

One-pot aerobic cleavage of mono-unsaturated lipids catalysed by mixed-oxides

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ABSTRACT: The oxidative cleavage of non-eatable monounsaturated lipids such as restaurant olive oil or oil extracted from high oleic sunflowers-HOSO is the way to produce useful C9 mono- and di-carboxylic acids, namely pelargonic and azelaic acid, respectively. In this paper we describe the synthesis and application of mixed oxides as cheap, recoverable and reusable catalysts for the one-pot conversion of non-eatable oils into products that may find application in several fields, from the cosmetic industry, to the agrochemical sector (pelargonic acid) and to the bio-polymer technologies (azelaic acid). The catalysts developed use oxygen as oxidant and the alcohol selected for producing the esters as solvent or can operate in solventless conditions. The same catalyst is used for oxidation and transesterification/ esterification. The oxidation is carried out under moderate P_{O2} (0.6-0.8 MPa) and temperature (413-433 K) in 2-3 h. The conversion yield and selectivity towards the

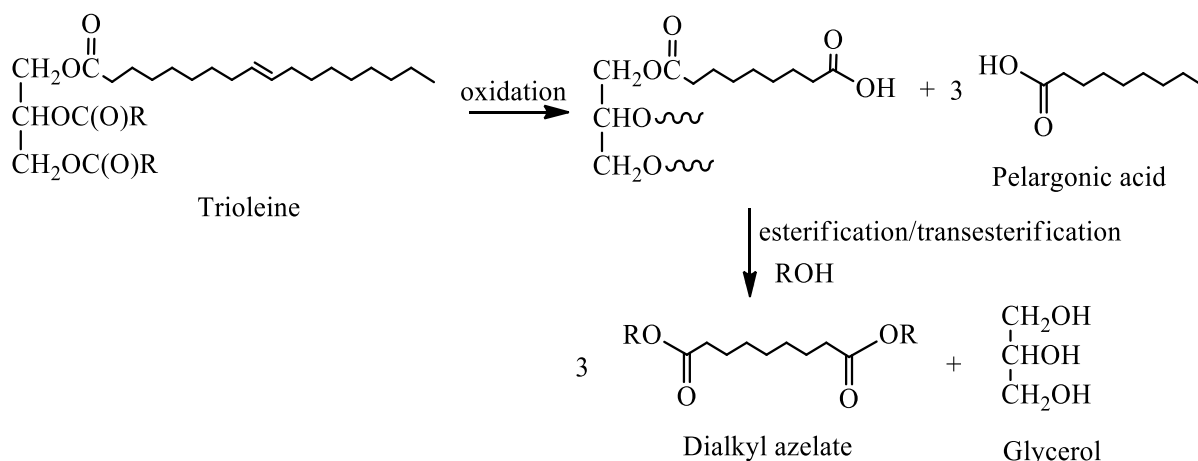
target products depend on both the catalyst composition and the reaction conditions. In best cases, 63-72% of a mixture of C7-C9 acids with 40-56% of C9 (% yield of C9 with respect to the starting oil) have been obtained that represent the best cases so far available. The reaction pathway has been revealed by using a flow-reactor that has allowed to detect along time the species formed and measure their concentration by GC-MS. This research has produced five key innovations, namely: i. One-pot one- or two-step process for the conversion of mono-unsaturated oils into mono- and di-carboxylic acids; ii. Use of oxygen as oxidant instead of ozone or hydrogen peroxide; iii. Elimination of sulphuric acid in the esterification/transesterification step; iv. Use of cheap-, recoverable-and reusable-mixed oxides as catalysts; v. Use of a single catalyst for both the oxidation and esterification-transesterification steps.

KEYWORDS: oxidative cleavage of lipids, mixed oxides, heterogeneous catalysis, oxygen as oxidant, catalyst recycle.

Introduction

The ever-increasing production and use of non-biodegradable fossil-C-based plastics has generated in last decades serious environmental problems. Despite the positive aspects such as the cheapness, easy manufacture and lightness of the materials that make them versatile for a variety of single-use applications, plastics having long timespan (decades) because of the stable chemical bonds in the extended polymeric structure, accumulate in natural compartments. Their relative physical resistance makes that can be converted into micro-particles (microplastics) that may cause serious damages to living organisms. Industries are yearly producing over 360 million tons-Mt/y of plastics, with more than 8 Mt/y used goods being dumped into oceans.¹ Although society is increasingly implementing the synthetic polymer recycling policy, nevertheless today less than 9% of polymeric waste is collected

and *ca.* 2% reused in high-value applications.² Developing sustainable polymeric materials from bio-based sources has drawn a great deal of interest, but bio-based polymers currently represent only 4.25% of the entire plastics market.³ Biomass derivatives are proving very successful as they can have characteristics very similar to fossil-C derivatives. However, bio-based plastics (not to be confused with bio-degradable items), being produced from renewable carbon resources, obey the concept of “carbon neutrality”.^{4,5} They are attracting major interest as a strategy for the efficient conversion of cheap renewable resources into bio-based large-scale materials. Until recently, bio-based precursors have been obtained from first-generation biomass resources, like glucose or starch, a use that directly competes with food and feed, even making a non-optimal use of arable land. More correctly, non-edible second-generation feedstock must be used to produce bio-monomers.⁶ Lignocellulosic material is an example, which requires chemical or microbial procedures for depolymerization to afford monomers⁷⁻¹⁰ or their derivatives.¹¹⁻¹⁴ An additional potential source of monomers are non-eatable lipids that are extracted in form of oil from seeds or animal-fat. Recycled restaurant-oils are also a useful matrix. Monounsaturated fatty acids (MUFAs), such as oleic acid that represent 99% of olive-oil and up to 80% of high-oleic sunflower oil, can be exploited to this end. In fact, the over-oxidation of the double bond at 9,10-C position of the oleic chain can produce two C9 moieties, a monocarboxylic acid (pelargonic acid) and a dicarboxylic acid (azelaic acid). Polymers derived from the latter have interesting properties, such as high impact strength, hydrolytic stability, hydrophobicity, low glass transition temperatures and flexibility.¹⁵ Azelaic acid or its esters are also used in the treatment of acne,¹⁶ as building block for the nylon synthesis^{17,18} or have other uses in the plastic industry. As mentioned before, triglycerides over-oxidation produces also pelargonic acid (used as surfactant, herbicide and in the cosmetic industry) and glycerine, as shown in Scheme 1.



Scheme 1. Conversion of tri-oleic lipids into mono- (pelargonic) and di-carboxylic acids (azelaic).

Such C9 mono- and di-carboxylic acids are rare in natural resources.¹⁹ In this paper, we present a simple one-pot synthetic approach to the heterogeneous aerobic catalytic oxidative double bond cleavage of MUFAs and in particular of the oleic fraction, bearing to the production of C7, C8 and C9 mono- and di-carboxylic acids and their esters. Our target in this work was the maximization of the selectivity towards azelaic and pelargonic acids/esters, using only molecular oxygen as oxidant, easily recoverable and Earth crust abundant mixed-metal-oxides as catalysts, in solvent-less conditions or using alcohol (methanol or, better, bio-butanol) as solvent and reagent for esterification-transesterification-reactions. The sequence of the reactions (“oxidation of net oil followed by esterification/transesterification” or “simultaneous oxidation in alcohol with transesterification of glycerides/esterification of free acids”), the reaction parameters (PO₂, temperature, time) and the recoverability/reusability of the catalyst have been investigated and the best “catalyst-parameter space” for maximizing the yield of C9 mono- and di-acids(esters) defined.

Experimental section

Materials. HOSO was a gift of NOVAMONT; Methanol anhydrous 99.8%, 1-Butanol anhydrous 99.8%, CeO₂ nanopowder, <25 nm particle size (BET), CeO₂ powder, 99.995% trace metals basis, Nb₂O₅ 99.99% trace metals basis, La₂O₃ 99.99% trace metals basis, Bi₂O₃ powder, 99.999% trace metals basis, K₂CO₃ reagent grade, ≥98%, powder, MgO ≥99.99% trace metals basis, TiO₂ powder, 99.8% trace metals basis, Ce(NH₄)₂(NO₃)₆ ≥ 99.99% trace metals basis, C₄H₄NNbO₉ 99.99% trace metals basis, La(NO₃)₃ · 6 H₂O 99.99% trace metals basis, Bi(NO₃)₃ · 5H₂O 99.999% trace metals basis, and TS-1 were purchased from Sigma-Aldrich. Oxygen and nitrogen cylinders were purchased from Rivoira.

Analytical methods. Glycerides gas-chromatographic analyses were carried out with a Thermo Trace GC Ultra on-column injector system equipped with FID detector and a Restek Rtx-5 capillary column. Mono carboxylic and dicarboxylic acids and esters yields were determined using a Shimadzu GC 2010 and Shimadzu GC-MS QP2020 plus using a Phenomenex Zebron ZB-5 column on both. The composition of the gas phase at the end of a catalytic run in a batch reactor was determined using a TCD-GC equipped with a capillary column Carboxen Plot 1010.

Mixed oxides were analysed using a Shimadzu EDX-700HS and the molar ratio of components determined.

Micromeritics Chemisorb 2750 was used for the determination of acid and basic sites and of the surface area of catalysts. NH₃ was used for the determination of acid sites, and CO₂ for the basic sites. The desorption was carried out in the interval 300-900 K. Weak sites desorb below 400 K, medium in the interval 400-600 K and strong above 600 K. Active sites were considered the medium- strong-sites. They were summed-up.

General procedure. All catalysts were dried at 403 K under vacuum for 2 hours before use and manipulated and stored under nitrogen to avoid surface contamination by air-born species, including water vapor.

Heating-cooling of the autoclave in the oxidation process. To better identify the reaction time and avoid inertia that might be different for the various tests, the heating system of the autoclave was preheated at the reaction temperature. After immersion in the heating jacket, the autoclave could reach the planned temperature in two minutes. Similarly, at the end of the reaction the autoclave was extracted from the heating jacket and immersed in a cooling bath so that room temperature was reached in almost 5-6 min in all cases.

Flow reactor. A Eylea Flow Master CCR-1100G, originally built for hydrogenation reactions, was adapted to the oxidation. The use of such equipment put a limit on the temperature (max 423 K) but allowed to dose the oxygen amount as it was possible to adjust the flow rate of the gas, keeping constant the flow of the substrate. The best parameters were found to be those reported in the text.

Preparation of the catalysts

Synthesis of MO1. MO1 was prepared as reported in the Patent cited in ref. 40.

Synthesis of MO1⁺⁺, MO1⁺⁺⁺, MO2, MO3. MO1⁺⁺, MO1⁺⁺⁺, MO2 and MO3 were prepared adding and mixing stoichiometric amounts of previous dried MO1 and single oxides in order to form a homogeneous solid dispersion. Such mixture was then mixed in a High Energy Milling-HEM apparatus for 2 hours at 750 rpm and calcined for 3 hours at 823 K. The calcined solids were transferred into a flask and stored under N₂ atmosphere to prevent uncontrolled surface deterioration prior to catalysis. The analysis by EDX confirmed their composition.

Synthesis of SMO1. SMO1, TiO₂ supported MO1, was prepared by wet impregnation technique: 0.38 g of Ce(NH₄)₂(NO₃)₆ + 0.42 g of C₄H₄NNbO₉ + 0.26 g of La(NO₃)₃ · 6 H₂O + 0.014 g of K₂CO₃ + 0.097 g of Bi(NO₃)₃ · 5H₂O and 4.19 g of TiO₂ were suspended in 50 mL of demineralized water and the final suspension was stirred for 10 minutes. The latter was dried using a rotavapor at 313 K under vacuum. Dry solid was calcined at 673 K for 4 hours. 4.55 g of white solid was obtained. The catalyst was reduced to powder, transferred into a flask and stored under N₂ atmosphere.

Synthesis of SMO2. SMO2 was prepared by deposition-precipitation technique: 0.38 g of Ce(NH₄)₂(NO₃)₆ + 0.42 g of C₄H₄NNbO₉ + 0.26 g of La(NO₃)₃ · 6 H₂O + 0.014 g of K₂CO₃ + 0.097 g of Bi(NO₃)₃ · 5H₂O and 4.19 g of TiO₂ were suspended in 50 mL of demineralized water. pH 10 was reached adding drop by drop NaOH 30% solution and then the suspension was stirred for further 1 hour at room temperature. After the solid product was decanted and water siphoned off. 150 mL of fresh demineralized water were used to wash the solid and removed and the solid was dried at 308 K for 14 h. The latter was calcined at 673 K for 4 hours. 4.61 g of white solid were obtained. The catalyst was reduced to powder, transferred into a flask and stored under N₂ atmosphere.

Synthesis of SMO3 and SMO4. 0.25 g of MO1 and 4.75 g of TS-1 were placed in agata jar in presence of 3 sphere of agata (Ø 10 mm) and mixed in HEM apparatus for 2 hours at 750 rpm and then calcined for 3 hours at 823 K. 4.91 g of white powder were obtained (SMO3). At the same manner 0.50 g of MO1 and 4.50 g of TS-1 were mixed by HEM and calcined. 4.96 g of white powder were obtained (SMO4). The catalysts were transferred into a flask and stored under N₂ atmosphere.

Transesterification of HOSO with MeOH/H₂SO₄. 600 mg of HOSO were dissolved in 3 mL of methanol, H₂SO₄ (2 mL, 1 M) were added and the mixture was refluxed for 6h under

N₂. After cooling to ambient temperature, the mixture was analysed by GC-MS and methyl-oleate and other compounds quantified by GC-MS. Results are reported in Table 3.

Transesterification of HOSO with TS-1 in methanol/butanol. 600 mg of HOSO were dissolved in 3 mL of methanol and the mixture was heated at 453 K for 5h under N₂ (0.6 MPa) in presence of 60 mg of TS-1. After cooling to ambient temperature, the mixture was analysed by GC-MS and methyl-oleate quantified (96+% with respect to 99% in the transesterification carried out with H₂SO₄).

The same reaction was carried out in butanol. A longer reaction time (6h) was necessary to reach the complete transesterification of HOSO.

Transesterification of HOSO with MO1+++. a) 600 mg of HOSO were dissolved in 3 mL of butanol and the mixture was heated at 453 K for 6h under N₂ (0.6 MPa) in presence of 60 mg of MO1+++ . After cooling to ambient temperature, the mixture was analysed by GC-MS and butyl-oleate quantified (97+% with respect to 99% in the transesterification carried out with H₂SO₄)

b) The same reaction was carried out in presence of butanoic acid (100 mg) and shown to be complete in 4 h. As butanoic acid is formed in the oxidation in butanol in the one-pot oxidation of HOSO, the transesterification was carried out for 4 h, as shown in Table 6.

Test on the stability of glycerol. Glycerol (2 mL) and the catalyst (200 mg) were treated in the conditions reported below and glycerol was quantified at the end of each test.

- i. Methanol (2 mL) was added to the above suspension and the mixture heated at 433 K for 3 h under N₂. Residual unreacted glycerol = 98+%
- ii. Glycerol and the catalyst were treated with O₂ (0.8 MPa) at 433 K for 2 h. Residual unreacted glycerol= 94%

iii. Mixture (i) was heated for 2 h under a $P_{O_2}=0.8$ MPa at 433 K. Residual unreacted glycerol=92-93%

Solvent-less oxidation of HOSO followed by homogeneous esterification/trans

esterification. 600 mg of HOSO and 60 mg of catalyst (Table 4) were placed in a 200 mL glass reactor with a magnetic stirrer and the reactor was put into the stainless-steel autoclave. The autoclave was charged with pure oxygen at desired pressure (see Table 4) and heated at 413 K or 433 K. After stirring for the reaction time as reported in Table 4, the autoclave was cooled to room temperature and the gas phase was either analysed or pumped off. To the resulting reaction mixture, 3 mL of solvent (methanol) were added and the catalyst was recovered by centrifugation. The liquid phase was subjected to esterification/transesterification with sulphuric acid at reflux for 3 hours. The resulting solution was analysed by GC (results are in Table 4).

Quantification of CO₂, O₂ and H₂. CO₂ and H₂ formed in a batch reaction were determined by TCD-GC analysis, by directly connecting the autoclave to the instrument: the total pressure in the autoclave was read and the gas phase was vent into the gas-loop system for injection. The relative amount of formed CO₂, H₂ and residual O₂ and their total quantity present in the autoclave were calculated using a calibration curve.

Oxidation of HOSO in absence of solvent followed by heterogeneous esterification/

transesterification. 600 mg of HOSO and 60 mg of catalyst (Table 5) were placed in a 200 mL glass reactor with a magnetic stirrer. The glass reactor was placed into the stainless-steel autoclave that was charged with pure oxygen as specified in Table 5 and heated at 433 K or 453 K. After stirring for the reaction time as reported in Table 5, the autoclave was cooled to room temperature and the gas phase was pumped off. To the resulting reaction mixture 6 mL of solvent (methanol) were added and the solution subjected to heterogeneous

esterification/transesterification with the same catalyst at 453 K, under different reaction time (see Table 5) and charging the autoclave with 6 bar of N₂. The resulting solution was analysed by GC as reported in Table 5.

One-pot catalytic oxidation and transesterification of HOSO. 600 mg of HOSO, 3 mL of butanol and 60 mg of catalyst (Table 6) were placed in a 200 mL glass reactor with a magnetic stirrer. The glass reactor was placed into the stainless-steel autoclave that was charged with pure oxygen at the desired pressure as reported in Table 6 and heated at 433 K or 453 K for the reported time (Table 6). After stirring for the given reaction time, the autoclave was cooled down to room temperature and the gas phase was pumped off. The resulting reaction mixture was analysed by GC and subjected to heterogeneous esterification/transesterification with the same catalyst after further adding 3 mL of butanol. The transesterification was carried out at 453 K charging the autoclave with 0.6 MPa of N₂. The resulting solution was analysed by GC-MS (see Table 6).

Flow reactor test. 3.0 g of MO1++ were mixed with the same amount of glass micro-beads and the mixture used to completely fill the EYALA reactor. The temperature was set at 423 K and through the reactor a solution of 600 mg of HOSO dissolved in 3 mL of butanol was flown with a rate of 5 mL/min mixed with oxygen (0.2 mL/min). A 0.1 mL sample of the solution was collected after each cycle and analysed by GC-MS. The evolution of the reaction is shown in Scheme 4.

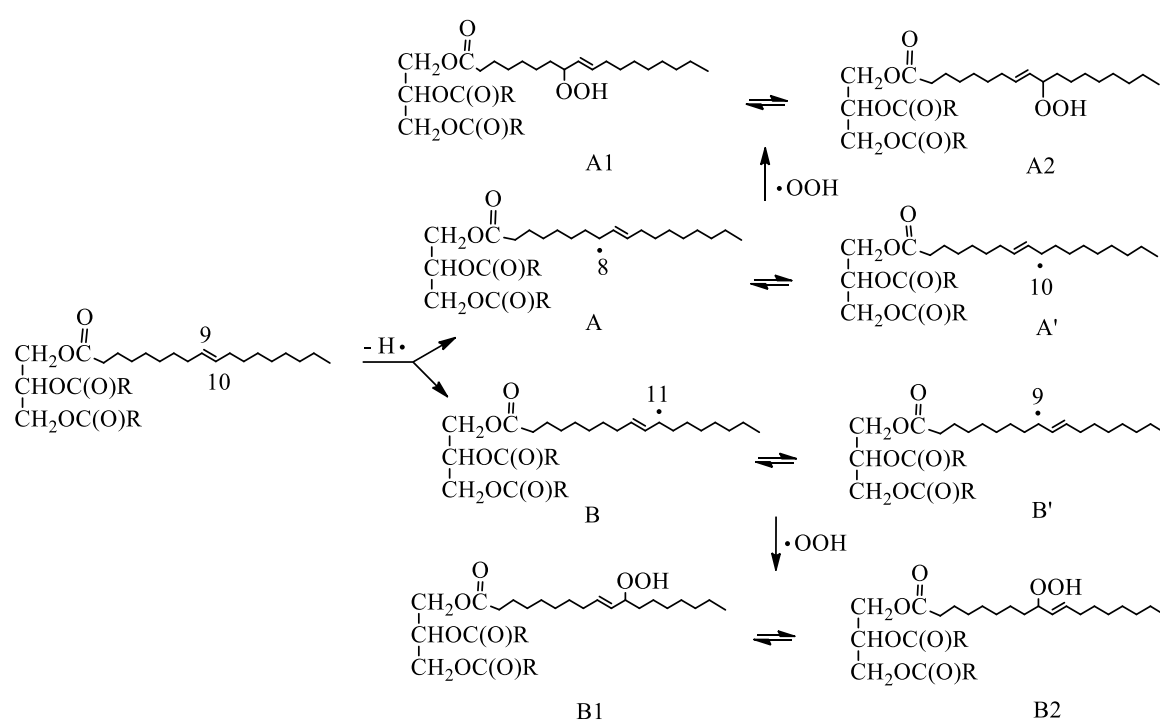
Results and discussion

Double bond oxidative cleavage of MUFAs. In principle, fatty acid double bond can be oxidized by either electron transfer to electrophiles or chemical oxidants. In the latter case, a variety of products can be formed such as epoxides, diols, aldehydes, ketones and carboxylic

mono- and di-acids, depending on the oxidant, catalyst and reaction conditions. Ozonolysis both in presence or absence of a metal promoter, is the most industrially applied process and produces aldehydes and carboxylic acids in very good yields (over 80 %) but with the disadvantage relative to the ozone toxicity and its production costs.²⁰⁻²² High performance is shown by ruthenium tetroxide RuO_4 that is formed in situ in a biphasic system under ultrasound technique using a catalytic amount of RuCl_3 or RuO_2 : this procedure however needs a stoichiometric supply of co-oxidant such as NaIO_4 , HIO_4 , NaClO , NaBrO_3 or $\text{CH}_3\text{CO}_3\text{H}$ that must be regenerated *via* an electrochemical process.²³ Hydrogen peroxide is widely used in epoxidation reactions and in any case does not over oxidize aldehydes into carboxylic acids by itself but needs metal assistance in the form of a Fe-complex,²⁴ molybdenum peroxo-complex²⁵ or vanadium catalyst followed by the cleavage of the diol with a cobalt halide catalyst.²⁶ An excess of concentrated hydrogen peroxide is necessary because the oxidant is lost during the reaction, resulting in increased process costs. Potassium permanganate shows a good activity and selectivity towards acids but after reaction MnO_2 precipitates in the medium and can hardly be reconverted into the permanganate moiety.²⁷ The use of molecular oxygen, considered as an ideal oxidant due to its natural abundance, inexpensiveness, and environmentally friendly characteristics, although has been known since long time in enzymatic²⁸ or photosensitized²⁹ reactions for oil-crushing, has not been deeply investigated from the point of view of selective and efficient carboxylic acid production³⁰ from triglycerides.

Use of dioxygen as oxidant. The direct interaction of dioxygen with unsaturated glycerides, commonly described as *autoxidation*, is a reaction occurring under a wide range of conditions. In absence of a metal centre, the oleic ester fraction of lipids reacts with triplet oxygen to form at least four products³¹ as shown in Scheme 2.

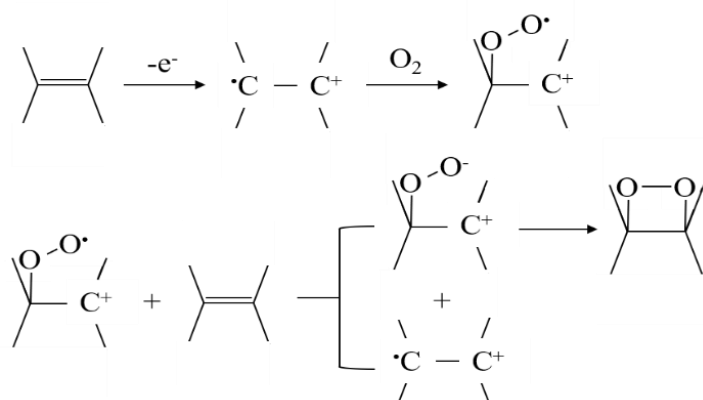
Oxygen in a triplet state at room conditions, acts as a di-radical $\cdot\text{O}-\text{O}\cdot$ and causes an hydrogen atom abstraction from the two oleate allylic positions affording two radical species (A and B in Scheme 2) that can resonate leading to a delocalized radical, which isomerizes, (faster at elevated temperatures) to give an isomeric allyl radical. In this way, isomers of C=9-10 oleic acid are formed, such as C=8-9 or C=10-11 species. The subsequent reaction of the isomeric allyl radical with molecular oxygen gives the oleate hydroperoxides (A1, A2, B1, B2 in Scheme 2).



Scheme 2. Autoxidation of MUFA

Reaction conditions such as temperature, oxygen pressure and reaction time are very important to define the number of hydroperoxide species formed, tuning the formation of kinetic or thermodynamic products. Also, the solvent can play an important role in the products distribution, for example if a good hydrogen-donor is present in the medium, the first-formed peroxy radicals are trapped and no rearrangement occurs with formation of only kinetic products. In any case, subsequent oxidation of hydroperoxyl species can occur, involving the homolytic cleavage of the oxygen-oxygen bond to

yield alkoxy and hydroxy free radicals; the alkoxy radical can then react to form an aldehyde and a new free radical³² that continues the process. It is important to observe that, in absence of initiators or catalysts, all mentioned reactions occur very slowly, over days or months. Correa et al.³³ have demonstrated that under high oxygen concentration and temperature, autoxidation of the various electron-rich substrates can be accommodated by a radical cation mechanism: the olefin can be oxidized to produce a relatively stable radical cation, which can be trapped by the triplet ground state oxygen molecule to yield an oxygenated radical cation, a potent oxidant, affording a stable dioxetane moiety (Scheme 3).



Scheme 3. Non catalysed conversion of the olefinic moiety of MUFAs into dioxetane caused by dioxygen

The thermal cleavage of a dioxetane would yield an aldehyde (site-specific cleavage), which under the reaction conditions might autoxidize to acid. The oleic acid double bond cleavage can occur under three different mechanisms namely one-step (in which directly aldehyde and carboxylic acids are obtained as final products), two step (with epoxy and diol intermediate) and three step (the terminal double bond of the intermediate would be oxidized to a keto-carboxylic acid which could also be cleaved).³⁴ Curiously, in the literature there are only few examples that report the oxidation of oleic acid or its methyl ester with molecular oxygen under heterogeneous catalysis: Table 1 summarizes the available data.

Despite the many positive aspects, first of all the easy recoverability, the application of heterogeneous catalysts in reactions with oils and fats has not been extensively applied, mainly because of the poor reactant/catalyst contact, pore diffusion limitations or low active site availability on the surface. As shown in Table 1, with the exception of the Fe/NaIO₄ system that requires very long reaction times (48h) and affords quite high amounts of azelaic acid (85%) together with nonanal, in all other cases a yield of *ca.* 32 % of azelaic acid is obtained.

Table 1. Literature data for oleic acid oxidation with a variety of oxidants

Catalytic system	Oxidant	Solvent	Temp. (K)	Time (h)	Product	Yield (%)	Ref
Nano Ru-HAP	NaIO ₄	1,2-C ₂ H ₄ Cl ₂ : H ₂ O	ca, 300	12	Nonanal	13	35
Silica supported W-oxide	H ₂ O ₂	t-BuOH	403	1	Azelaic acid	32	36
					Pelargonic acid	36	
H ₂ WO ₄	H ₂ O ₂	---	373	24	Azelaic acid	71	37
					Pelargonic acid	50	
[Fe(OTf) ₂ (6-Me-PyTACN)]	NaIO ₄	CH ₃ CN	<i>ca.</i> 300	48	Nonanal	5	38
					Azelaic acid	85	
Cr on MCM-41	O ₂	SC-CO ₂	353	8	Azelaic acid	32.4	39
					Pelargonic acid	32.2	

Use of mixed oxides as catalysts in HOSO oxidative cleavage. We have recently patented (WO2017202955A1) a catalyst formed by 5 cheap and easily available oxides on the Earth crust able to promote the oxidative cleavage of methyl oleate double bond in a single step using molecular oxygen as oxidant⁴⁰ affording mono- and di-carboxylic acids, with an interesting selectivity towards C9 species, namely pelargonic acid and azelaic acid. In the present work, we have developed the direct *one-step* over-oxidation of the unsaturated fatty esters double bond into carboxylic acids, using a High Oleic Sunflower Oil (HOSO). The oxidation reaction was studied under progressively evolving conditions. We started with the heterogeneously catalysed oxidation of net oil followed by homogeneous (H₂SO₄)

esterification of free acids/transesterification of glycerides bearing attached the residual oxidized part of the original C18 long chain.

This approach was then evolved into the heterogeneous oxidation of the net oil followed by heterogeneously driven esterification/transesterification. Finally, we have developed the one-pot heterogeneous oxidation and esterification/transesterification using the same modified catalyst.

The glycerides (tri-, di-, mono-) composition of original HOSO was defined through on column-GC analysis (Table 2) and the length and nature of the FAs chains was identified using GC-MS after transesterification with methanol in presence of sulphuric acid (Table 3).

Table 2. HOSO glycerides composition

	Tri-glycerides	Di-glycerides	Mono-glycerides	Free Glycerol	Other
HOSO [%w/w]	99.1	0.35	0.1	0	0.45

Table 3. HOSO fatty acid composition

Fatty acid	C18:0	C18:1	C18:2	C18:3	C16:0	C16:1
%	4.85	81.6	7.7	0.15	5.4	0.3

We have modified the original catalyst composition for the metal oxide ratio and metal oxide type.

The catalysts used in this work are described below. They are essentially derived from the catalyst (MO1) described in ref. 40. We have tested the same catalyst in the oxidation of HOSO, to verify if the redox and acid/base properties of the catalyst play a role during the entire oxidation-esterification-transesterification process towards the overall acids yield and selectivity.

Six catalysts will be described in this paper, namely:

- i. **MO1** (catalyst described in ref. 40)
- ii. **MO1+** = MO1 with 10% w/w added Nb₂O₅

- iii. **MO1++** = MO1 with 15% w/w added Nb₂O₅
- iv. **MO1+++** = MO1 with 20% w/w added Nb₂O₅
- v. **MO2** = MO1 in which La₂O₃ is substituted with TiO₂
- vi. **MO3** = MO1 in which K₂O is substituted with MgO.

All catalysts were prepared by High Energy Milling-HEM technique, as reported in ref. 40. **Table 4** reports main data collected under different reaction conditions. At the end of the oxidation, the reaction mixture was treated with the selected alcohol, filtered for catalyst recovery, and esterified with H₂SO₄. The recovered catalyst was washed twice with diethyl ether and calcined at 823 K for one hour before re-use.

A first important point to emphasize is that CO₂ is formed during the oxidation that is in agreement with the fact that shorter chains (C4-C8) are found in the reaction solution. Noteworthy, depending on the catalyst, either mono- or di-carboxylic acids were decarboxylated preferentially. The gas phase analyses at the end of each oxidation reaction have demonstrated that, the higher the temperature and reaction time, the greater the amount of CO₂ formed. The presence of solvent also increases the carbon dioxide production, probably due to its oxidation and subsequent decarboxylation. H₂ is simultaneously formed but revealed in quantities lower than expected (with respect to CO₂) because of in situ water formation in the presence of high oxygen concentration. Figure 1 shows the chromatogram of the gas phase of the reaction reported in Entry 5, Table 4.

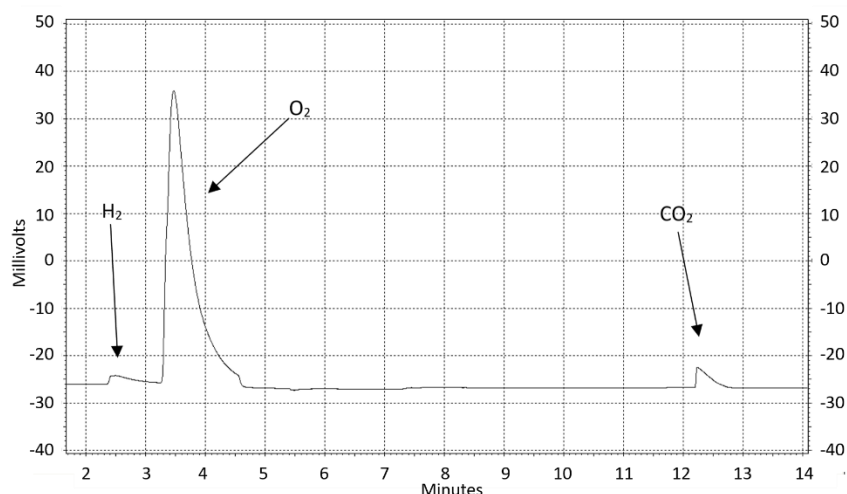


Figure 1: Chromatogram of the gas phase of the oxidation reaction described in Entry 5, Table 4 showing (from left to right): H₂, O₂ and CO₂.

The pH of the reaction mixture after oxidation ranges from 4 to 5. C10 mono- and di-carboxylic acid esters are also found (*ca.* 2%) as effect of the isomerization of oleic acid moving the double bond from the original C=9-10 to the C=8-9 or C=10-11 position.

Table 4. Effect of catalysts in the oxidative cleavage of HOSO

Entry	Catalyst	Time (h)	P _{O2} (bar)	Temp (K)	MMC Yield (%)	DMC Yield (%)	Selectivity MP (%)	Selectivity DMA (%)	n _a /n _b
1	None	15	8	413	6.5	6	42	50	
2	None	15	8	433	18	15	43	40	
3	MO1 not calc.	15	8	413	16	14	39	43	19.6
4	MO1 calc	15	8	413	28	20	45	50	1.06
5	MO1 calc	15	8	433	20	20	37	41	
6	MO1 calc	3	8	433	30	26	48	50	
7	MO1 calc	3	13	433	43	48	42	43	
8	MO1++ calc	2	8	413	30	71	44	36	2.15
9	MO1+++ calc	2	8	413	30	60	46	43	2.73
10	MO2 calc	15	8	413	29	26	45	56	0.98
11	MO3 calc	15	8	413	24	22	42	44	1.47

Reaction conditions in batch: All figures are the average of three tests. Catalyst 10% w/w with respect to the substrate was used in all tests; esterification/transesterification: 3 h at reflux with methanol and H₂SO₄ conc.; 98 % of HOSO was converted in all reactions after transesterification. MMC: total monocarboxylic acid methyl esters; DMC: Total Dicarboxylic acids methyl esters. MP: Methyl Pelargonate % in MMC; DMA: DiMethyl Azelate % in DMC. Calc: calcined at 823 K; not calc: not calcined. n_a/n_b= molar ratio of (medium+strong) acid sites to (medium+strong) basic sites. Medium strength are sites with desorption in the range 400-600 K; strong sites desorb > 600 K.

Also, stearic acid and palmitic acid esters are found unaltered, matching the original composition (see Table 3). Esterified oleic acid is present only in traces. Glycerol and its methylated species were detected in low amount and quantified in the solution after treatment with H₂SO₄/methanol. Ad hoc tests made with pure glycerol showed that carrying out the net oxidation, or oxidation in presence of methanol or even simple treatment with methanol under N₂ in the reaction conditions, 93-92-98 % of glycerol remained unreacted, respectively.

Entries 1 and 2 in Table 4 show that the oxidative cleavage occurs also in absence of catalysts, but at lower conversion yield and requires long time (15 h were necessary for observing a measurable effect). Increasing the temperature from 413 to 433 K (Entries 1 and 2, respectively), increases the total yield of carboxylic acids (w/w% with respect to the starting substrate) but as mentioned above, favours the decarboxylation, lowering the selectivity towards C₉ mono- and di-carboxylic species as C₇ and C₈ (or even lower) species are formed. As selectivity is meant the % of C₉ mono- or di-carboxylic acids in the overall mono-and di-carboxylic acids formed. In absence of catalysts, species with number of C-atoms less than 7 are observed at a low extent.

All listed catalysts are active in the oleic double bond oxidative cleavage (compare with the reaction without catalyst, Entries 1 and 2, Table 4), except the not-calcined catalyst (rich of -OH moieties on the surface as confirmed by the determination of surface acid sites-last column in Table 4) that does not show a great effect (Entry 3). This means that the surface area of the metal oxide plays a key role in the oxidation process. In fact, the oxidation reaction occurs essentially on the surface of the catalyst as the dimension of the starting lipids prevents their migration into pores.

Consequently, we find that nano-sized catalysts (20-100 nm) are more efficient than

micro-sized (100-500 μm) ones by 30+%. The first attempts were done using the same oxidation time as in the non-catalysed reactions (15 h, Entries 3-5): low overall yields of C7-C9 mono- and di-carboxylic acids were observed coupled to significant amounts of short chain acids ($n < 7$) and large volumes of CO_2 . Reducing the oxidation time to from 15 to 3 and 2 h (Entries 5-6-7), causes the increase of the yield of MMC and DMC, meaning that the shorter time causes less chain-cut and CO_2 production, as confirmed by the quantification of formed CO_2 . In fact, we have measured the amount of CO_2 formed in reactions corresponding to Entries 5 and 6 in Table 4 and have found that reducing the reaction time from 15 to 3 h, keeping all other parameters constant, causes the reduction of CO_2 formation from 4.97 to 2.54 mmol, as measured by TCD of the gas phase.

The use of radical catching species (β -carotene) does not improve too much the selectivity towards C9 species, our specific target. In general, Table 4 shows that the overall carboxylic acids yield and C9 selectivity can be differently influenced by catalyst properties and reaction conditions. An increase of temperature, reaction time and/or oxygen pressure influences both the overall diacids yield and selectivity towards C9 species (Entries 4-7, Table 4). However, if by one hand higher oxygen pressure and temperature act positively on the double bond cleavage probably because of higher diffusion rate and decrease of viscosity that improve the substrate-catalyst contact, on the other hand the de-carboxylation process takes place more easily with the formation of shorter chain carboxylic acids decreasing the selectivity toward azelaic and pelargonic acid. We have played on catalyst acid/base properties and electron density distribution on its surface for understanding how such properties influence the reaction. Noteworthy, replacing in MO1 La_2O_3 with TiO_2 (MO2) or K_2O with MgO (MO3) or loading Nb_2O_5 (MO1++ and MO1+++), the overall oxidation

yield and/or selectivity towards C9 mono- or di- carboxylic acids can be slightly tuned (Entries 8-11, Table 4)

Figure 2 shows how the properties of the catalyst are modified upon changing the composition: along the series MO1, MO1+, MO1++, MO1+++, increasing the content of the acid oxide Nb₂O₅ the strength of bonding on NH₃ increases. Along the same series the binding of CO₂ decreases in strength. (Figure 3)

It is also worth noting that, catalyst MO₂ does not show any higher oxidation power than MO1. The not too different basic properties of magnesium (MO3) with respect to potassium (MO1) make that the two catalysts almost retain the same properties. On the other hand, increasing the amount of Nb₂O₅ increases the acidity of the catalyst: comparing Entries 4,8 and 9 in Table 4, one can observe some interesting differences. MO1++ is the most active catalyst, also showing a good selectivity towards C9.

Considering the positive effect of titanium on the azelaic acid selectivity (Entry 10), MO1 was dispersed at different concentrations on two kind of titanium-based support, namely: titanium oxide and titano-silicalite1 (TS-1) using different techniques, obtaining new solids which contain only 5-10% w/w of MO1.

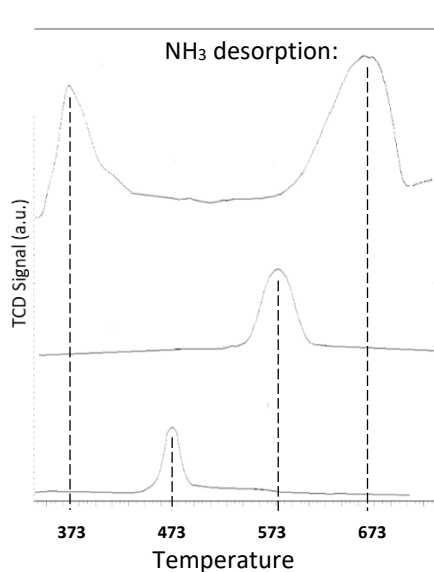


Figure 2: NH₃ desorption curves for catalysts MO1 (*bottom*), MO1++ (*middle*), MO1+++ (*top*) containing increasing amounts of Nb₂O₅. Increasing the amount of the acid oxide Nb₂O₅

increases the strength of bonding of NH_3 . Weak sites in MO1^{+++} are due to excess free Nb_2O_5 .

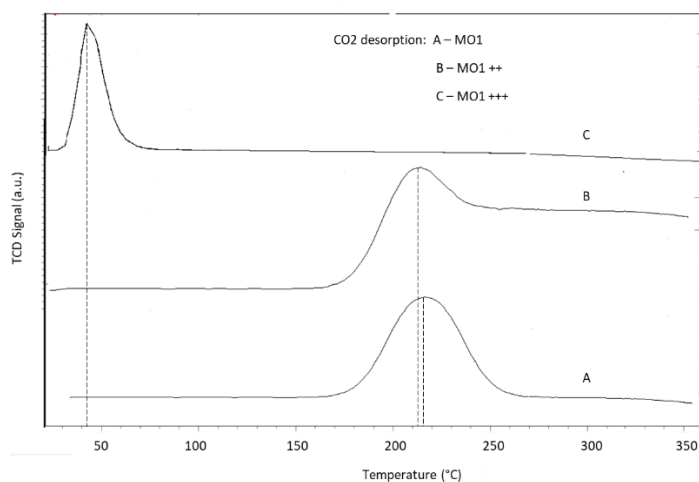


Figure 3: TPD of CO_2 for catalysts MO1 , MO1^{++} and MO1^{+++} : the addition of the acid oxide Nb_2O_5 weakens the CO_2 - catalyst bonding.

The new series of catalysts is made of:

- vii. MO1 (10%) supported on TiO_2 by wet impregnation, SMO1
- viii. MO1 (10%) supported on TiO_2 by deposition-precipitation, SMO2
- ix. MO1 (5%) supported on TS-1 by HEM, SMO3
- x. MO1 (10%) supported on TS-1 by HEM, SMO5 .

The n_a/n_b [ratio of (strong+medium) acid sites to (strong+medium) basic sites] for SMO1 and SMO5 are respectively 0.31 and 2.27, indicating the strong influence of TS-1 on the catalyst properties. The surface area also varies from MO1^{++} ($162 \text{ m}^2/\text{g}$) to SMO1 ($112 \text{ m}^2/\text{g}$, and SMO5 ($124 \text{ m}^2/\text{g}$).

We also have verified that TS-1 can act as transesterification agent on lipids under N_2 . Based on such finding, catalysts (vii-x) were tested on net HOSO oxidation and the reaction solution was then subjected to esterification/transesterification with methanol in presence of the same catalyst without use of sulphuric acid. Simply, after the oxidation time was elapsed, O_2 was pumped off the reactor, MeOH was added under

N₂ which pressure was then risen to the value given in Table 5 and the transesterification continued for the time reported and at 453 K.

Table 5. Behaviour of TiO₂-supported MO1 in the aerobic oxidative cleavage of HOSO and transesterification/esterification of resulting C9 species.

Entry	Catalyst	Time (h)	Press (bar)	Temp (K)	Y MCE (%)	Y DCE (%)	C7-C9 sel (%)	C9 select (%)
1	SMO1	1.5	12 O ₂	433	18	13	60	28
	+ CH ₃ OH	3	6 N ₂	453				
2	SMO1	2	12 O ₂	433	12	15	69	34
	+ CH ₃ OH	3	6 N ₂	453				
3	SMO1	2.5	12 O ₂	433	22	33	65	32
	+ CH ₃ OH	3	6 N ₂	453				
4	SMO1	1.5	12 O ₂	453	13	19	41	18
	+ CH ₃ OH	3	6 N ₂	453				
5	SMO1	2	12 O ₂	453	14	12	58	26
	+ CH ₃ OH	3	6 N ₂	453				
6	SMO1	2.5	12 O ₂	453	8	19	36	13
	+ CH ₃ OH	3	6 N ₂	453				

Reaction conditions in batch: All figures are the average of three tests. Catalyst 10% w/w with respect to the oil was used in all tests; 98-99 % of substrate was converted in each test; esterification/transesterification: 3h under reflux with methanol using the same oxidation catalyst. After the end of the oxidation, O₂ was pumped off the reaction mixture, MeOH added and the esterification-transesterification completed under N₂ at the reported pressure. MMC: total monocarboxylic acid methylesters; DMC: Total Dicarboxylic acid methylesters. Selectivity of MP: Methyl Pelargonate % in MMC; Selectivity of DMA: DiMethyl Azelate % in DMC.

As shown in Table 5, when MO1 was dispersed on the Ti-support with a load of 10 % (SMO1, Entry 1), the performance of the catalyst was, obviously, relatively poor due to the low amount of oxidants, the overall C7-C9 carboxylic acids yield slightly increased, while the C9 selectivity remained almost the same as those of MO1 (Table 4, Entry 4).

TS-1 alone is active in the reaction, but the presence of MO1 increases yield and selectivity. The time of reaction was also important. A long time if from one hand increases the conversion of the substrate from the other increases the chain-cut process reducing the selectivity towards C9 species. Reaction time was shortened to 2h

oxidation and 3h trans-esterification. Interestingly, the TiO₂-supported catalysts result active also in the trans-esterification reaction.

Such findings have pushed us to develop the one pot oxidation/esterification-transesterification in presence of an alcohol, using the same catalyst for both reactions. One-pot catalytic oxidative-cleavage and transesterification/ esterification of HOSO. However, we decided to test the oxidation of HOSO in butanol using the same catalyst as oxidant and transesterification/ esterification agent. Butanol was selected as solvent and esterification reagent because it is of bio-origin and is excellent solvent for HOSO, for the high boiling point and considering that butyl ester of azelaic acid present several industrial applications. HOSO was dissolved in the opportune volume of butanol (at least 20 times the amount necessary for esterification and transesterification to compensate losses for oxidation, *vide infra*) and the solution submitted to oxidation, as reported in Table 6. At the end of the oxidation reaction, O₂ was pumped off and N₂ admitted at a pressure between 6 and 8 atm. We have carried out over 300 catalytic tests using the catalysts SMO1, SMO2, SMO3, SMO5, MO1, MO1+, MO1++, MO1+++, and varying the P_{O₂} (6-8-10-12 atm), temperature (433-453 K), time of transesterification (3-4.5 h), using in the post-oxidation transesterification either the same catalyst used in the oxidation or adding a fresh catalyst (the same used in the oxidation), or adding SMO5 to check the effect of more acidic catalysts. Noteworthy, butanoic acid, formed from butanol during the oxidation reaction, has a beneficial effect on the release of C_n-moieties from the glyceride, as demonstrated by ad hoc transesterification tests carried out on HOSO in presence of only the catalyst or the catalyst plus butanoic acid.

In Table 6 we summarize the most representative results to show the effect of catalyst, oxidation conditions and time of transesterification.

Table 6. Use of MO1 derived catalysts in *one-pot* aerobic HOSO oxidation in butanol followed by transesterification under N₂

Entry	Catalyst	Time (h)	Pressure (bar)	Temp (K)	C7-C9DBE yield (%)	C9 DBA yield (%)
1	SMO1	2	12 O ₂	433	52	27
	"	3	6 N ₂	453		
2	SMO5	1.5	12 O ₂	453	23	9
	"	3	6 N ₂	453		
3	SMO5	2.5	12 O ₂	433	50	26
	"	3	6 N ₂	453		
4	MO1	2	8 O ₂	433	64	37
	"	3	6 N ₂	453		
5	MO1	2	8 O ₂	433	61	35
	"	4.5	6 N ₂	453		
6	MO1	1.5	12 O ₂	433	72	40
	SMO5	3	6 N ₂	453		
7	MO1	2	8 O ₂	433	61	34
	" + MO1+	3.5	6 N ₂	453		
8	MO1+	2	8 O ₂	433	57	31
	" + fresh	4	6 N ₂	453		
9	MO1++	2	8 O ₂	433	63	56
	"	4	6 N ₂	453		
10	MO1+++	2	8 O ₂	433	72	38
	"	4	6 N ₂	453		

Reaction conditions in batch: All figures are the average of three tests. Catalyst 10% w/w with respect to the oil was used in all tests; 98-99 % of the substrate was converted in each test; esterification/transesterification: 3h under reflux using the same oxidation catalyst. After the end of the oxidation, O₂ was pumped off the reaction mixture, BuOH was added and the esterification-transesterification completed under N₂ at the reported pressure. Fresh: the same fresh catalyst was added. C7-C9 DBE yield: total yield of C7-C9 butyl esters in the final reaction mixture; C9 DBA yield: Dibutyl Azelate % in the mixture. The difference between C7-C9 DBE and C9 DBE is represented by the decarboxylated forms C7 and C8 dibutyl esters.

It is worth to recall that, under the new reaction conditions, during the oxidation phase the monocarboxylic acids can be formed either free or esterified with butanol (both are detected by GC-MS, we consider the total amount in our calculations). Conversely, the dicarboxylic acid can be found in a variety of different forms: free diacids, monoesters, diesters or even remain attached to glycerol (short chain glycerides are detected by HPLC): the final transesterification reaction plays an important role for the total release of diacid esters and their correct quantification. In order to check whether glycerides were completely trans-

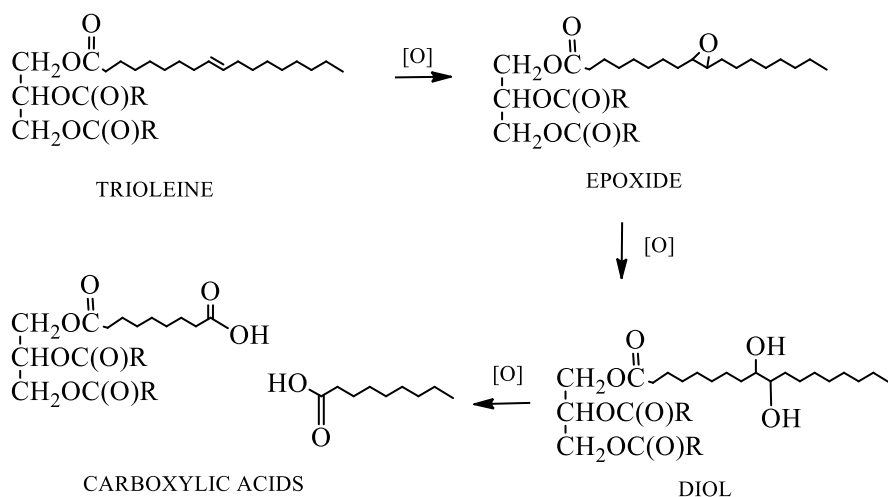
esterified, a further reaction with H₂SO₄ in butanol (some more butanol was added to the amount already present in the reaction mixture) was carried out after centrifugation of the solid catalyst and the yield of DCA-esters (and monoesters) was compared to the amount found after transesterification with only the solid catalyst. Such operation revealed that using MO1++ or MO1+++ the transesterification under N₂ was enough to release 98-99+% of the DCA-diester and esterify monoacids. For example, when the reaction 9 solution (separated from the solid catalyst MO1++) was subjected to esterification with H₂SO₄ the yield of diesters increased by only less than 1% with respect to the values reported in Table 6.

Other catalysts were not so effective in the transesterification (lower acidity) so that the yield of diesters after H₂SO₄ esterification/trans-esterification was even 5-7 points higher. This is not surprising and is on line with our previous publications and patents^{41,42} that have shown that mixed oxides of opportune composition act as effective catalysts in transesterification of lipids containing up to 20% excess free acid: in the present case, the acids' concentration may be higher than 20%, then more acidic catalysts were used to avoid leaching of basic oxides. It must be emphasized that the butyl ester of butanoic acid was always found among reaction products, being formed upon oxidation of butanol followed by esterification. Moreover, even in this case butyl esters of C10 mono- and di-carboxylic acids were found at a rate of *ca.* 1%. The best yields were found with MO1++ catalyst which produced 63% of overall C7-C9 diacid esters and 56% of azelaic acid esters. (Entry 9). When MO1 was used in the oxidation and SMO5 (containing TiS-1) was added in the transesterification reaction, 72 % of diacids were obtained, but only 40 % of azelaic acid (Entry 6). This is due to the decarboxylation reaction which is favored by SiO₂. MO1 added with SMO5 is very close to MO+++ . MO1++ benefits of the load of Nb₂O₅ that, due to its acidity, improves the yield in the trans-esterification/esterification phase. The Ti-supported

catalysts are less active in oxidation and show a good performance in the trans-esterification/esterification process, but TS-1 may push the de-carboxylation reaction producing shorter diacids.

Rising the temperature during the oxidation from 433 to 453 K (Entries 2 and 3) reduces the yield of azelaic acid, the same effect is caused by the increase of P_{O_2} from 6-8 to 12 atm. However, the best operative conditions were set at 433 K, 6-8 atm P_{O_2} , 2-2.5 h oxidation reaction, followed by esterification/transesterification under N_2 (6 atm) for 3-4 h at 453 K, using MO1++.

The reaction pathway. To detect the reaction pathway, we have used an Eyring flow-reactor and the reaction run at 423 K (maximum allowed temperature for the Eyring flow-reactor). The reactor was charged with MO1++ catalyst (*ca.* 3 g) mixed with glass-microbeads. A nano-sized filter was placed on the head and tail of the reactor to avoid loss of catalyst. HOSO dissolved in butanol was added with defined amounts of oxygen and the mixture flown through the reactor as specified in the Experimental Section. The solution was recycled several times. Samples were taken after each cycle, treated with sulphuric acid for releasing the MUFAs, and the organic phase was analysed by GC-MS. The first species that appeared was the epoxide (Cycle 2, 0.5% yield with respect to starting oil) followed by the diol (Cycle 3). The C9-acids (Scheme 4) appeared only after the fifth cycle (0.3% with respect to starting oil). The fact that the latter remain in solution, causes their decarboxylation with time. The reaction is slower than in the bulk reactor, because both the temperature and pressure of oxygen are lower than in the bulk experiments, even if the ratio catalyst/substrate is much higher in the flow experiments. After 20 cycles a conversion of the substrate equal to 35% was observed with a few units % of acids and esters. This technique was useful for revealing the steps through which the oxidation proceeds, but needs substantial improvement (temperature, ratio O_2 to substrate, permanence time) for real application.



Scheme 4. Appearance of species in the oxidative cleavage of HOSO in a flow-reactor

The investigation of the stability and reusability of the catalyst were performed using the catalyst MO1++, that demonstrated the best properties in the aerobic oxidative cleavage of MUFAs. At the end of the normal oxidation run, the catalyst was isolated by filtration or centrifugation, washed twice with diethyl-ether and then calcined at 823 K for 2 h. The catalyst was reused for five times and the efficiency evaluated on the basis of the following parameters: conversion of MUFAs, production of C7-C9 mono and diacids, selectivity towards C9.

The catalyst maintained its activity through five cycles, with a minor homogeneous decrease of the three properties amounting at *ca.* 1 % per cycle, altogether. The first recycle produced the same figures as in the first cycle, so happened for the second recycle. From the third to the fifth recycle an overall decrease of *ca.* 5% was detected.

Conclusions

HOSO (or restaurant olive oil) have been subjected to oxidative cleavage using heterogeneous catalysts, in solvent-less conditions or using the alcohol selected for esterification of the acids as solvent and using oxygen as oxidant. Several catalysts,

based on the original one covered by a EP-patent⁴⁰, have been evaluated in a variety of operative conditions. In all cases, CO₂ was produced as the effect of decarboxylation of acids (mono- and di-carboxylic) or oxidation of the solvent. Such reaction needs to be controlled as decreases the yield of target products (C9 acids). The best catalysts, in terms of conversion of the substrate and yield of C7-C9 acids, are represented by the original catalyst MO1 added with Nb₂O₅ that confers acidity to the catalyst and promotes the esterification/transesterification at the point that such catalyst (MO1++) is able to drive both the oxidation and esterification/transesterification reaction, with much simplification of the entire process, avoiding the use of sulphuric acid and making it quite benign and environmentally friendly. This is a unique example in the literature of a catalysts performing both oxidation and esterification/transesterification. So far only examples of heterogeneous catalysts able to carry out esterification/transesterification were described.⁴¹⁻⁴⁴ The improvement of the catalyst continues to be investigated in our labs.

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

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ABBREVIATIONS

HOSO, high oleic sunflower oil; MUFAs, monounsaturated fatty acids; BET, Brunauer–Emmett–Teller; FID, flame ionization detector; TCD, Thermal Conductivity Detector; GC, gas chromatograph; GC-MS, gas chromatography-mass spectrometry; HEM, High Energy Milling; MO, mixed oxide; MMC, methyl ester of mono carboxylic acid; DMC, dimethyl ester of di-carboxylic acids; PA, pelargonic acid (C9 monocarboxylic acid); AA, azelaic acid (C9 dicarboxylic acid).

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