. [118] Moreover, the outcomes showed in Table 2.8 stregthen the hypothesis that the use of different halides could favor SN_1 or SN_2 mechanism.

In the SN_2 pathway, aliphatic carbonate anion attacks the C_β atom (**C**). Thus, the relative -*cis* configuration of substrate *cis*-**4a** is retained and only *cis*-**5a** will be produced. In the SN_1 pathway, the halide initially dissociates from the linear carbonate anion (**D**) and, then, the formation of a carbenium ion (**E**) enables the formation of both *cis*-**5a** and *trans*-**5a**. Therefore, it can be assumed that *cis*-**5a** is the kinetically favored carbonate, while *trans*-**5a** is the thermodynamically favored carbonate.[118]

This trend explains the main differences in term of conversion and *cis:trans* ratio when bromide or iodide were employed. Iodide is a better nucleophile than bromide (in the presence of hydrogen bond donor)[119] but it also a better leaving group than bromide, hence iodide dissociates easier beacuse the anion is bigger and better stabilized than bromide. The SN_1 pathway is favored when iodide was used because iodide dissociation is faster than the attack of carbonate anion (COO-) to C_β atom.

Finally, -*trans* EMO (*trans*-**4a**) and over-oxidized ketone (**6a**) are most reasonably formed due to epoxy-ring closing (**G**) or Meinwald rearrangement (**H**) of intermediate (**F**).[118]

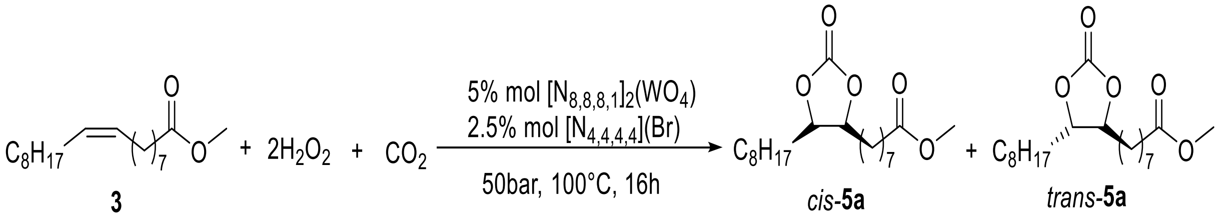


Scheme 2.14: Proposed mechanism for the carbonation of *cis*-**4a.**

2.5 One-Pot Tandem Reaction

The optimized epoxidation and carbonation processes were finally gathered togheter in order to develop a one-pot tandem synthesis protocol in which methyl oleate is directly converted into the corresponding cyclic carbonates **5a**.

A one-pot auto-tandem methodology was initially considered. Methyl oleate (2g, 6.76mmol), H_2O_2 (30% v/v, 2equiv), **2a** (5% mol) and $[N_{4,4,4,4}](Br)$ (2.5% mol) were added in a round-bottom-glass flask that was then placed inside a stainless steel autoclave. The autoclave was sealed, degassed via three vacuum-N_2 cylces and pressurized with 50 bar of CO_2 and, finally, heated at 100°C for 16 hours (Scheme 2.15).



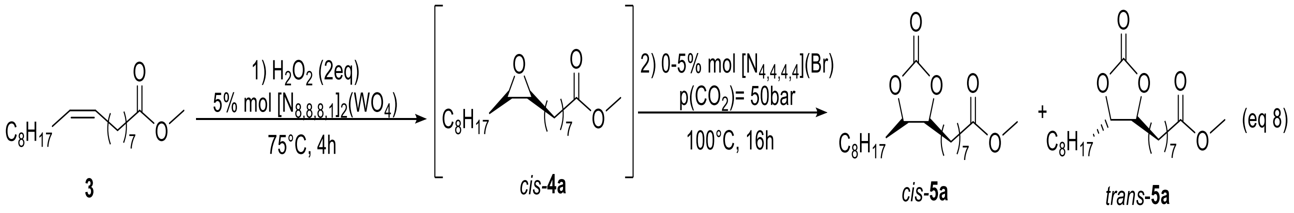
Scheme 2.15: Initial one-pot auto-tandem procedure for the formation of carbonates **5a**

Under these conditions, no formation of carbonates was observed. This preliminary outcome showed the unfeasability of a one-pot auto-tandem methodology, hence two steps are required and an assisted tandem catalysis was applied.

In a conventional procedure, a round-bottom-glass flask methyl oleate (2g, 6.76mmol) and H_2O_2 (30% v/v, 2equiv) were set to react with **2a** (5% mol) at 75°C until a complete conversion was achieved, usually after 4 hours. Then, the glass flask was placed inside a stainless steel autoclave and $[N_{4,4,4,4}](Br)$ (0.055g, 0.169mmol) was added. The autoclave was sealed, degassed via three vacuum-N_2 cycles and pressurized with 50 bar of CO_2. At the end, the autoclave was heated at 100°C for 16 hours (eq 8).

For every one-pot assisted-tandem synthesis, carbonation did not occur until methyl oleate was completely converted into its -*cis* epoxidized methyl oleate (*cis*-**4a**). Samples of mixture were withdrawn after about 4 hours of reaction and analyzed both by ^{1}H-NMR and GC-MS in order to follow the course of the reaction. The results are plotted in Table 2.9.

Table 2.9: Outcomes of one-pot assisted-tandem methodology



Entry	**[N$_{4,4,4,4}$](Br) (mol%)**	**Conversion** ***cis*-4a (%)**	**Selectivity 5a (%)**	***Cis : Trans* Ratio** ***cis*-5a : *trans*-5a**
1^{a}		5	7	99 : 1
2	2.5	33	≈100	99 : 1
3	5	45	≈100	99 : 1

Reaction conditions: 6.76mmol **3**, 5 mol% catalyst (**2a**), p(CO2, 100°C)=50 bar, 100°C, 16h, solvent-free. The conversion of MO (**3**) and the selectivity toward *cis*-**4a** are always quantitative (≈100%). (a) Reaction was conducted in absence of co-catalyst.

Initially, the assisted-tandem synthesis was conducted in absence of co-catalyst $[N_{4,4,4,4}](Br)$ (entry 1) and a very low conversion (5%) and selectivity (7%) were achieved. This initial outcome demonstrated that the presence of halides is required in order to achieve a good conversion.

Higher conversion of *cis*-**4a** and complete selectivity toward carbonates **5a** were achieved when the catalyst (**2a**) was coupled with 2.5% molar of co-catalyst $[N_{4,4,4,4}](Br)$ (entry 2).

Finally, when 5% molar of $[N_{4,4,4,4}](Br)$ was adopted (entry 3) conversions were increased to 45% yet still inadequate.

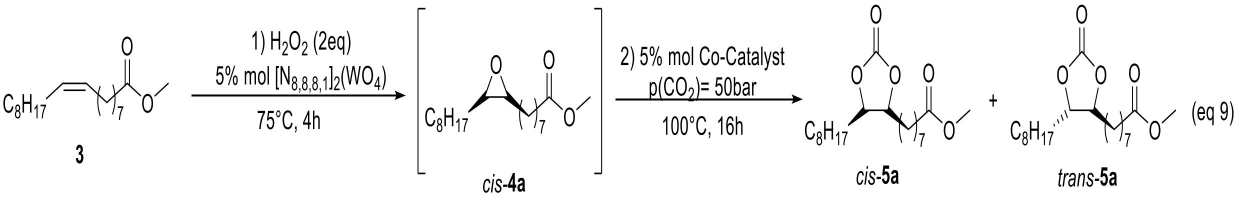
These unsuccessful results probably depended on the presence of a biphasic system. As the organic phase was not extracted and collected, $[N_{4,4,4,4}](Br)$ may split in both organic and aqueous phase and perform worse than in the simple CO_2 fixation step in absence of water.

Several compounds have then been tested as potential substitute co-catalyst to improve the cyclic carbonates yield in the tandem process.

2.5.1 The effect of various co-catalysts

Many organic and inorganic salts have been tested as co-catalysts in the assisted one-pot tandem reaction (eq 9). Firstly, keeping fixed the $[N_{4,4,4,4}]^+$ cation, other halides than bromide were tried as counter ions (especially chloride and iodide). Lately, several inorganic salts, whose solubility in water is higher than $[N_{4,4,4,4}](Br)$'s one, were employed. Results are reported in Table 2.10.

Table 2.10: Outcomes of the other co-catalysts employed



Entry	Co-Catalyst	Conversion *cis*-4a (%)	Selectivity 5a (%)	*Cis : Trans* Ratio *cis*-5a : *trans*-5a
1	$[N_{4,4,4,4}]Cl$	12	≈100	99 : 1
2	$[N_{4,4,4,4}]Br$	45	≈100	99 : 1
3	$[N_{4,4,4,4}]I$	81	85	68 : 32
4	NaCl	22	≈100	99 : 1
5	NaBr	48	≈100	97 : 3
6	NaI	73	73	34 : 66
7	KCl	11	≈100	99 : 1
8	KBr	67	≈100	90 : 10
9	KI	79	88	46 : 54

Reaction conditions: 6.76mmol **3**, 5 mol% catalyst (**2a**), 5 mol% co-catalyst, p(CO2, 100°C)=50 bar, 100°C, 16h, solvent-free. The conversion of MO (**3**) and selectivity toward *cis*-**4a** are always quantitative (≈100%).

The worst conversions were obtained when chloride was used as counter ion (entry 1, entry 4 and entry 7). Chloride is the worst leaving group among the halides, hence SN_1 pathway is the sole walkable path. This allows only the production of -*cis* carbonate without any byproducts' formation. Additionally, in the presence of hydrogen bond donor, chloride is also the worst nucleophiles and is not able to open the epoxy-ring: this negatively influences the conversion.[119]

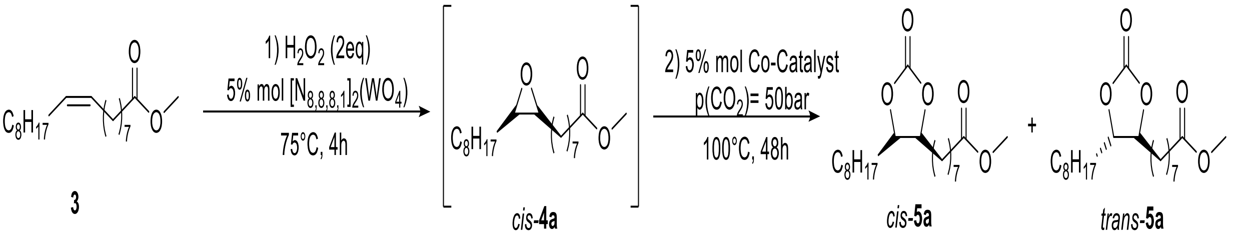
Higher results in term of conversion were reached when bromide was adopted as counter ion (entry 2, entry 5 and entry 8). This trend follows what already stated about the possible mechanism for the carbonation (*e.g.*, paragraph 2.4.4): bromide is a better leaving group and positively influences the conversion but -*trans* carbonate formation occurred as SN_2 pathway is more accessible. The lower conversion of NaBr (entry 4) than KBr (entry 7) may be due to the higher polarizability of K^+ that better stabilize the halo-alkoxide intermediate. Indeed, more -*trans* carbonate was formed when KBr was used, as bromide had more time to dissociate. Finally, when iodide was used (entry 2, entry 5 and entry 8), conversions were the highest but selectivity partially decrease as *trans*-**4a**, diol **6b** and ketone **6a** were formed. In addition, *cis:trans* ratio is shifted toward the -*trans* carbonate when NaI (entry 5) and KI (entry 8) were used. This trend seems to decrease with the increase of the interaction between cation and anion in the halide salt (entry 3).

If we compare the different outcomes obtained by NaI and NaBr in the tandem protocol in a two-phase system (entry 5 and entry 6, Table 2.10) and the sole CO_2 fixation process in the organic phase (entry 1 and entry 2, Table 2.8), better performances were achieved in the biphasic system. The one-pot assisted-tandem methodology allow to improve the performances of the inorganic salts in terms of both conversion and selectivity. Thus, during the epoxidation process $[N_{8,8,8,1}]_2(WO_4)$ (**2a**) acts as a hydrogen peroxide activator and as a catalyst for the reaction; in the CO_2 fixation process, **2a** acts as Lewis acid boosting the diastereoselectivity toward the formation of -*cis* carbonate and as a phase-transfer catalyst allowing simple inorganic salts to have a high catalytic activity in a biphasic system.

2.5.2 Consideration over time

In order to increase the overall yield of the one-pot tandem process (eq 10), the final carbonation reaction has been enlarged in time (48h). Sodium and potassium salts have been used as co-catalysts. The results after 48h of carbonation reaction are shown in Table 2.11.

Table 2.11: One-pot tandem reaction with 48h of carbonation



(eq 10)

ENTRY	Co-Catalyst	Conversion cis-4a (%)	Selectivity 5a (%)	***Cis* : *Trans* Ratio** *cis*-**5a** : *trans*-**5a**
1	NaBr	54	70	93 : 7
2	NaI	72	72	42 : 58
3	KBr	≈100	≈100	92 : 8
4	KI	93	93	67 : 34

Reaction conditions: 6.76mmol **3**, 5 mol% catalyst (**2a**), 5 mol% co-catalyst, p(CO2, 100°C)=50 bar, 100°C, 16h, solvent-free. The conversion of MO (**3**) and selectivity toward *cis*-**4a** are always quantitative (≈100%).

As reported in Table 2.11, the conversion with NaBr (entry 1) was slightly increased when the reaction was prolonged to 48 h but the selectivity dropped down to 70%. Unsatisfactory results were also obtained with NaI (entry 2): no improvements were observed if compared to the reaction (entry 6, Table 2.9) conducted for 16h. Better outcomes were achieved in terms of conversion (93%) and selectivity (93%) with KI (entry 4) in a prolonged time.

A quantitative conversion and selectivity toward the carbonates were achieved when KBr was employed (entry 3); *cis:trans* ratio (92:8) was almost completely shifted toward *cis*-**5a**. Moreover, potassium bromide is the cheapest salts among the inorganic salts adopted: it costs 0.0934 €/g for a 500g stock (NaI 0.594 €/g, KI 0.316 €/g and NaBr 0.138€/g).

This is the first ever reported investigation describing a one-pot assisted-tandem catalysis to produce oleo-carbonates directly from renewable oil-based feedstocks. Furthermore, this process allows to produce of both -*cis* epoxidized methyl oleate and carbonated methyl oleate with a quantitative conversion and selectivity.

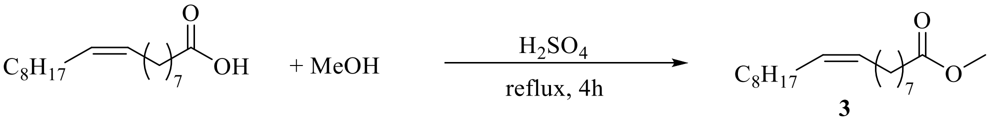
CHAPTER III

CONCLUSIONS

3.1 Conclusions

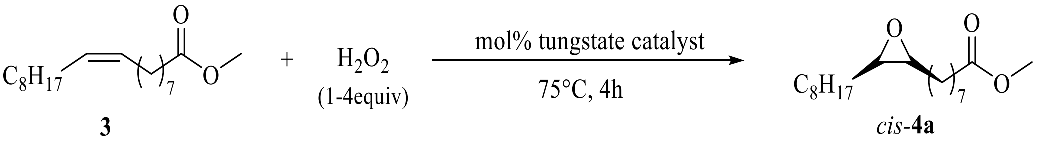
Internal cyclic carbonates are compounds useful as softening agents, fuel additives, polymer precursors, lubricants or chemical solvents, as well as plasticizers or biomedical products. The possibility to develop a new strategy to produce them from oleochemicals and, additionally, to exploit carbon dioxide as a C_1 building block, has collected much interest from both environmental and economic standpoint. Usually, olefins are converted into epoxides that must undergo tedious work-up for their isolation and purification. Epoxides are successively reacted with CO_2 to form cyclic organic carbonates. In this context, this Thesis work has been aimed at developing a new one-pot tandem methodology exploiting oleochemicals as starting materials and avoiding the intermediate isolation of the epoxide.

Initially, the transformation of oleic acid to methyl oleate (**3**) was conducted through an esterification acid-catalyzed protocol previously reported in literature:[102] oleic acid and an excess of methanol were set to react at reflux temperature for 4 hours, in the presence of sulfuric acid (Scheme 3.1). This reaction proceeded with good yields, always up to 90%.



Scheme 3.1: Esterification of oleic acid into methyl oleate (**3**)

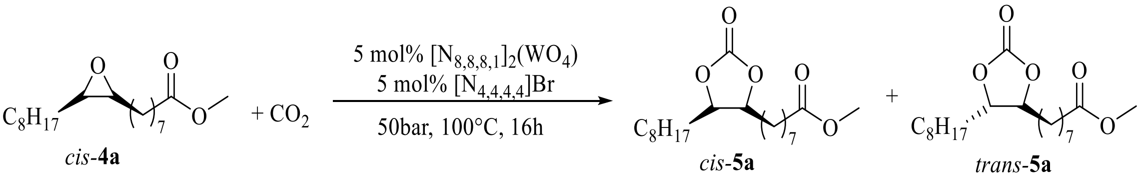
Then, the epoxidation of methyl oleate and the CO_2 fixation into epoxidized methyl oleate have been investigated individually. The epoxidation process (Scheme 3.2) was investigated at different temperature (25°C – 75°C) and by varying catalyst, catalysts amount and hydrogen peroxide amount to optimize the reaction conditions in absence of any extra solvent.



Scheme 3.2: Synthesis of epoxidized methyl oleate (*cis*-**4a**).

The optimized procedure promoted a quantitative conversion (~100%) of methyl oleate at 75°C after 4 hours with a slight excess of H_2O_2 (molar ratio H_2O_2:MO=Q=*2*) and 5% of trioctylmethylammonium-tungstate (**2a**). The reaction obviously proceeds with retention of stereochemistry and only -*cis* epoxide (*cis*-**4a**) was obtained. The epoxidized methyl oleate was then purified to be ready for the further carbonation reaction: usually, an extraction with ethyl acetate was sufficient to reach the pure product.

The CO_2 fixation process has been investigated through different CO_2 pressure (1-50 bar), temperature (70-120°C), co-catalyst and amount of co-catalyst. At 100°C for 16 hours, under 50bar of CO_2, with 5% of **2a**, as catalysts, 5% of tetrabutylmethylammonium bromide ($[N_{4,4,4,4}]Br$), as co-catalysts (Scheme 3.3), the optimum conditions were achieved, in terms of carbonates selectivity (conversion above 97%) and reaction stereoselectivity (*cis:trans*= 80:20).



Scheme 3.3: Synthesis of both -cis and -trans cyclic carbonates via CO_2 fixation.

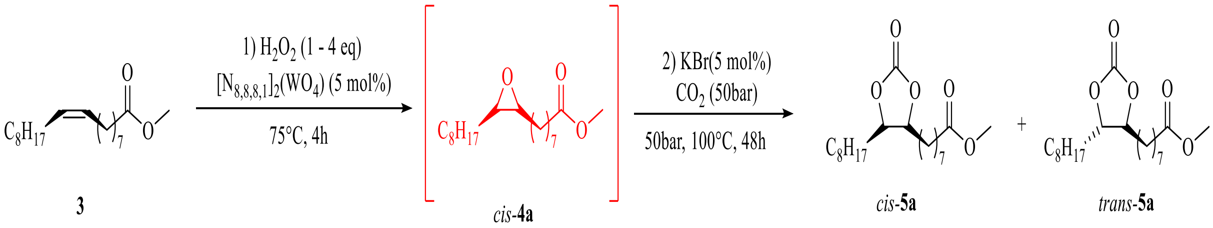
Finally, both reactions have been gathered together in order to develop a one-pot tandem synthesis. In this case, after the complete conversion of methyl oleate, the epoxide was set to react with CO_2, without any earlier work-up or purification process. Herein, the mainly issues occurred due to the presence of a biphasic system, as the organic phase was not extracted and collected. Thus, while the first step was kept fixed, some variations were done to the second one with the purpose of increase the carbonates yields, which was disappointing with the conditions just presented (see Scheme 3.3).

Different co-catalysts were studied based on two main features:

A) Co-catalysts whose solubility in water is greater than the solubility of $[N_{4,4,4,4}](Br)$: many sod/ium and potassium salts have been studied;

B) Co-catalysts with different counter ions than bromide: chloride and iodide were investigated as potential counter ion for the tetrabutylammonium salt.

Moreover, time was extended to increase the overall yield. Due to its greater solubility and a good leaving group, potassium bromide has proved to be the best co-catalyst for the CO_2 insertion (Scheme 3.4) in a biphasic system.



Scheme 3.4: Complete one-pot assisted-tandem reaction of methyl oleate (**3**).

The overall conversion and selectivity toward carbonates were quantitative (≈100%), with a good diastereoselectivity (*cis:trans* ratio = 92:8).

This Thesis study has proved that a two-phase system, composed by trioctylmethylammoium tungstate ionic liquid (**2a**) and aqueous hydrogen peroxide (H_2O_2), is highly efficient and selective for the production of epoxidized fatty acid esters (*i.e.*, *cis*-9,10-epoxystearate(*cis*-**4a**)). Furthermore, the study of carbonation reaction has demonstrated that trioctylmethylammonium tungstate enables the conversion of epoxidized methyl oleate to the corresponding cyclic organic carbonates but high conversion and selectivity were not affordable in absence of a halide co-catalyst. We also demonstrated the feasibility of unexpensive inorganic salts as epoxy ring-opening activators and a mechanism for the carbonation has been proposed in accordance with the obtained results and mechanisms proposed in literature.

Finally, this Thesis work has proved as well the feasibility of a one-pot tandem methodology for the conversion of fatty acids ester into internal cyclic carbonates A reproducible protocol has been implemented by an assisted tandem procedure in which CO_2 (50 bar) and the halide source co-catalyst are added after the completion of the epoxidation step (without any intermediate work-up or purification of the reaction mixture) to avoid detrimental interactions of halide source with the hydrogen peroxide activated by tungstate catalyst.

To the best of our knowledge, this is the first ever reported investigation describing a one-pot tandem reaction to produce oleocarbonates directly from renewable oil-based feedstocks.

CHAPTER IV

EXPERIMENTAL PART

4.1 General

Reagents. Trioctylamine (TOA), trioctylphosphine (TOP), 1-butylimidazole (MIM), dimethyl carbonate (DMC), tetrabutylammonium iodide (TBAI), sodium iodide (NaI), sodium bromide (NaBr), potassium bromide (KBr), potassium iodide (KI), methanol (MeOH), diethyl ether (Et_2O), dichloromethane (CH_2Cl_2), oleic acid (OA) were from Sigma-Aldrich. Sodium chloride (NaCl) was from Fluka. Tetrabutylammonium bromide (TBABr) was from Cognis. Tetrabutylammonium chloride (TBACl) was synthetized by another research laboratory. All reagents were ACS grade, and if not otherwise specified, they were employed without further purification. Water was of milli-Q grade.

Analyses. GC/MS (EI, 70 eV) analyses were run using a HP5-MS capillary column (L=30 m, Ø=0.32 mm, film=0.25 μm). The following conditions were used. Carrier gas: He; flow rate: 1,2 mL/min; split ratio: 10:1; initial T: 100° C (2 min), ramp rate: 20 °C/min; final T: 300 °C. ^{1}H NMR and ^{13}C NMR were recorded on a Bruker NMR spectrometer (400 MHz for ^{1}H-NMR, 100MHz for ^{13}C-NMR and 162MHz for ^{31}P-NMR).

Chemical shifts were reported in δ values downfield from TMS; d-Chloroform ($CDCl_3$), dimethyl sulfoxide-d6 (C_2D_6OS) and oxide deuterium (D_2O) were used as deuterated solvents.

4.2 Syntheses of reagents and catalysts

All the ionic liquids (trioctylmethylammonium-tungstate (**2a**), phosphotungstate (**2b**), trioctylphosphonium-tungstate (**2c**), 1-butyl-3-methylimidazolium tungstate (**2d**)) and methyl oleate (**3**) were prepared by adjusting methods previously reported by our and other research groups.

4.2.1 Syntheses of ionic liquids with dimethyl carbonate (DMC)

In a typical procedure, TOA (20 mL, 45.2 mmol), DMC (30 mL, 356 mmol) and methanol (20 mL) were combined in a 200 mL stainless steel autoclave fitted with a pressure gauge and a thermocouple for temperature control. Three vacuum-N_2 cycles were applied. The autoclave was heated for 20 h at 140 °C with magnetic stirring (1000rpm). Then the autoclave was allowed to cooled and vented. Methanol and residual DMC were removed from the mixture by rotary evaporation to give $[N_{8,8,8,1}](CH_3OCOO)$ (**1a**) (19.18g, 95%).

The same procedure was adopted to synthetize both $[P_{8,8,8,1}](CH_3OCOO)$ (**1b**) and $[BMIM](CH_3OCOO)$ mixture (**1c**). All the methyl carbonate-onium salts were characterized by ^{1}H-NMR and ^{13}C-NMR.

4.2.2 Syntheses of tungstate-based ionic liquids (TILCs)

In a conventional procedure, H_2WO_4 (3.450g, 13.8 mmol) was slowly added to an aqueous solution of $[N_{8,8,8,1}](CH_3OCOO)$ (10,072g, 22.7mmol) heated at 50 °C. The solution was stirred for 3h during which time the initial opalescent solution turned yellow. The solution was cooled and, then, extracted with ethyl acetate. The ionic liquid was finally concentrated under vacuum to reach a 9.547g $[N_{8,8,8,1}]_2(WO_4)$ (**2a**) (yield=85%).

This procedure was also adopted for the synthesis of $[P_{8,8,8,1}]_2(WO_4)$ (**2c**) and $[BMIM]_2(WO_4)$ (**2d**). The other TILC (**2b**) were synthetized with the same methodology, exploiting $H_3PW_{12}O_{40}$ as Brønsted acid.

The tungstate-based ionic liquids were fully characterized by ^{1}H-NMR, ^{13}C-NMR, ^{31}P-NMR, ^{183}W-NMR and FT-IR. Spectra are reported and commented in the Appendix.

4.2.3 Esterification acid-catalyzed of oleic acid

In a typical procedure, a 250-mL round-bottomed flask equipped with a condenser was charged with oleic acid (20,032g, 71 mmol) and a large excess methanol (100mL, 247mmol). The solution was pre-heated at 50°C, then concentrated H_2SO_4 (95%) was added dropwise until a light white solution was formed. The reaction was then performed under reflux with magnetic stirring (1100 rpm) for 4 hours. The solution was allowed to cool at room temperature. A saturated solution of $NaHCO_3$ was added in order to reach a pH=7. The two-phase solution was then extracted with dichloromethane and dried over sodium sulfate. The solution is then filtered and concentrated under rotary evaporator to reach 19.189g of methyl oleate (yield = 91%).

The product was fully characterized by GC/MS, ^{1}H-NMR and ^{13}C NMR. Spectra are reported and commented in the Appendix

4.3 Reaction Procedures

4.3.1 Epoxidation of methyl oleate with H_2O_2 and TILCs catalyst.

In a typical procedure, a 50-mL round-bottomed flask equipped with a condenser was charged with methyl oleate (**3**, 500mg, 1.67 mmol), H_2O_2 30% (w/w) (0.32 mL), 200µL of mesitylene (as internal standard) and the catalyst (**2a**) in a 1:2:0.05 molar ratio, respectively. The reaction was then performed at 75°C, by heating the mixture under magnetic stirring (1100 rpm). At intervals of one hour, the mixture was sampled and samples were analyzed by ^{1}H-NMR. Reactions were usually followed up to 4 hours. The solution was then extracted with dichloromethane, dried over sodium sulfate and filtered. The organic phase was concentrated under rotatory evaporator to reach 475 mg of isolated *cis*-**4a** (yield= 91%). The described procedure was also used by increasing the H_2O:**3** molar ratio up to 4, and by varying the catalyst:**3** molar ratio to 0.025. Initial tests were done in the presence of 2.5% mol of H_3PO_4. An additional test was also performed at 75 °C in the absence of any catalyst by setting the H_2O_2:**3** molar ratio at 2.

*4.3.2 Carbonation of cis-***4a** *under CO_2 pressure*

In a typical procedure, a stainless-steel autoclave with an internal volume of 200 mL, equipped with a pressure gauge, a thermocouple and two valves, was charged with a mixture of epoxidized methyl oleate (400mg, 1.28 mmol), **2a** and [$N_{4,4,4,4}$](Br) in a 1:0.05:0.025 molar ratio, respectively. The autoclave was purged at room temperature by three vacuum-CO_2/N_2 purge cycles and pressurized with CO_2 (50 bar). The autoclave was then heated at 100°C and the reaction was magnetically stirred (1000rpm) for the desired time (16h). The autogenous pressure was 70 bar. After 16 hours, the autoclave was allowed to cool, vented, and opened. The brown liquid was then extracted with dichloromethane, dried over sodium sulfate and filtered. The organic phase was concentrated under rotatory evaporator to reach 364 mg of isolated **5a** (yield = 79%)

The previous procedure was used to evaluate the effect of the temperature, the pressure and the co-catalyst's load. Additional experiments were performed by varying:

1) the **2a**:[$N_{4,4,4,4}$](Br) molar ratio in the range from 1:0.25 to 1:1 respectively; 2) the temperature was shifted to 70 and 120°C; 3) different pressures were tested, from 1 to 50 bar.

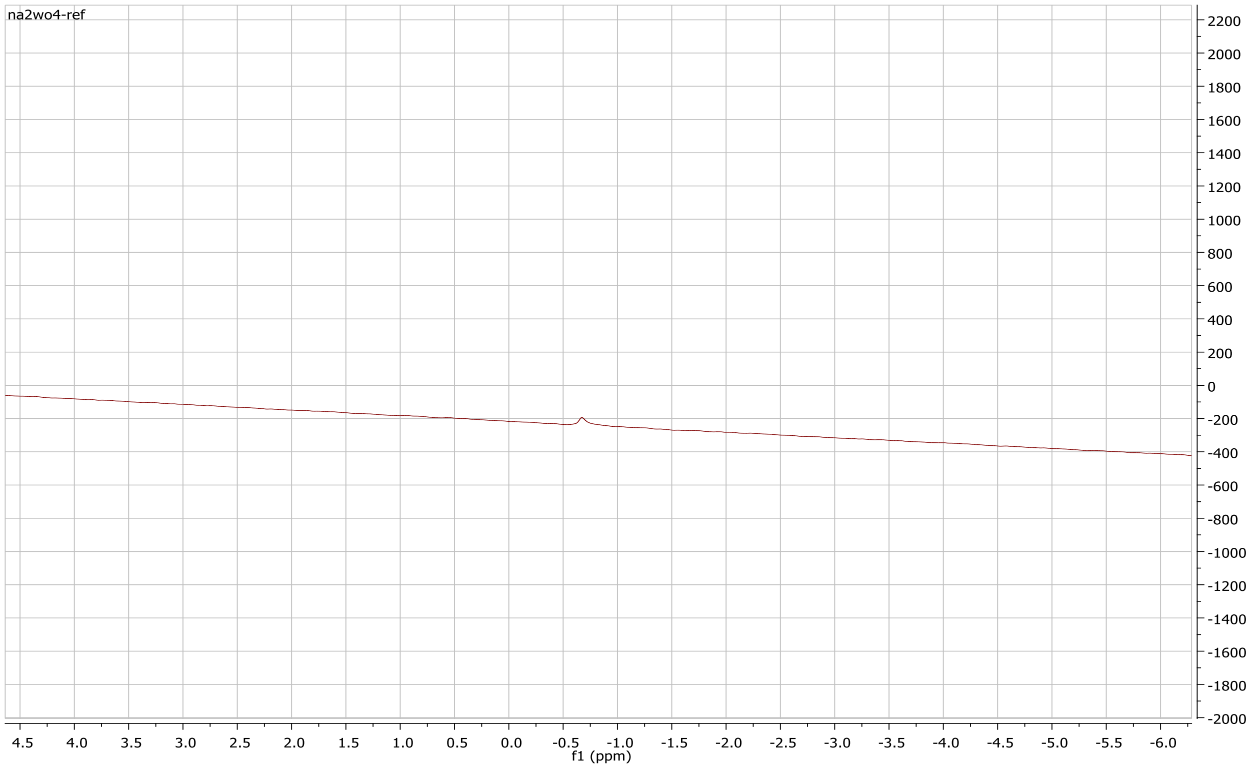
4.3.3 One-Pot Tandem Reaction

In a typical procedure, a 50-mL round-bottomed flask equipped with a condenser was charged with methyl oleate (**3**, 500mg, 1.67 mmol), H_2O_2 30% (w/w) (0.32 mL), 200µL of mesitylene (as internal standard) and the catalyst (**2a,** 80mg, 0.08mmol) in a 1:2:0.05 molar ratio, respectively. The reaction was then performed at 75°C, by heating the mixture under magnetic stirring (1100 rpm) for 4 hours. At intervals, the mixture was sampled and samples were analyzed by ^{1}H-NMR and GC-MS in order to follow the course of the epoxidation process. Once the reaction has reached a complete conversion, the biphasic solution was allowed to cool at room temperature. $[N_{4,4,4,4}](Br)$ (12.8mg, 0.04mmol) was then added as co-catalyst and the round-bottom glass flask was fitted inside a stainless-steel autoclave (internal volume: 200 mL) equipped with a pressure gauge, a thermocouple and two valves. The autoclave was purged at room temperature by three vacuum-N_2 purge cycles and pressurized with CO_2 (50 bar). The autoclave was then heated at 100°C and the reaction was magnetically stirred (1000rpm) for 16 hours. The autogenous pressure was 70 bar. After the reaction's time, the autoclave was allowed to cool, vented, and opened.

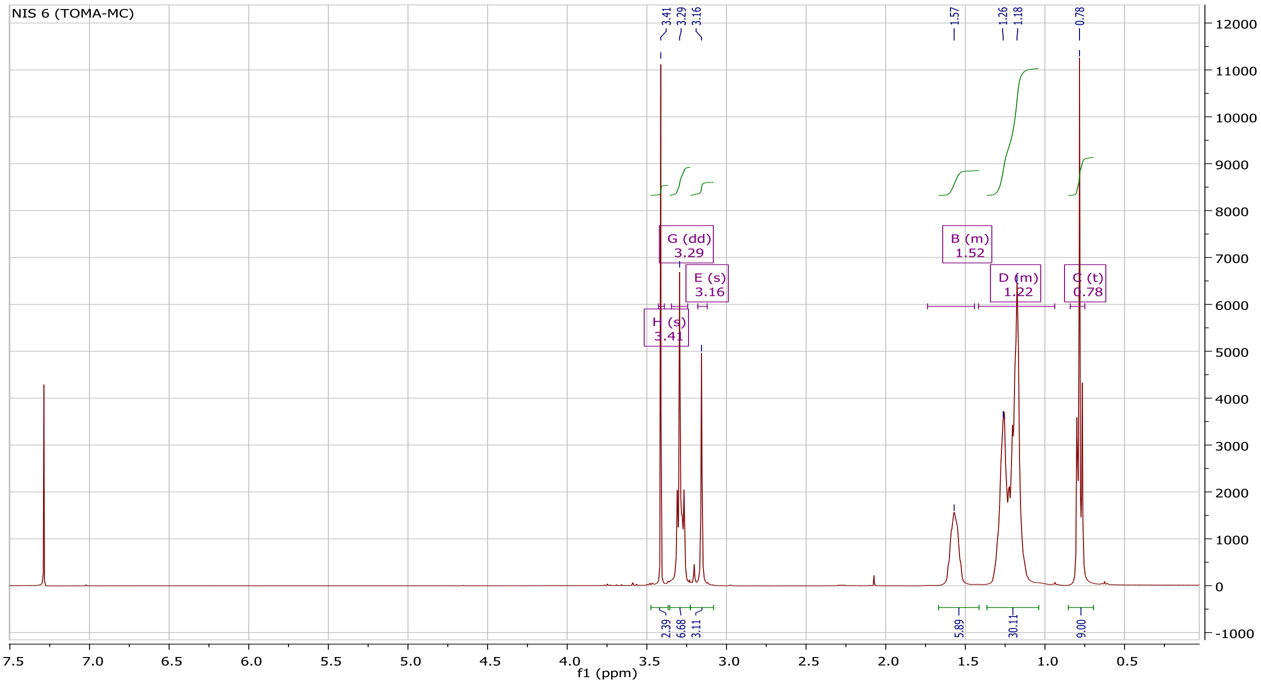
This procedure was also performed to evaluate the applicability of other co-catalyst (organic and inorganic salts) and the effect of enlarged time (48h). Additionally, this procedure was performed in absence of any co-catalysts.

APPENDIX

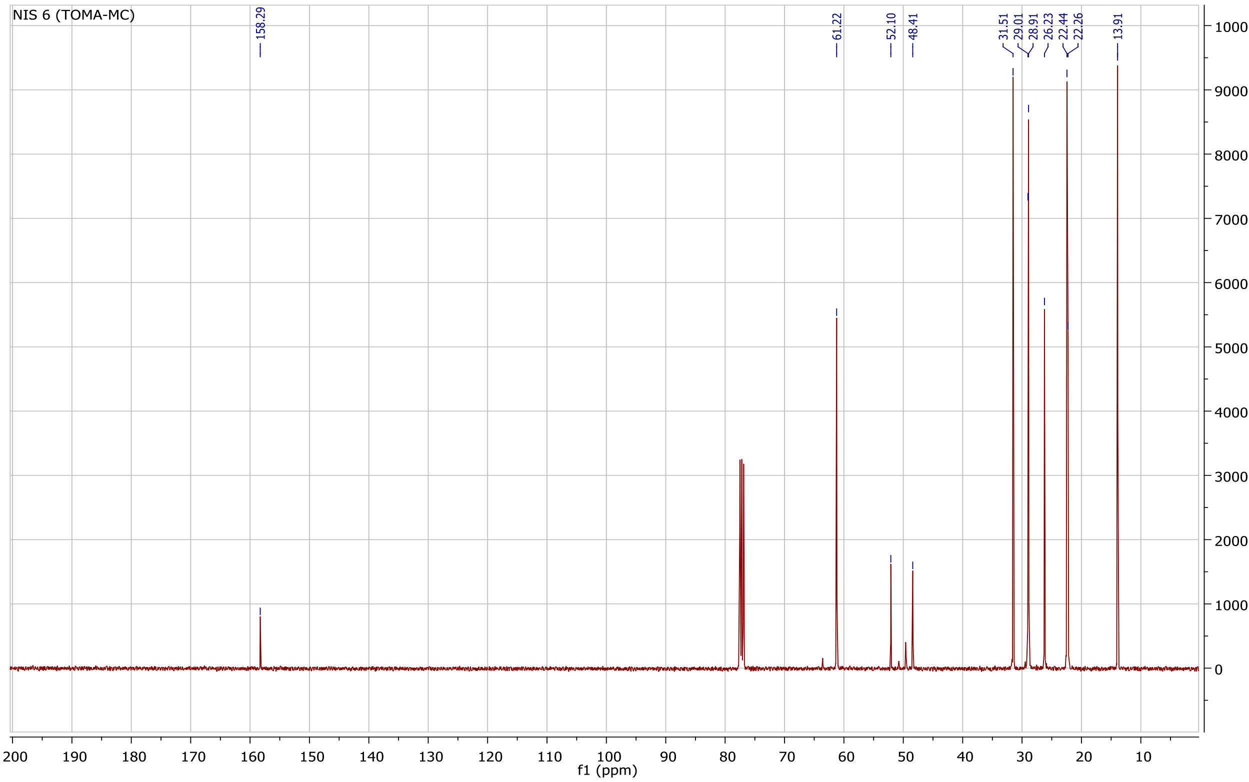
^{183}W-NMR of Sodium Tungstate (Na_2WO_4) as reference



Trioctylmethylammonium-methyl carbonate ([$N_{8,8,8,1}$](CH_3OCOO), **1a**)

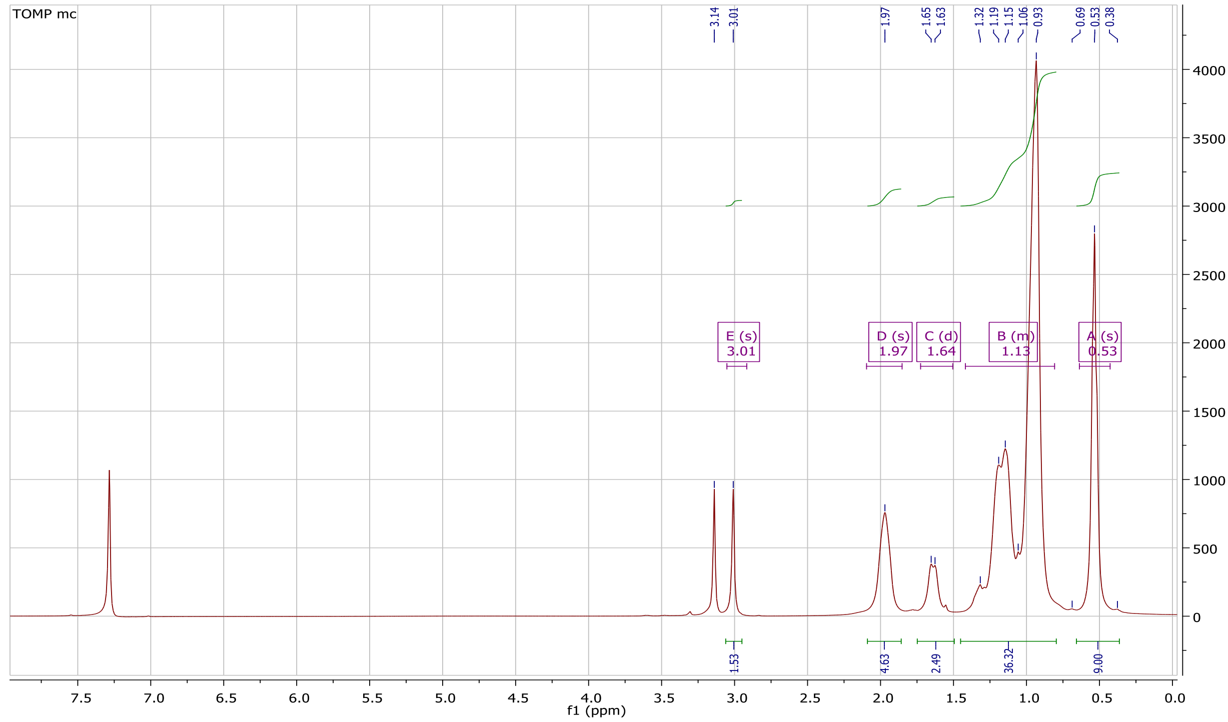


^{1}H-NMR (400MHz, $CDCl_3$): δ = 0.78 (t, J=6.90, 9H), 1.18 (m, 30H), 1.57 (m, 6H), 3.16 (s, 3H), 3.29 (dd, J=5.56, 11.40hHz, 6H), 3.40 (s, 3H).

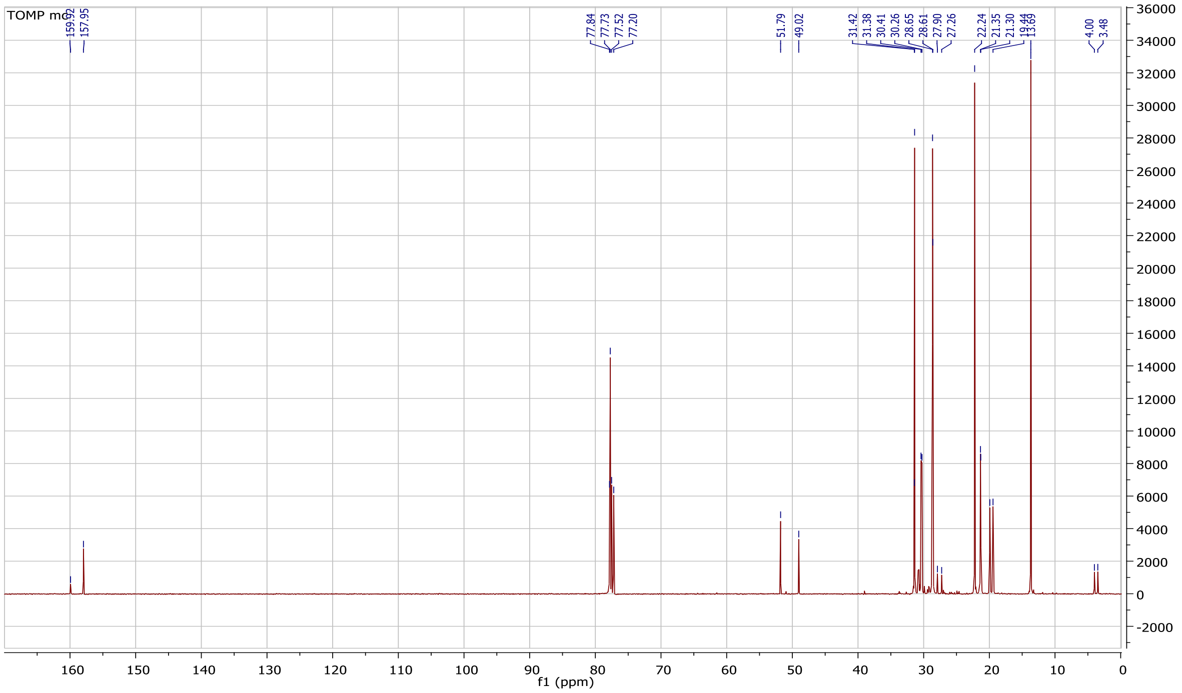


^{13}C-NMR (100MHz, CDCl$_3$): δ = 13.91, 22.26, 22.44, 26.33, 28.91, 29.01, 31.51, 48.41, 52.10, 61.22, 158.29.

Trioctylmethylphosphonium-methyl carbonate ([P$_{8,8,8,1}$](CH$_3$OCOO), **1b**)

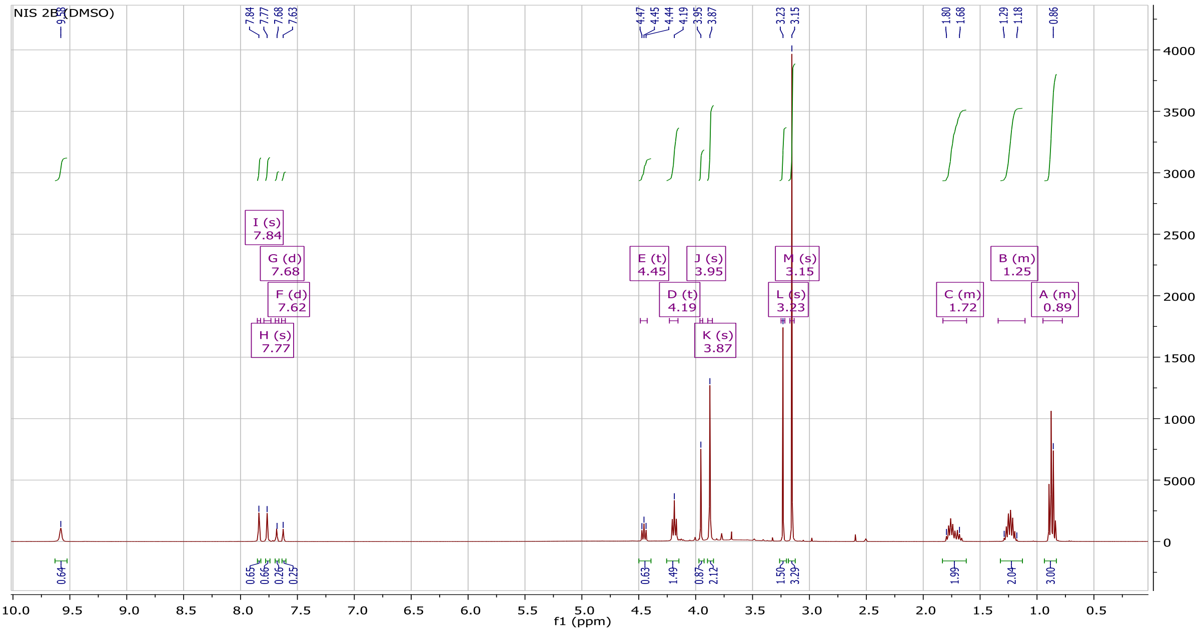


^{1}H-NMR (400MHz, CDCl$_3$): δ = 0.53 (s, 9H), 0.93-1.32(m, 36H), 1.64 (d, J=10.6MHz, 3H), 1.976 (s, 6H), 3.01 (s, 3H).



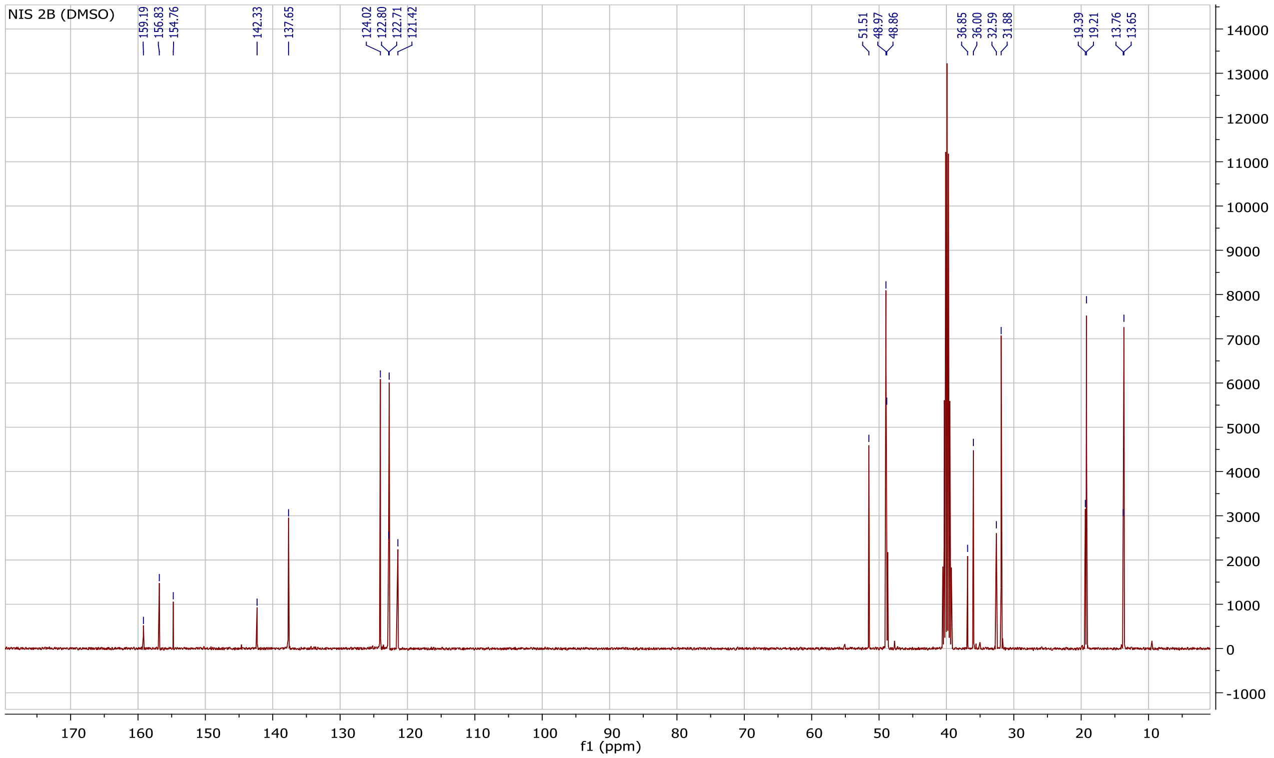
^{13}C-NMR (100MHz, CDCl$_3$): δ = 3.48, 4.00, 13.69, 19.44, 19.92, 21.30, 21.15, 22.24, 27.90, 28.61, 28.65, 30.26, 30.41, 31.38, 31.42, 49.02, 51.79, 77.20, 77.52, 77.73, 77.84, 157.95, 159.92.

1-Butyl-3-methylimidazolium–methyl carbonate / 1-butyl-3-methylimidazolium-2-carboxylate (**1c**)



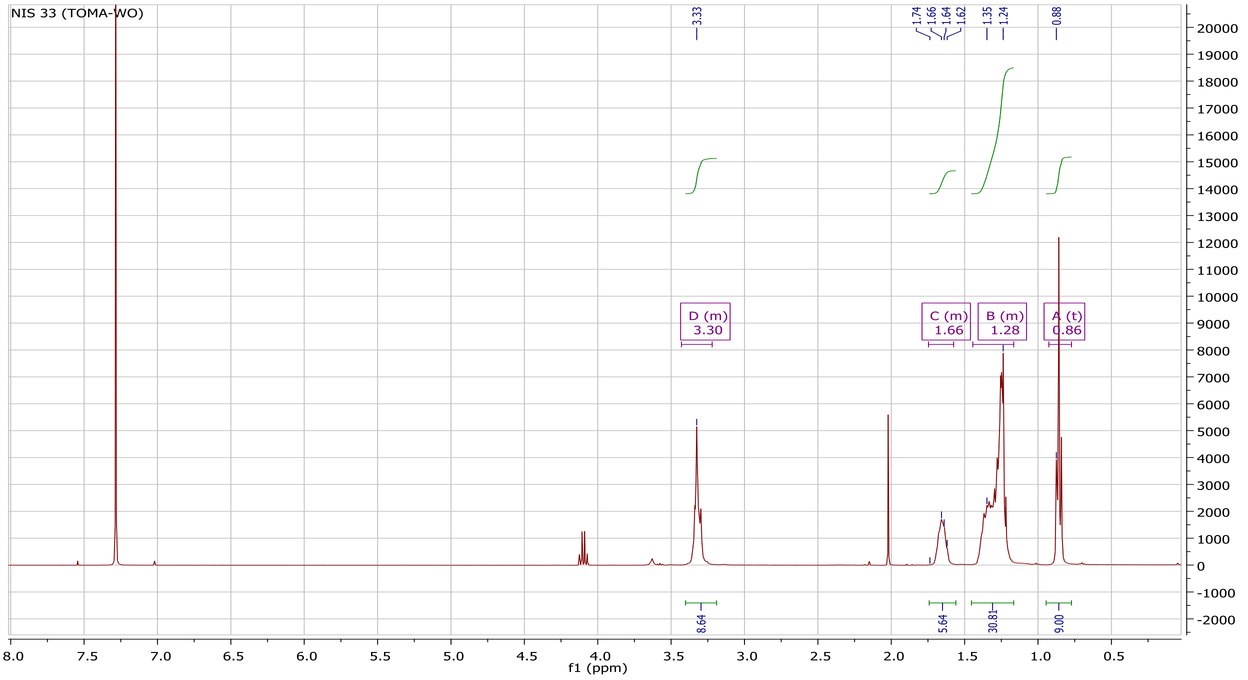
^{1}H-NMR (400MHz, DMSO) (1-Butyl-3-Methyl-2-Carboxy-Imidazolium): δ = 0.89 (m, 3H), 1.25 (m, 2H), 1.72 (m, 2H), 3.95 (s, 3H), 4.45 (t, J= 7.3, 2H), 7.62 (d, J=1.68Hz, 1H), 7.68 (d, J=1.57Hz, 1H).

^{1}H-NMR (400MHz, DMSO) (BMIM-MC): δ = 0.88 (t, 3H), 1.25 (m, 2H), 1.76 (m, 2H), 3.23 (s, 3H), 3.87 (s, 3H), 4.19 (t, J=7.2Hz, 2H), 7.77 (s, 1H), 7.84 (s, 1H), 9.58 (bs, 1H).

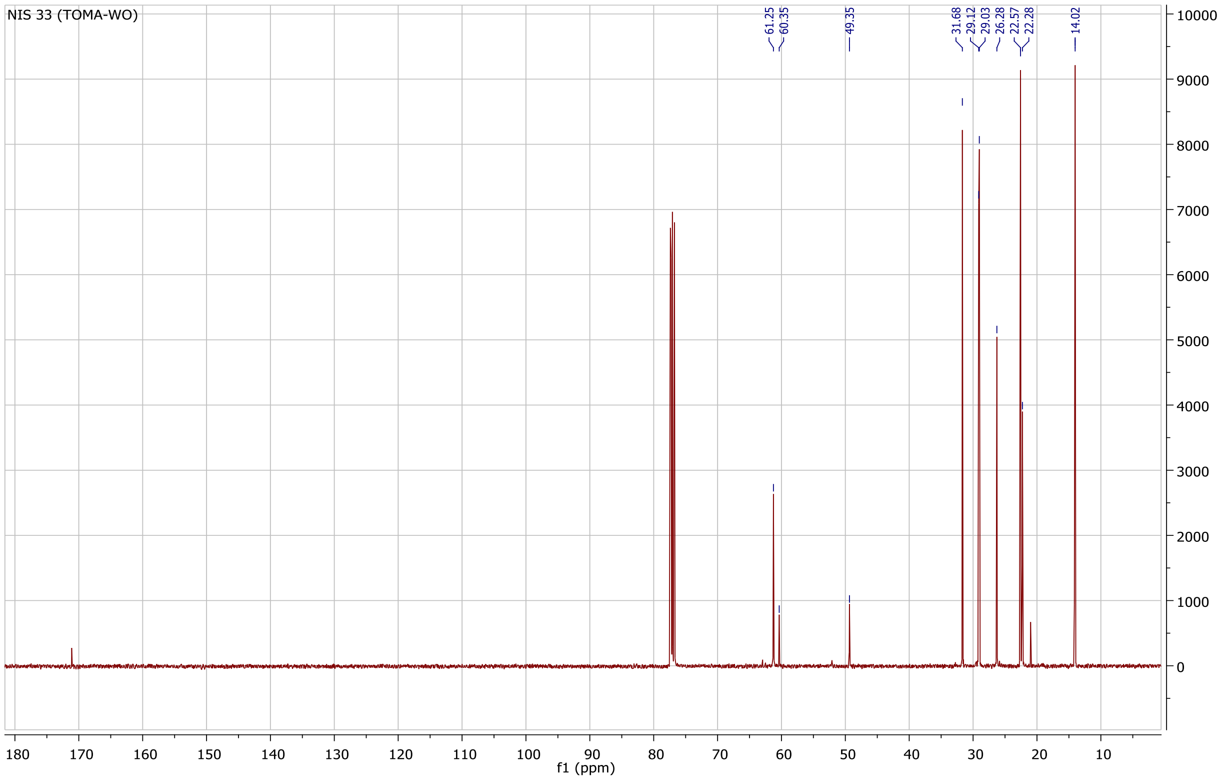


^{13}C-NMR (100MHz, DMSO) (1-Butyl-3-Methyl-2-Carboxy-Imidazolium): δ = 13.76, 19.39, 32.59, 36.85, 48.97, 112.8, 121.42, 122.8, 159.19.
^{13}C-NMR (100MHz, DMSO) (BMIM-MC): δ = 13.65, 19.21, 31.88, 36.00, 48.97, 51.51, 122.71, 124.02, 137.65, 156.83.

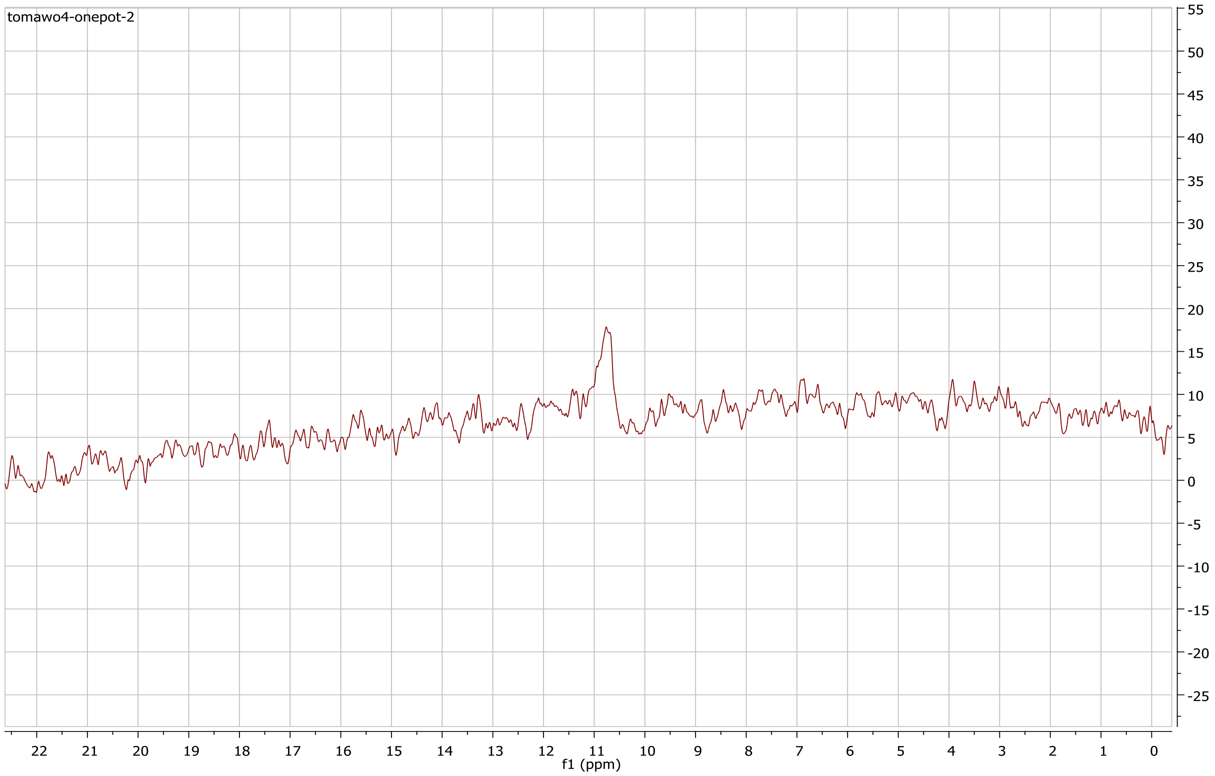
Trioctylmethylammonium-tungstate ($[N_{8,8,8,1}]_2(WO_4)$, **2a**)



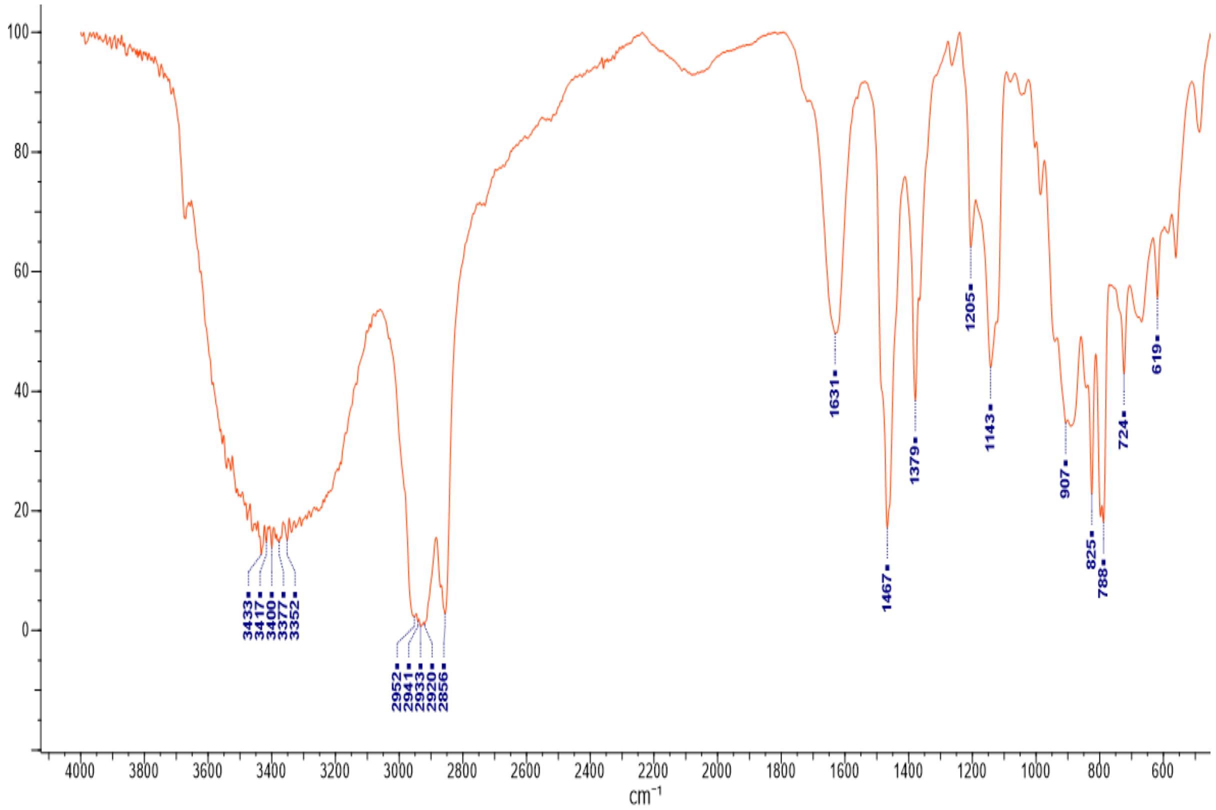
^{1}H-NMR (400MHz, $CDCl_3$): δ = 0.86 (t, J=6.9Hz, 9H), 1.17-1.45 (m, 30H), 1.67 (m, 6H), 3.36(s, 3H), 3.38 (m, 6H)



^{13}C-NMR (100MHz, CDCl$_3$): δ = 61.25, 49.35, 31.68, 29.12, 26.28, 22.57, 22.28, 14.02.

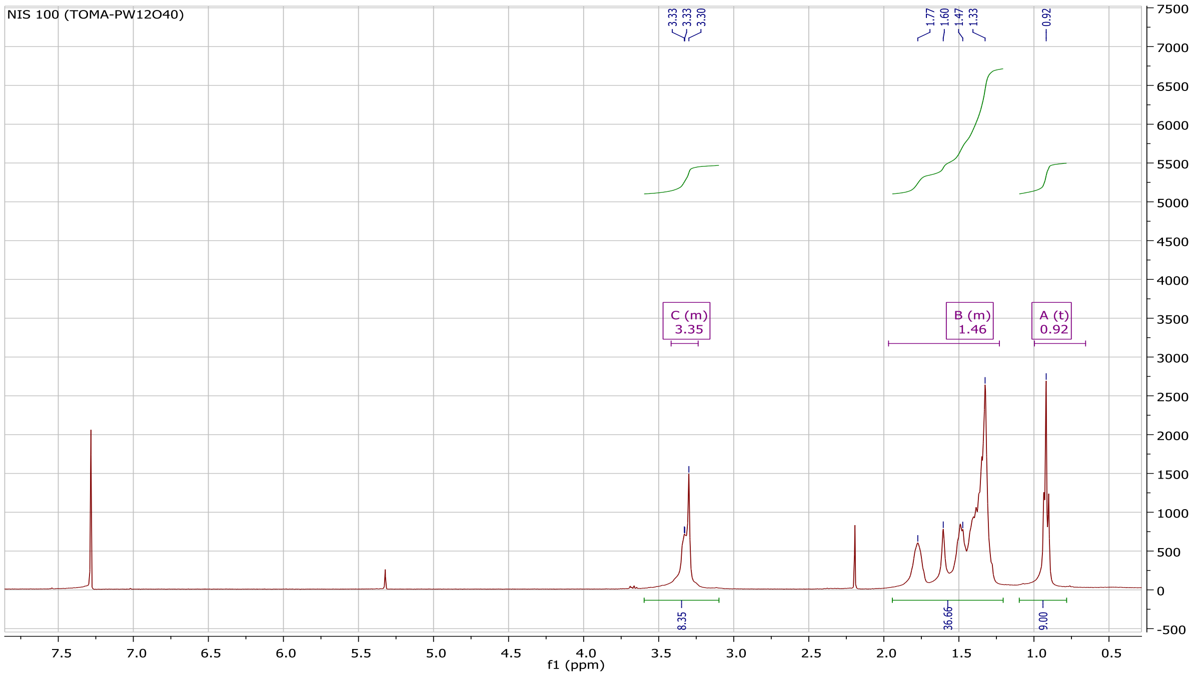


^{183}W-NMR

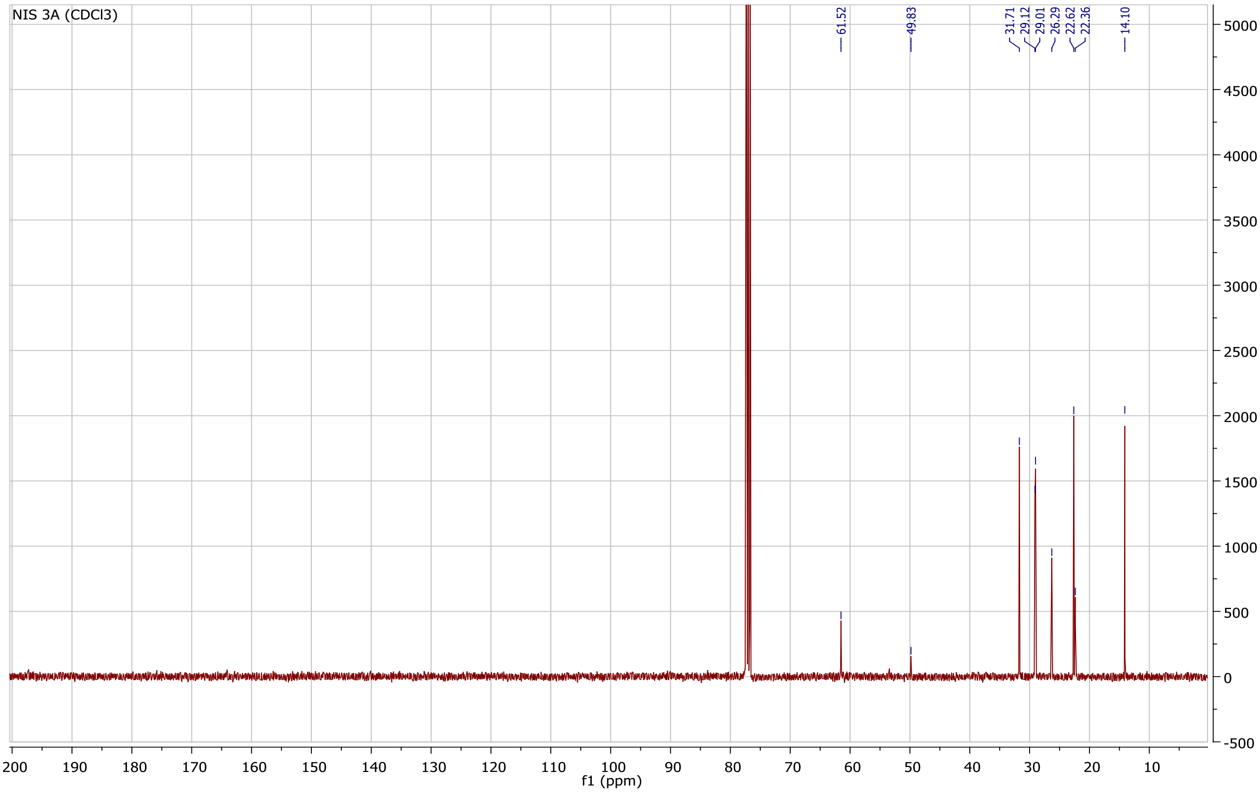


FT-IR

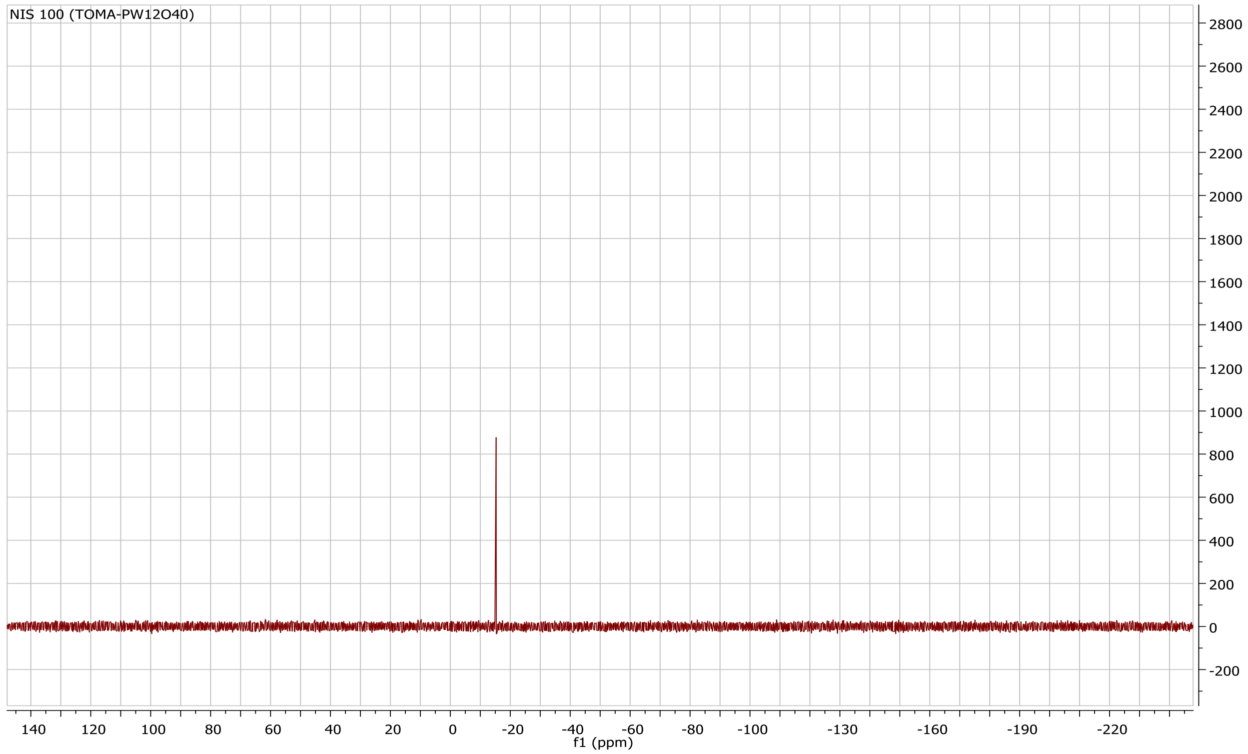
Trioctylmethylammonium-phosphotungstate ($[N_{8,8,8,1}]_3(PW_{12}O_{40})$, **2b**)



^{1}H-NMR (400MHz, $CDCl_3$): δ = 0.87 (t, J=6.9Hz, 9H), 1.25-1.72 (m, 36H), 3.37-3.75(m, 8H).

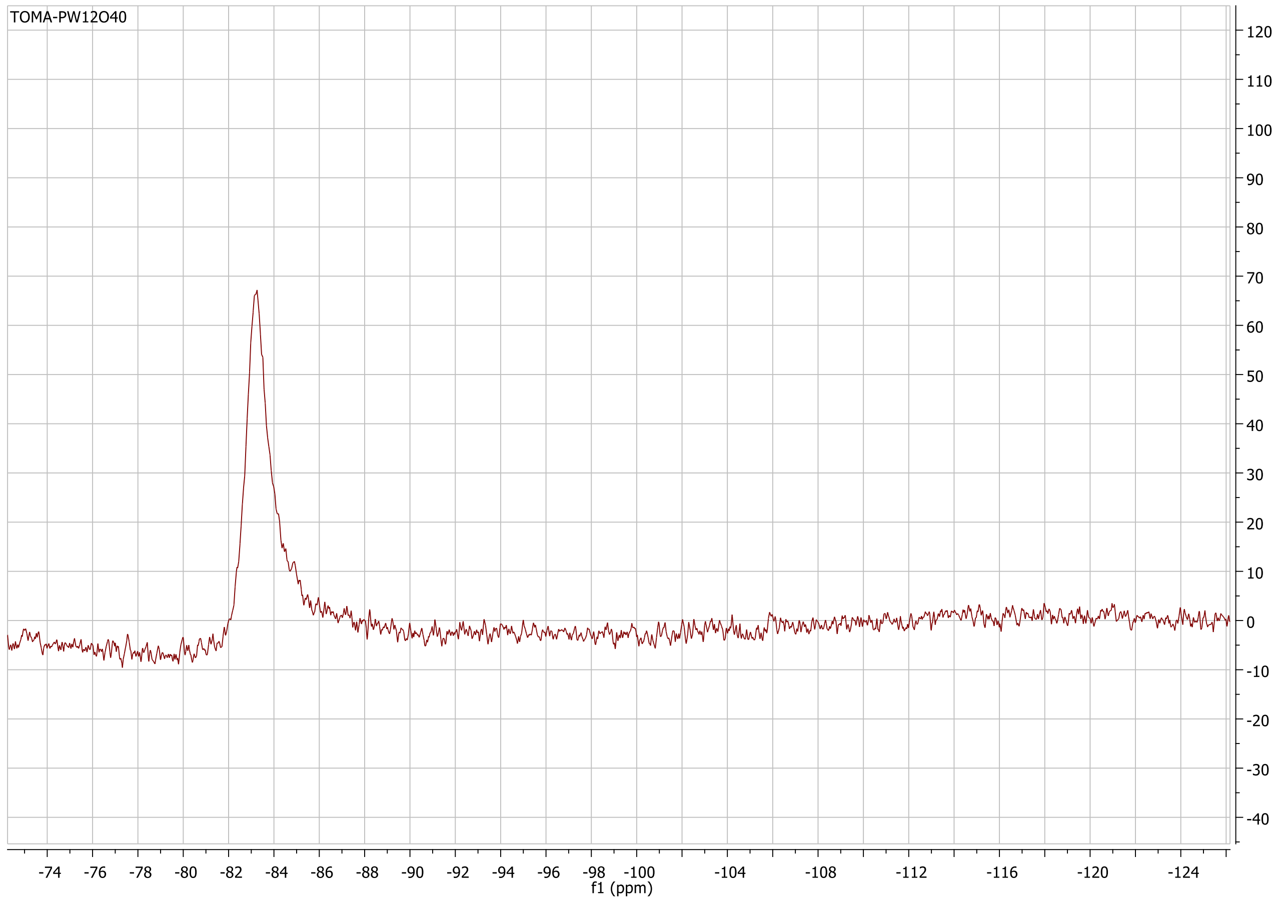


^{13}**C-NMR (100MHz, CDCl$_3$):** δ = 14.1, 22.36, 22.62, 26.29, 29.01, 29.12, 31.71, 49.83, 61.52

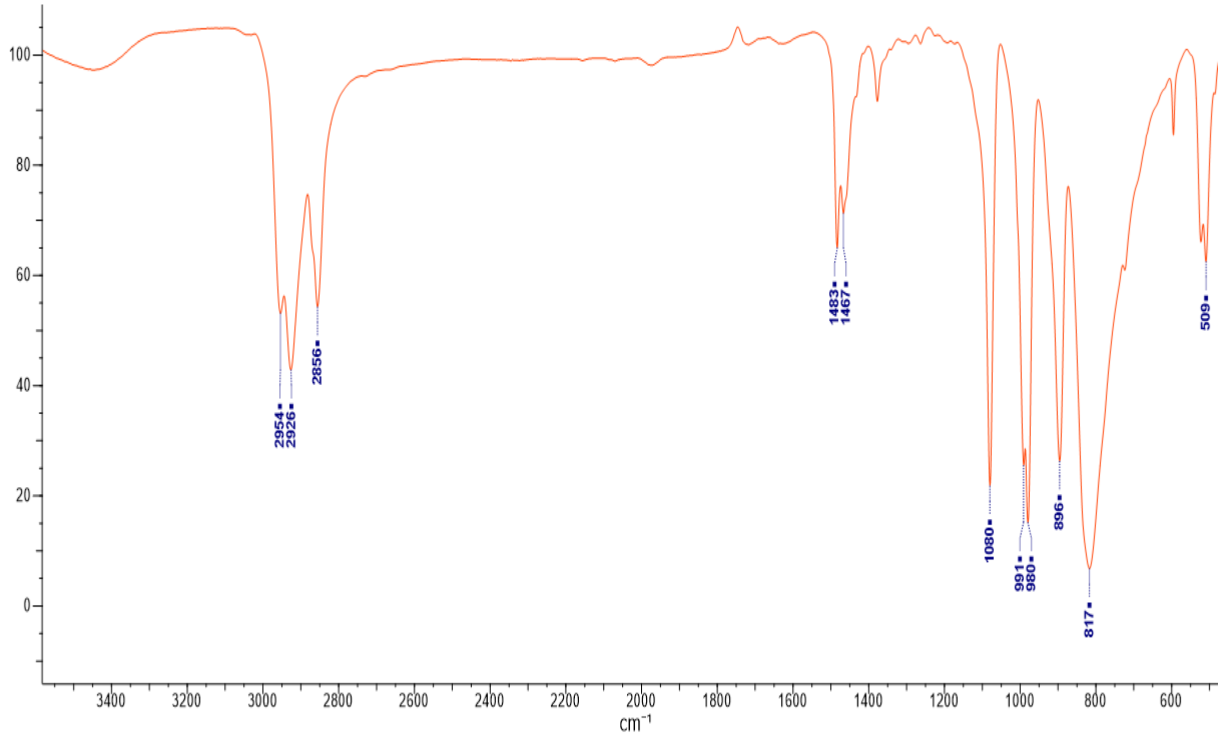


^{31}**P-NMR (162MHz, CDCl$_3$):** δ = -15.29.

-

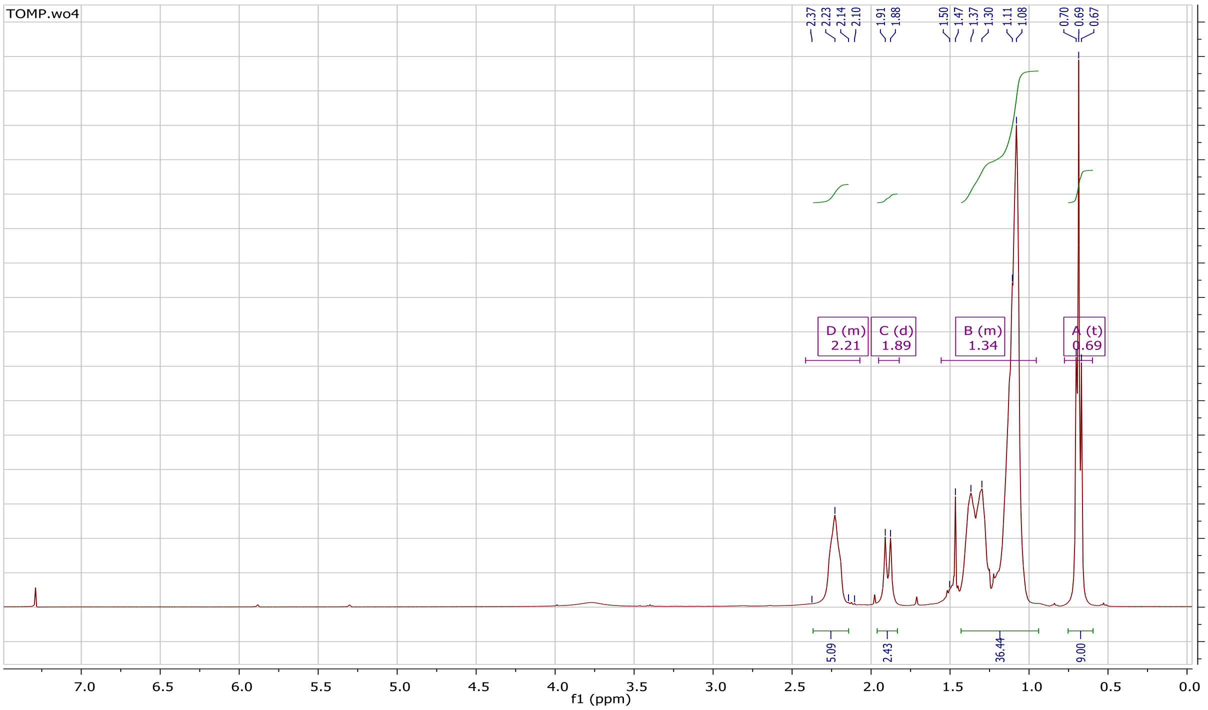


^{183}**W-NMR**

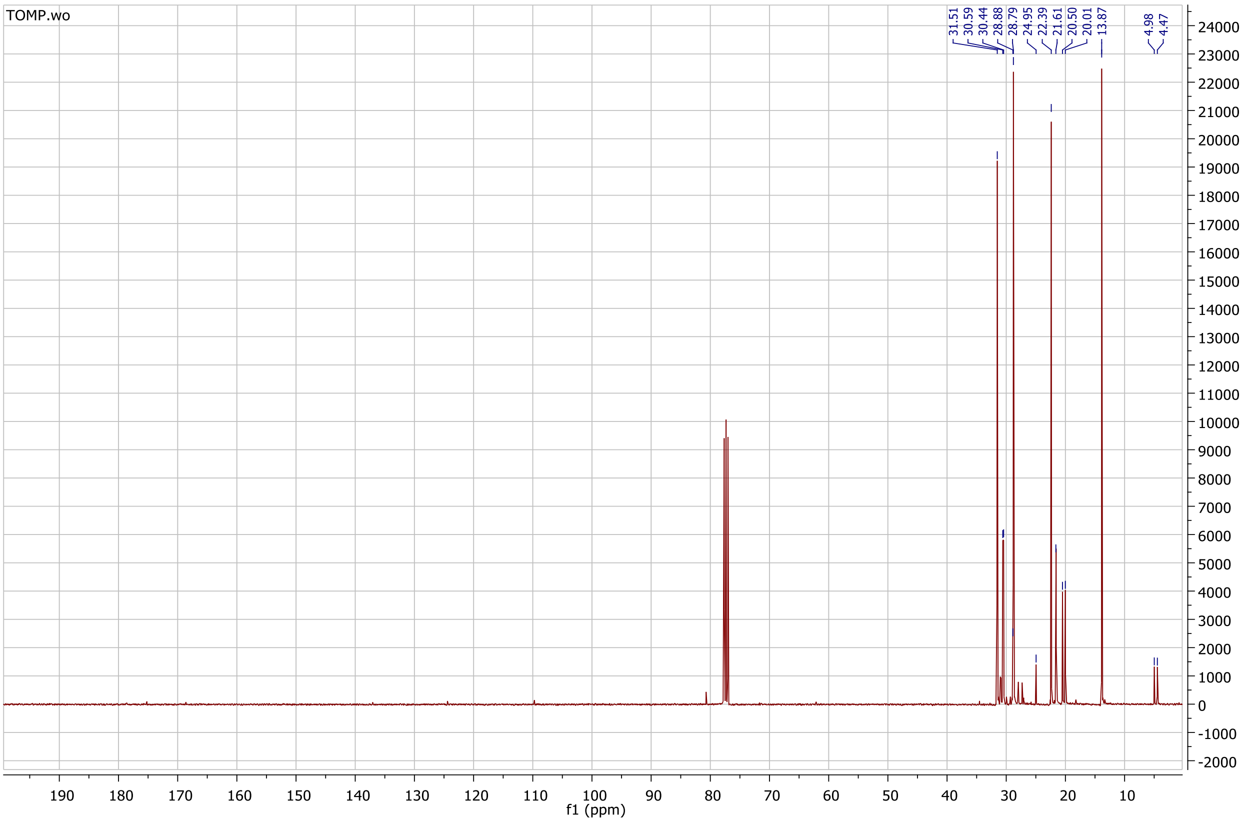


FT-IR

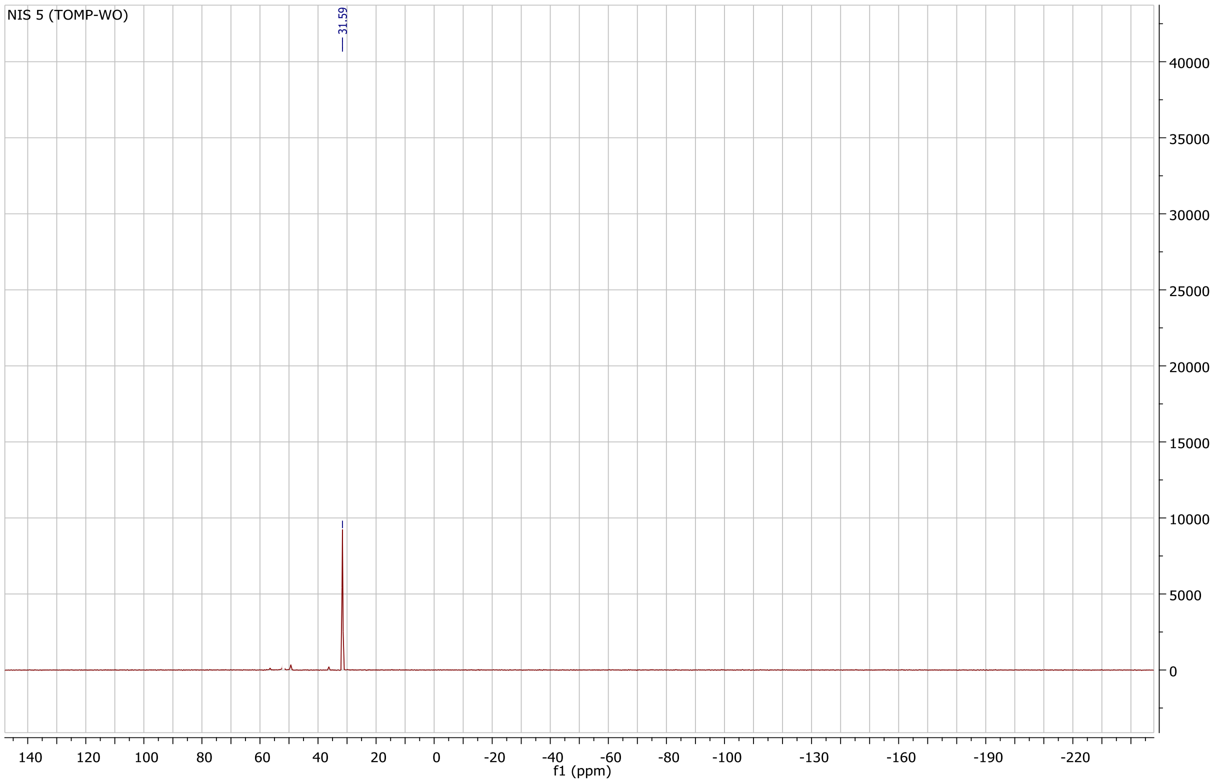
Trioctylmethylphosphonium-tungstate ($[P_{8,8,8,1}]_2(WO_4)$, **2c**)



^{1}H-NMR (400MHz, CDCl$_3$): δ = 0.69 (t, J=6.7Hz, 9H), 1.00-1.50 (m, 36H), 1.85-1.95(d, J=13.3Hz, 3H), 2.21 (m, 6H).



^{13}C-NMR (100MHz, CDCl$_3$): δ = 4.47, 4.98, 13.87, 20.01, 20.50, 21.61, 22.39, 24.95, 28.79, 28.88, 30.44, 30.59, 31.51.



^{31}P-NMR (162MHz, CDCl$_3$): δ = 31.53.

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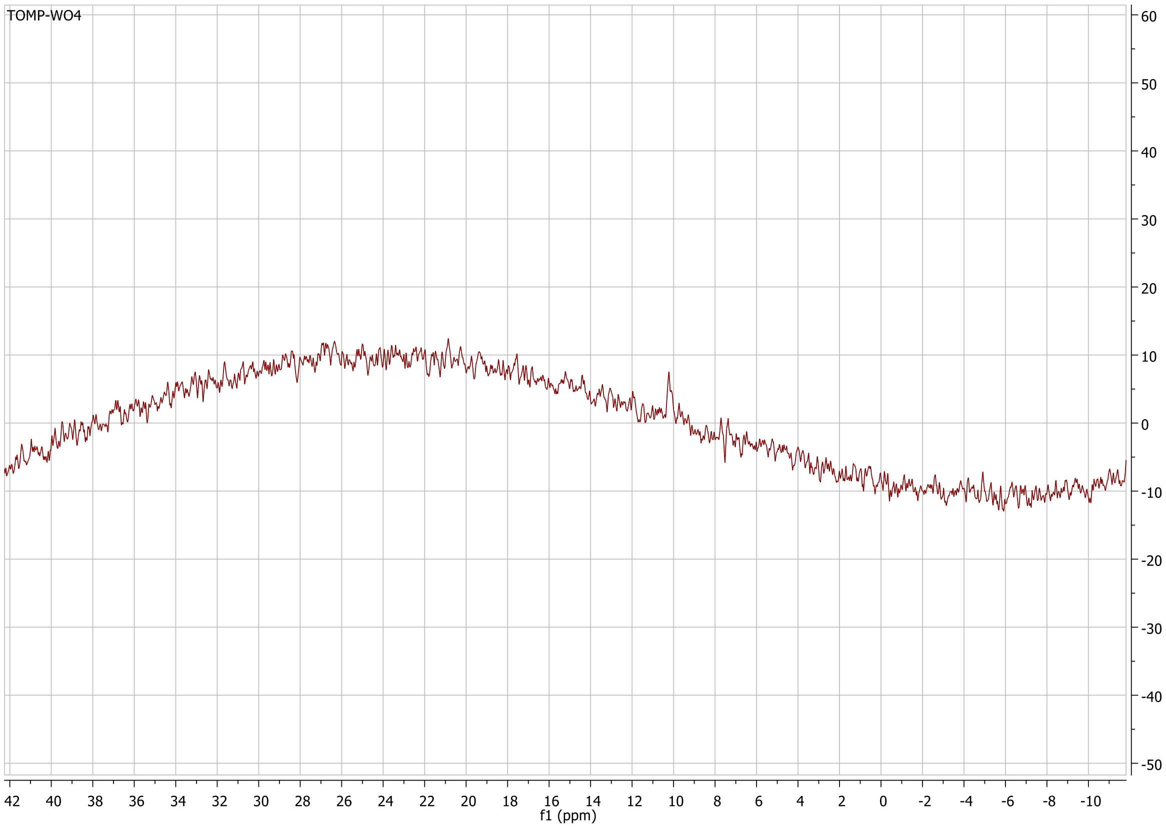
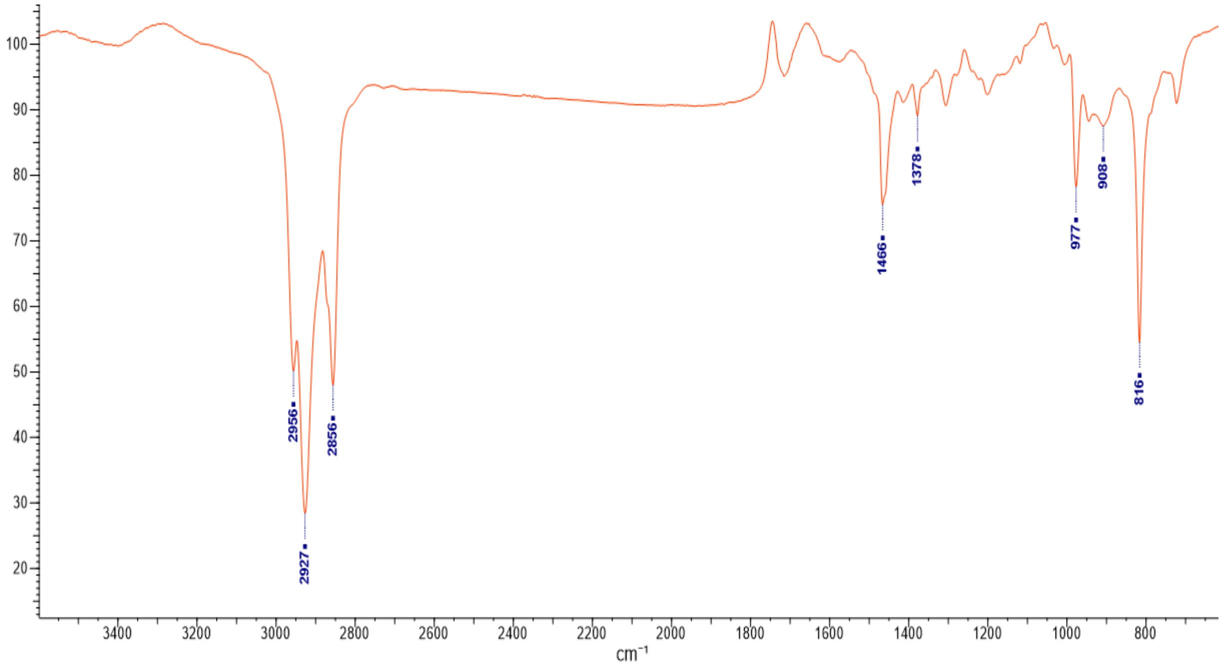
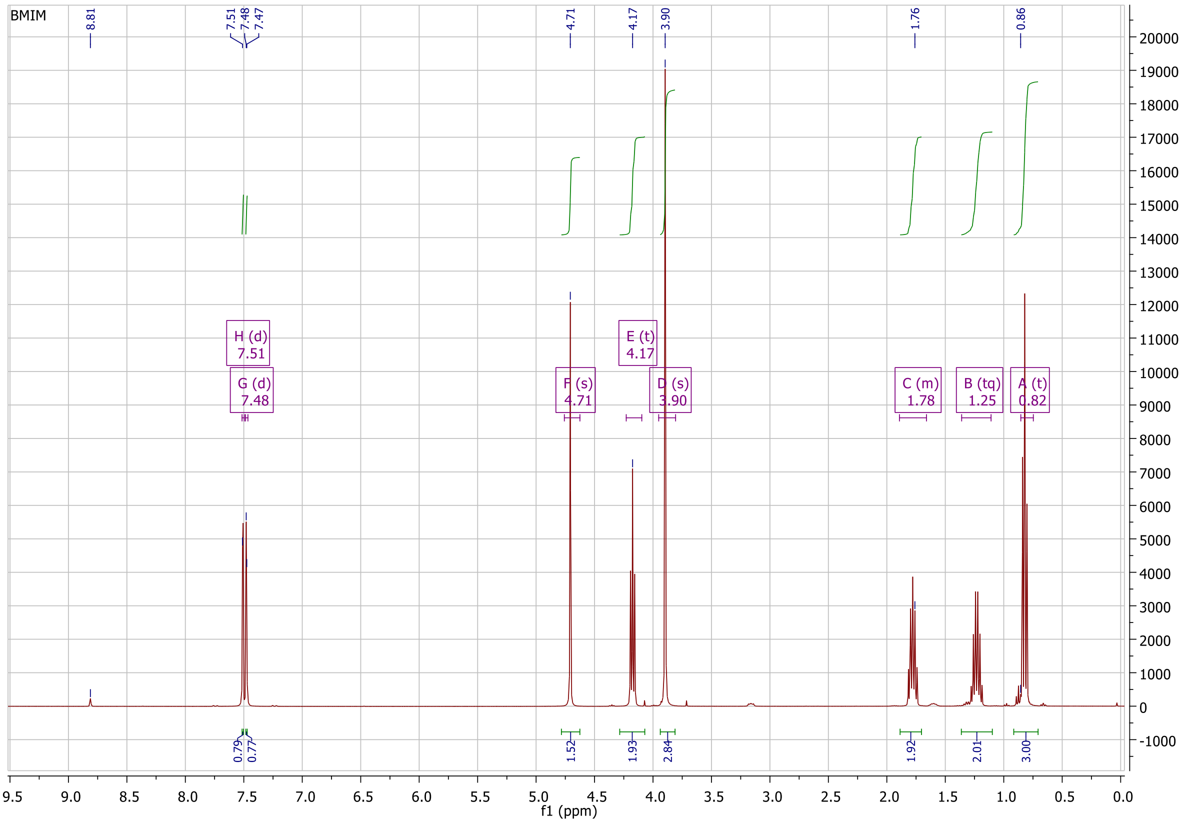


^{183}W-NMR

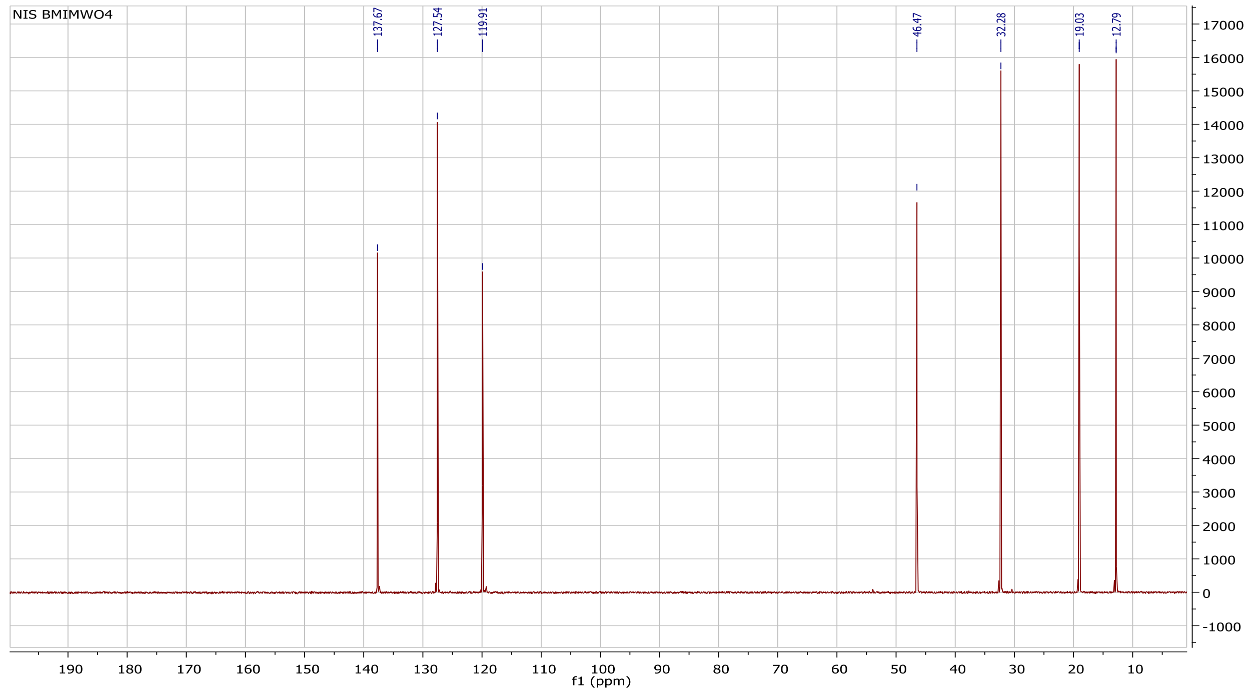


FT-IR

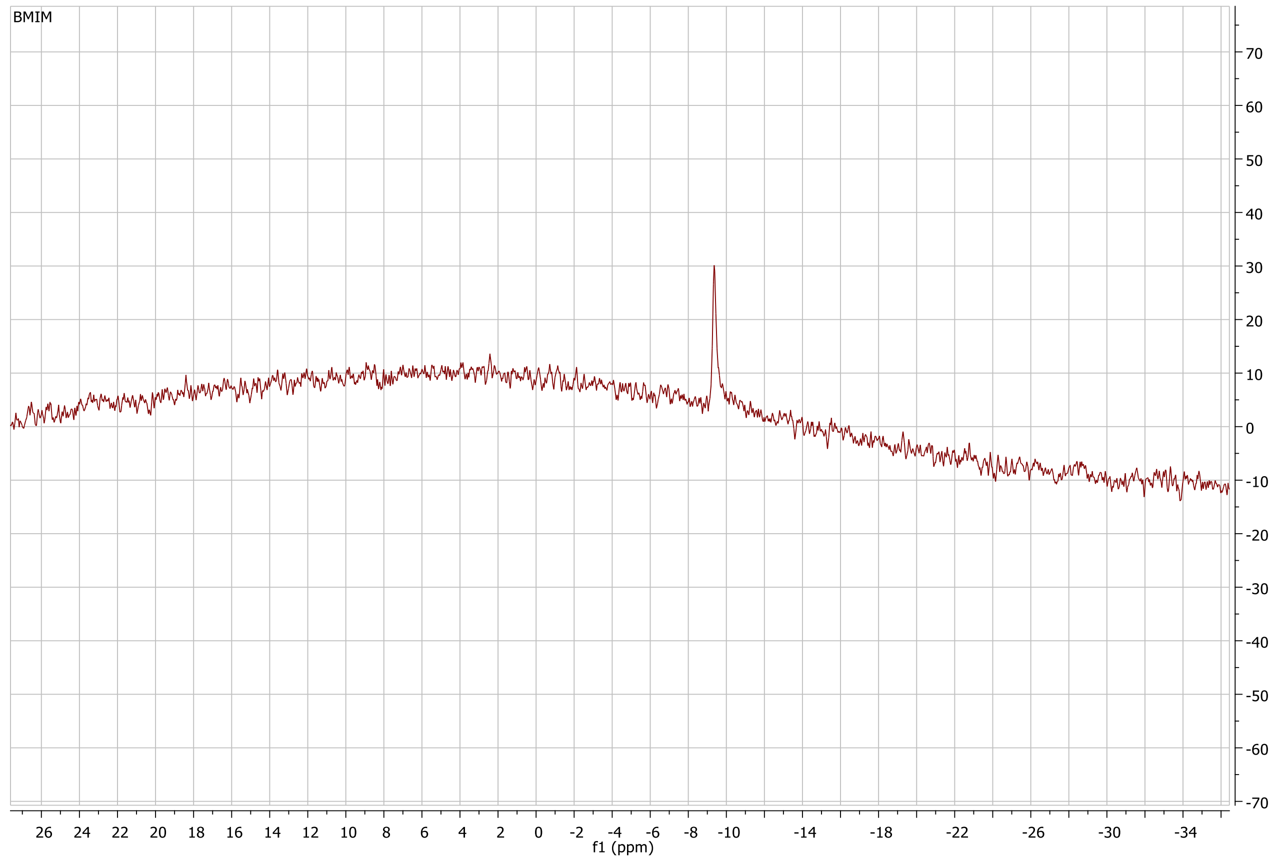
1-butyl-3-methyl-ammonium tungstate ([BMIM]$_2$(WO$_4$), **2d**)



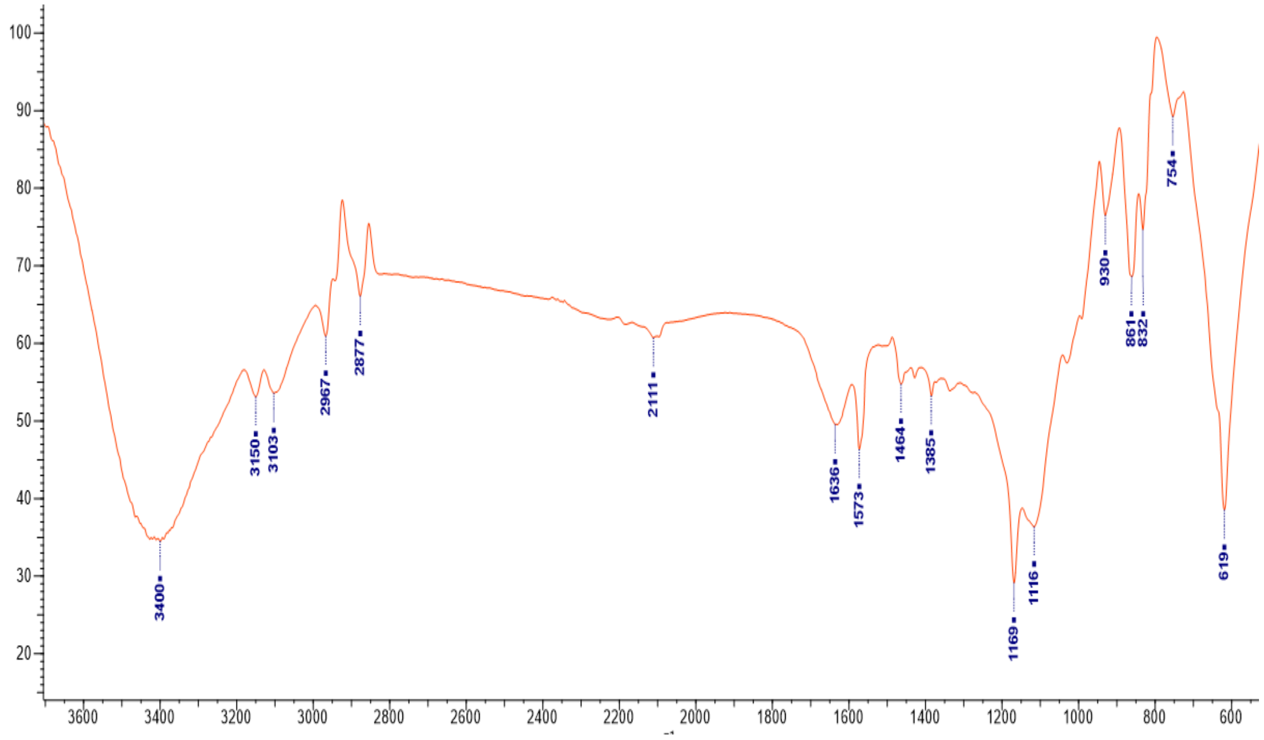
^{1}H-NMR (400MHz, D$_2$O): δ = 0.82 (t, J=7.4Hz, 3H), 1.18-1.29 (tq, J=14.8, 7.3Hz, 2H), 1.74-1.81(m, 2H), 3.90 (s, 3H), 4.17 (t, J=7.2Hz, 2H), 4.71 (s, 1H), 7.48 (d, J=2.0Hz, 1H), 7.51 (d, J=2.0Hz, 1H), 8.81 (bs, 1H).



^{13}C-NMR (100MHz, D_2O): δ = 12.79, 19.03, 32.28, 46.47, 119.91, 127.54, 137.67.

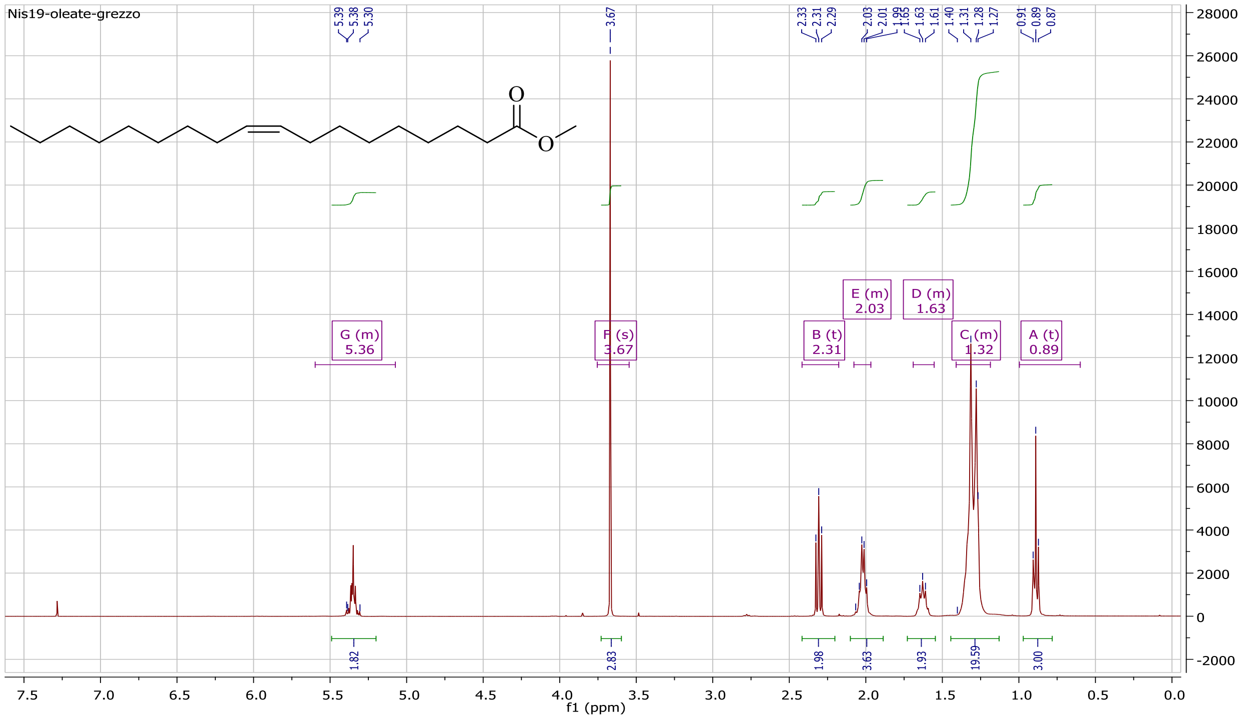


^{183}W-NMR

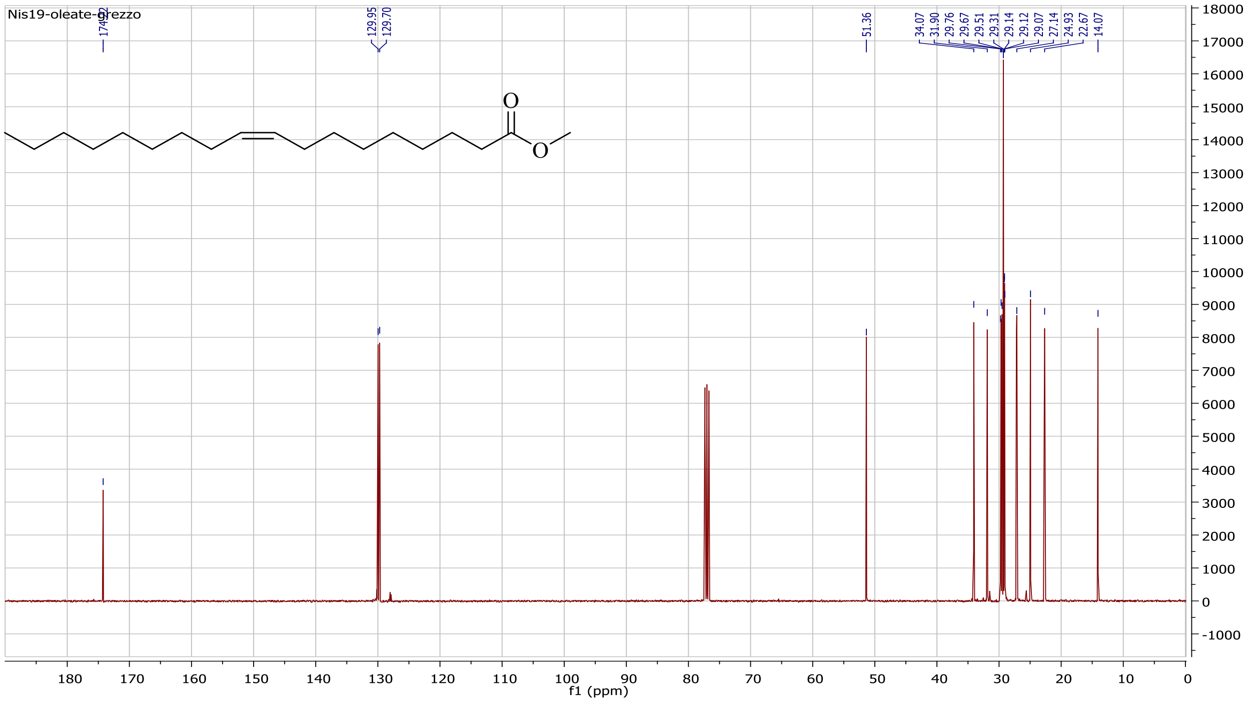


FT-IR

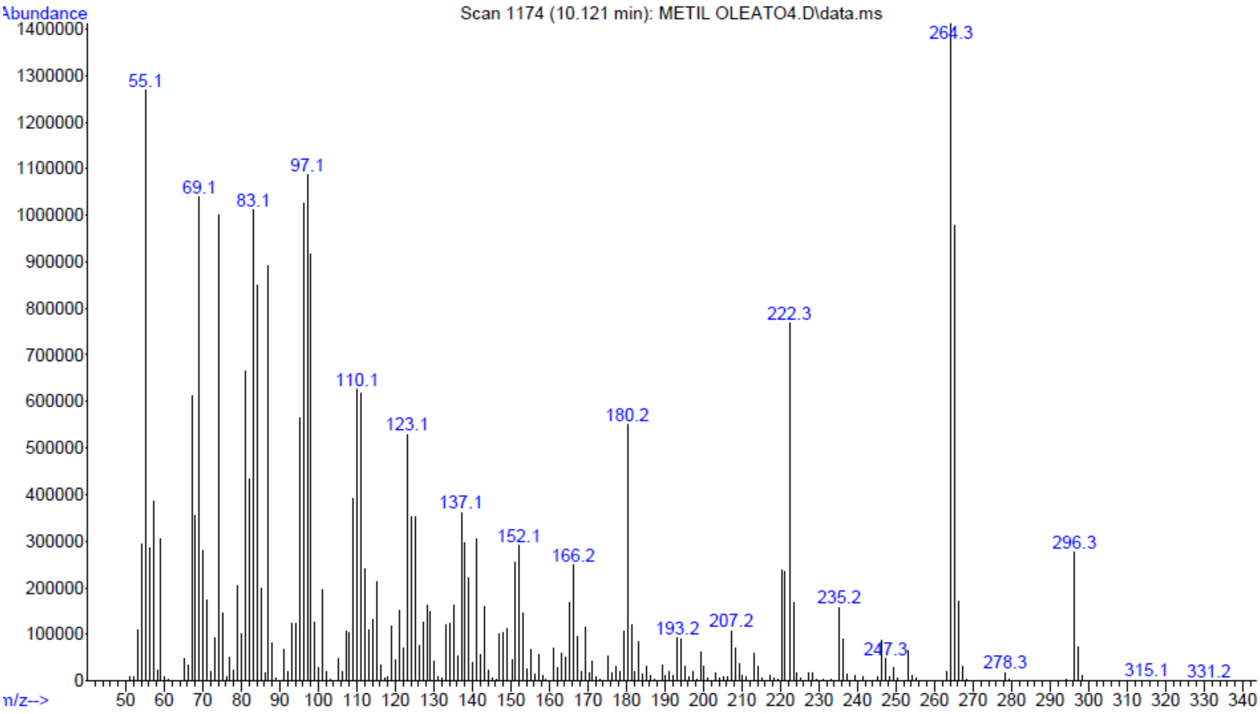
Methyl Oleate (**3**)



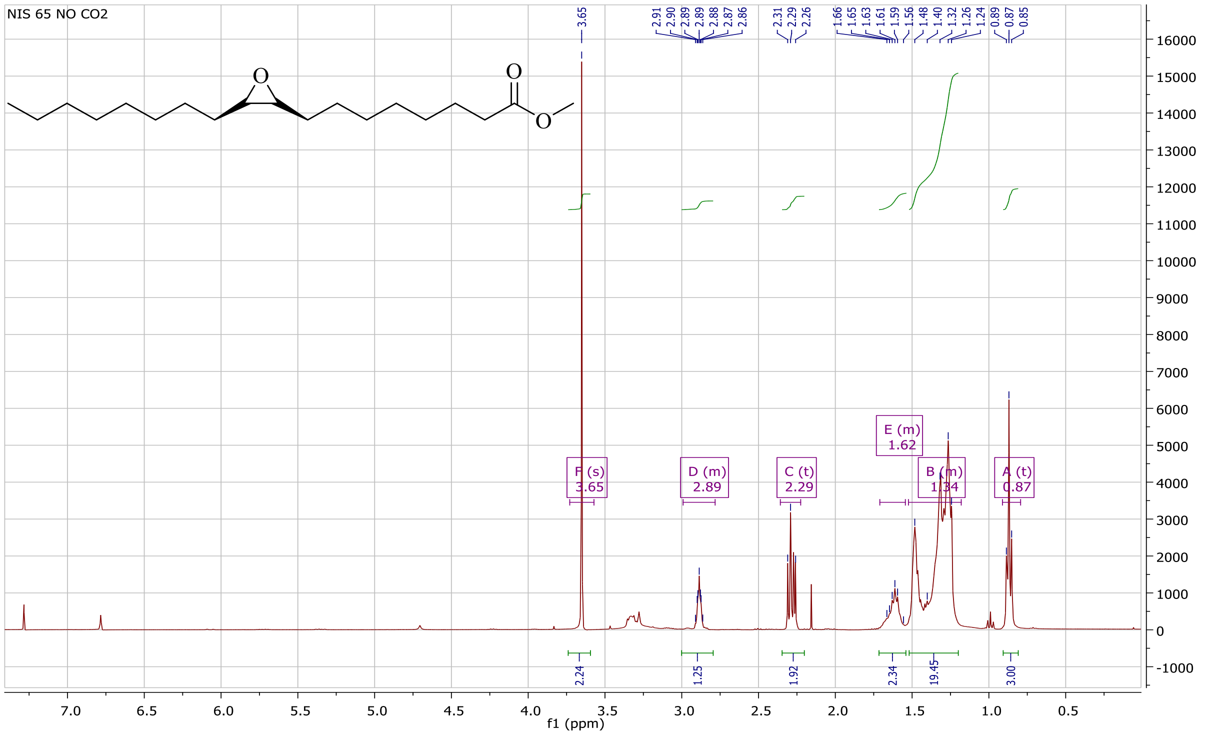
^{1}H-NMR (400MHz, CDCl$_3$): δ = 0.89 (t, J=6.9Hz, 3H), 1.25-1.40 (m, 20H), 1.63 (m, 2H), 2.03 (m, 4H), 2.31 (t, J=7.6Hz, 4H), 3.67 (s, 3H), 5.30-5.39 (m, 2H).



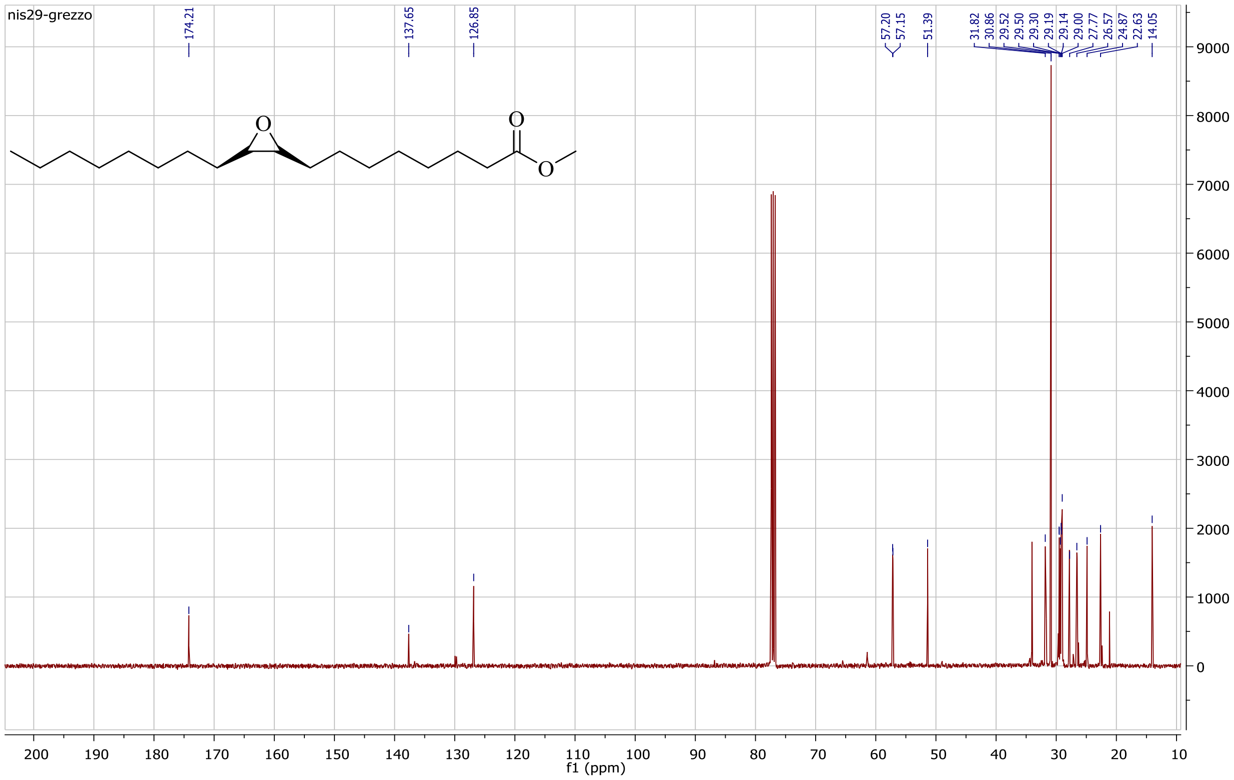
^{13}C-NMR (100MHz, CDCl$_3$): δ = 14.07, 22.67, 24.93, 27.14, 27.20, 29.07, 29.12, 29.14, 29.31, 29.51, 29.67, 29.76, 31.90, 34.07, 51.36, 129.70, 129.95, 174.42.



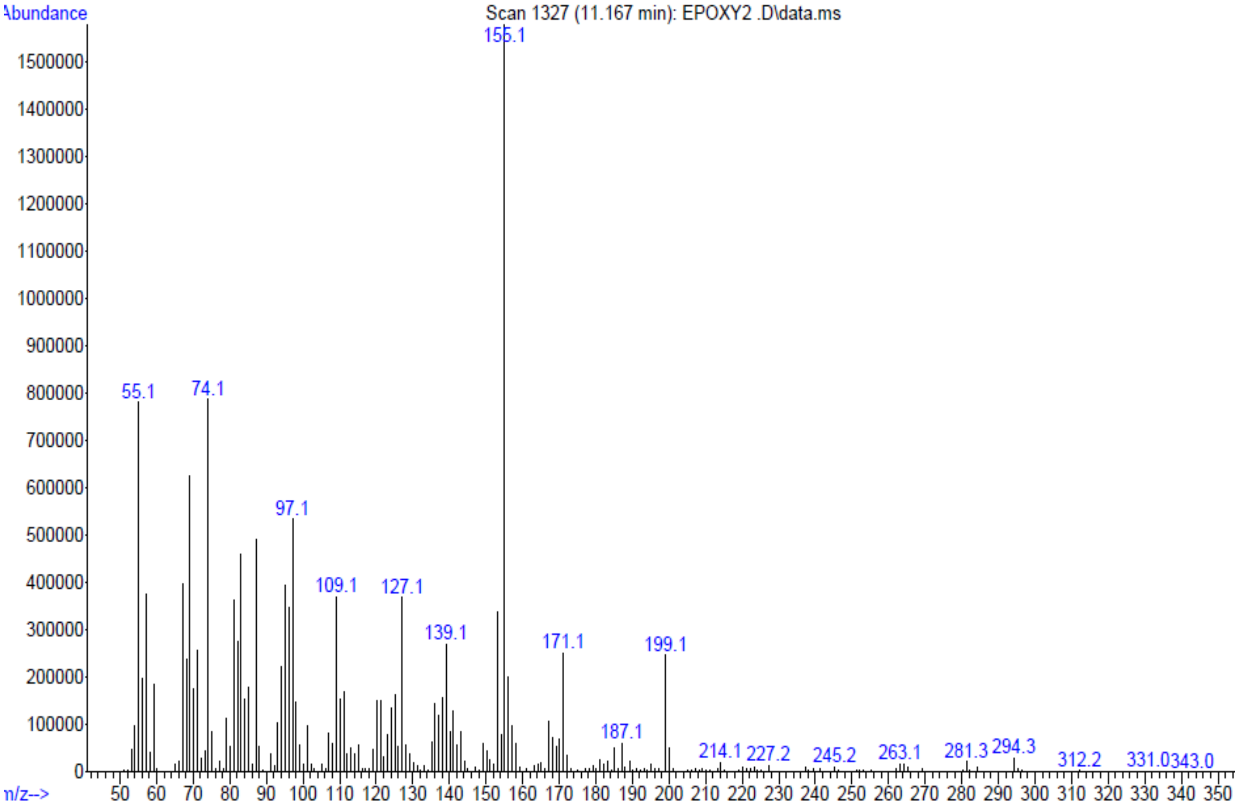
methyl 8-((2R,3S)-3-octyloxiran-2-yl) octanoate (*cis*-**4a**)



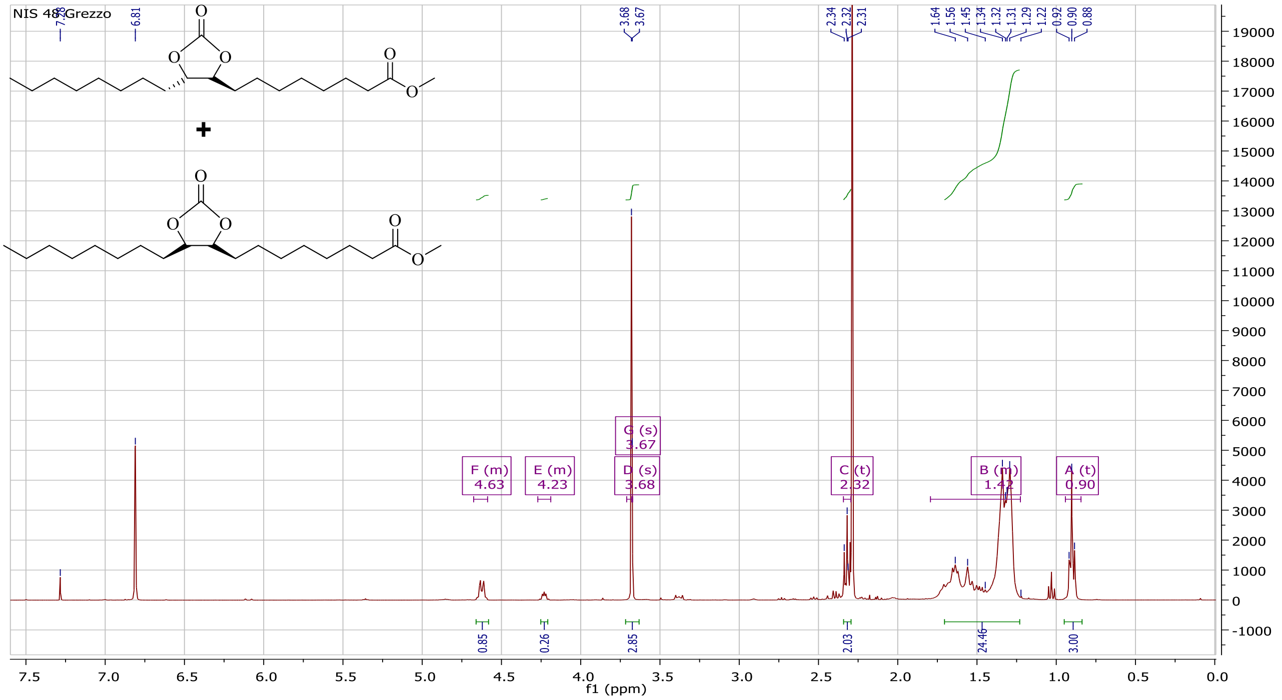
^{1}H-NMR (400MHz, CDCl$_3$): δ = 0.87 (t, J=6.9Hz, 3H), 1.20-1.55 (m, 20H), 1.55-1.70 (m, 2H), 2.25-2.32 (t, J=10.32Hz, 2H), 2.89 (m, 2H), 3.65 (s, 3H).



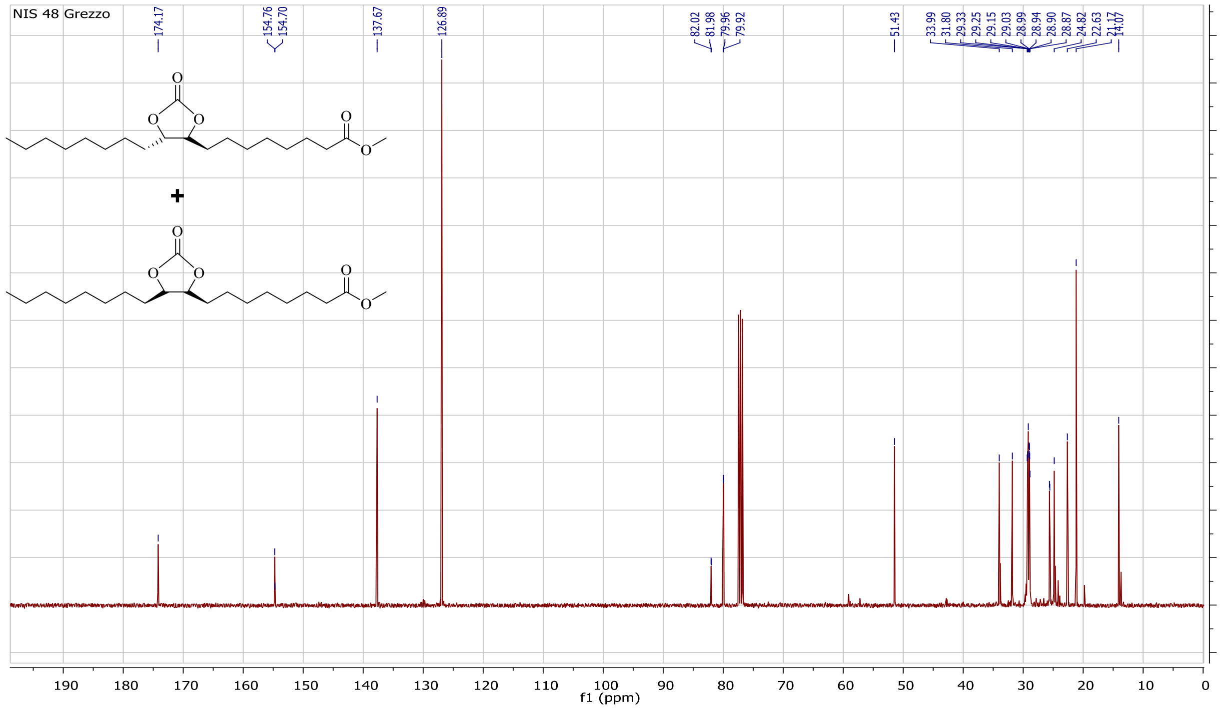
^{13}C-NMR (100MHz, CDCl$_3$): δ = 14.05, 22.63, 24.87, 26.57, 27.77, 29.00, 29.14, 29.19, 29.30, 29.50, 29.52, 30.86, 31.82, 51.39, 57.15, 57.20, 174.21.



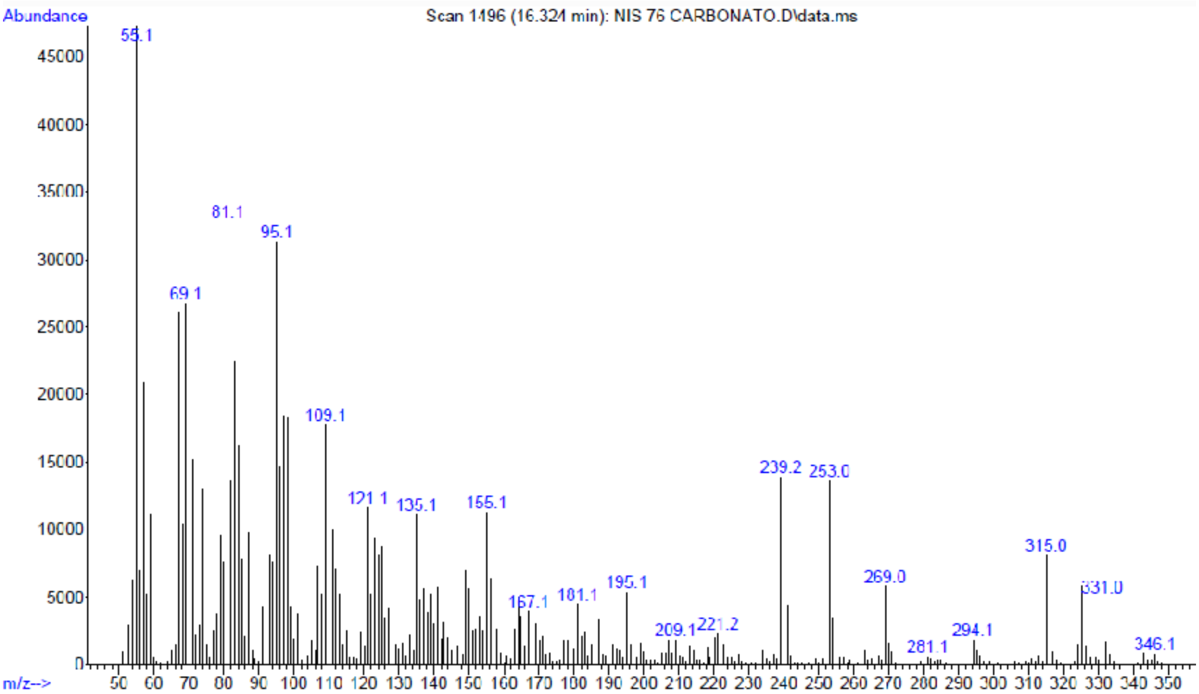
methyl 8-(5-octyl-2-oxo-1,3-dioxolan-4-yl) octanoate (-*cis* and -*trans* **5a**)



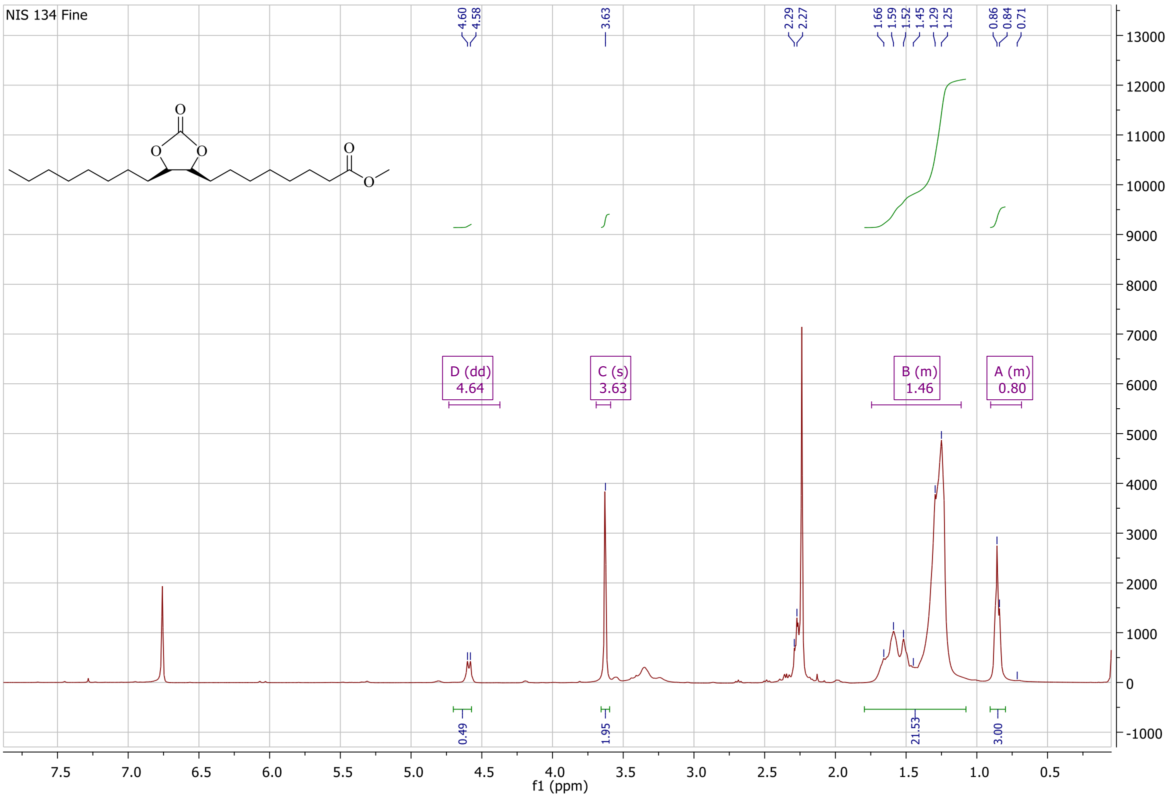
^{1}**H-NMR (400MHz, CDCl$_3$):** δ = 0.90 (t, J=6.9Hz, 3H), 1,25-1,75 (m, 24H), 2.37 (t, J=4.9Hz, 2H), 3.67 (s, 3H), 3.68 (s, 3H), 4.23 (m, 2H), 4.63 (m, 2H).



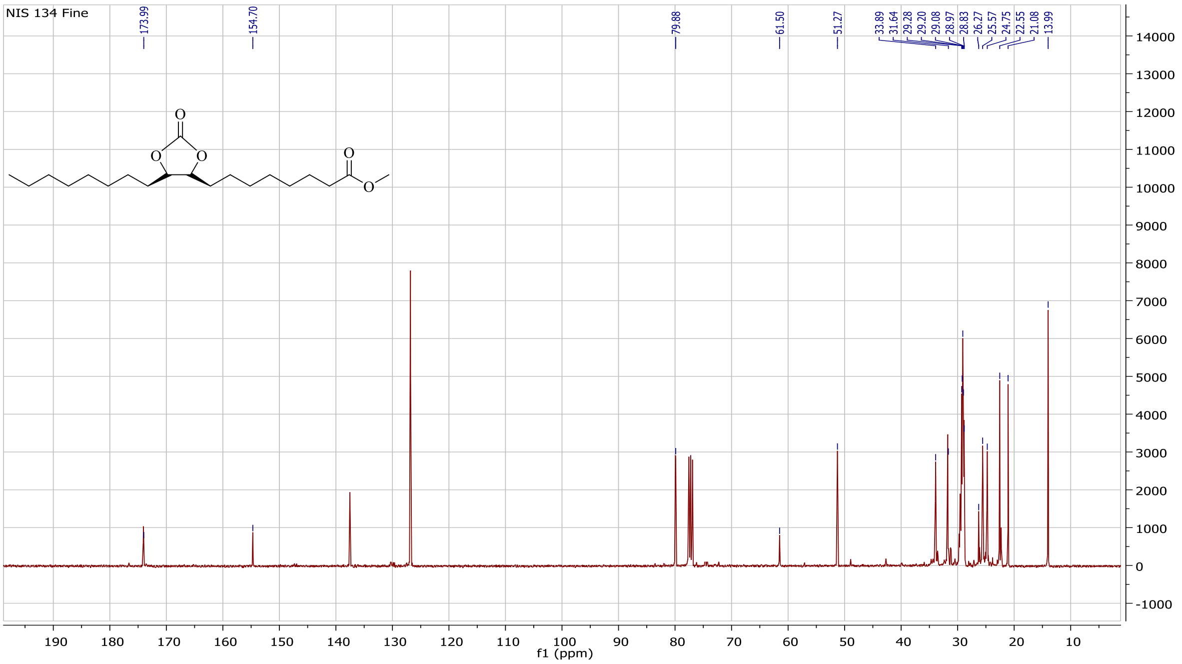
^{13}C-NMR (100MHz, CDCl$_3$): δ = 13.68, 14.07, 21.17, 22.63, 24.82, 25.55, 25.61, 28.87, 28.90, 28.94, 29.03, 29.12, 29.15, 29.18, 29.25, 29.33, 31.80, 33.90, 51.40, 51.43, 79.92, 79.96, 137.67, 154.70, 154.76, 174.17



cis-methyl 8-(5-octyl-2-oxo-1,3-dioxolan-4-yl) octanoate (*cis*-**5a**)



^{1}H-NMR (400MHz, CDCl$_3$): δ = 0.80 (m, 3H), 1.25-1.66 (m, 24H), 2.27 (m, 2H), 3.63 (s, 3H), 4.64 (m, 2H).



^{13}C-NMR (100MHz, CDCl$_3$): δ = 13.99, 21.08, 22.25,22.57, 24.75, 25.57, 26.27, 28.83, 28.97, 29.01, 29.08, 29.20, 29.28, 31.64, 33.89, 51.27, 61.50, 79.88, 154.70, 173.99.

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