



HAL
open science

Oxidative cyclization of linoleic acid in the presence of hydrogen peroxide and phosphotungstic acid

Nahla Araji, Gregory Chatel, Audrey Moores, François Jerome, Karine de Oliveira Vigier

► **To cite this version:**

Nahla Araji, Gregory Chatel, Audrey Moores, François Jerome, Karine de Oliveira Vigier. Oxidative cyclization of linoleic acid in the presence of hydrogen peroxide and phosphotungstic acid. *Molecular Catalysis*, 2020, 493, pp.111084. 10.1016/j.mcat.2020.111084 . hal-03015077

HAL Id: hal-03015077

<https://hal.science/hal-03015077>

Submitted on 19 Nov 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Oxidative cyclization of linoleic acid in the presence of hydrogen peroxide and phosphotungstic acid

Nahla Araji,^a Gregory Chatel,^{b,} Audrey Moores,^{c,*} François Jérôme,^a Karine De Oliveira Vigier^{a,*}*

^aIC2MP, UMR CNRS 7285-Université de Poitiers, France, ENSIP, B1, 1 rue Marcel Doré, TSA 41105, 86073 Poitiers Cedex 9, France. karine.vigier@univ-poitiers.fr

^b Univ. Savoie Mont Blanc, LCME, F-73000 Chambéry, France. Gregory.Chatel@univ-smb.fr

^c Centre for Green Chemistry and Catalysis, Department of Chemistry, McGill University, 801 Sherbrooke St. West, Montreal, H3A0B8, Quebec, Canada. audrey.moores@mcgill.ca

Abstract:

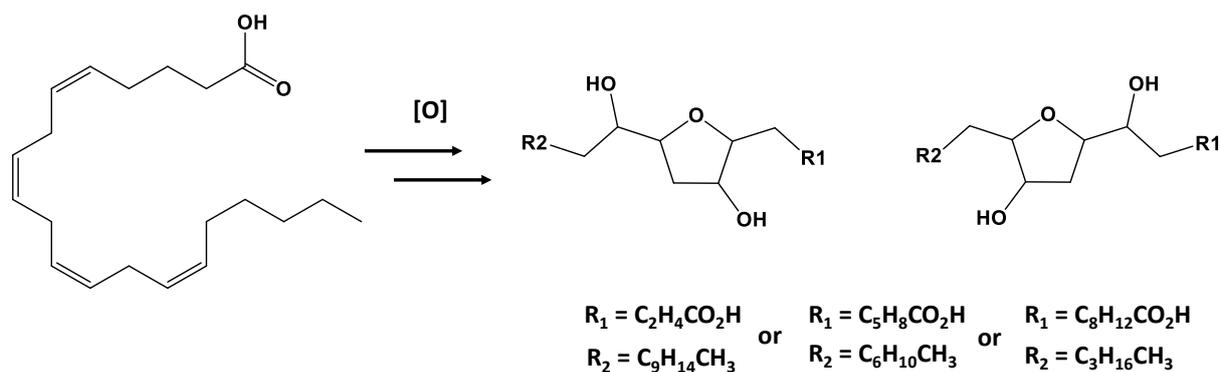
The synthesis of THF and tetrahydro-2H-pyran is of interest due to the applications of such molecules as antitumour, pesticidal, antiprotozoal and antimicrobial agents for instance. Here, an original approach was performed to prepare these derivatives starting from linoleic acid in the presence of hydrogen peroxide and phosphotungstic acid in the absence of a phase transfer agent. A maximum cyclic compounds yield of 99% was obtained under mild conditions of temperature. A heterogeneous catalyst was synthesized by exchanging proton by Cs to obtain Cs_{2,3}H_{0,7}PW₁₂O₄₀ that was recycled up to 3 cycles. It is one of the best yield to these products observed in the literature from fatty acids.

KEYWORDS: linoleic acid; heteropolyacids; tungsten catalyst; hydrogen peroxide; THF derivatives.

1. Introduction

Nowadays, vegetable oils are used as renewable raw materials for the manufacture of industrial products such as biofuels, lubricants, surfactants and pharmaceutical and cosmetic products [1]. To access these products, vegetable oils undergo chemical treatments such as hydrolysis, transesterification, oxidation, hydrogenation, metathesis, etc [2]. The presence of one or more C=C double bonds in the fatty chain of these molecules provides a chemical manifold and makes their functionalization a center of interest for several domains such as polymer synthesis, cosmetics and others. Hydroxylation reactions can lead to vicinal alcohols which are an interesting class of molecules in the formulation of several products, such as paints, surface coating, food emulsifiers, soap surfactants, biofuel additives, etc. [3]. These vicinal alcohols also act as an intermediate for the production of dicarboxylic acids such as azelaic and pelargonic acids, which are valuable specialty monomers [4]. In the literature, the hydroxylation of polyunsaturated fatty esters is generally followed by a cyclization process leading to the formation of substituted tetrahydrofurans (THFs). These compounds are of interest due to their biological activity in areas such as polyether antibiotics and *Annonaceous* acetogenins [5-6]. Hence, *Annonaceous* acetogenins constituted of THF and Tetrahydro-2H-pyran derivatives are bioactives as antitumour, immunosuppressive, pesticidal, antiprotozoal, antifeedant, anthelmintic and antimicrobial agents. Several acetogenins were isolated such as 4-acetyl gigantetrocin A [7], 4-acetyl annonacin [8] and 4-acetyl xylomaticin [8], annohexocin [9] and murihexocins [10]. The synthesis of these types of molecules *via* oxidative cyclization of fatty acid methyl ester such as linoleic acid has been little investigated. Yet it is a desirable approach with benefits for simplicity and atom-economy if developed with green catalysts.

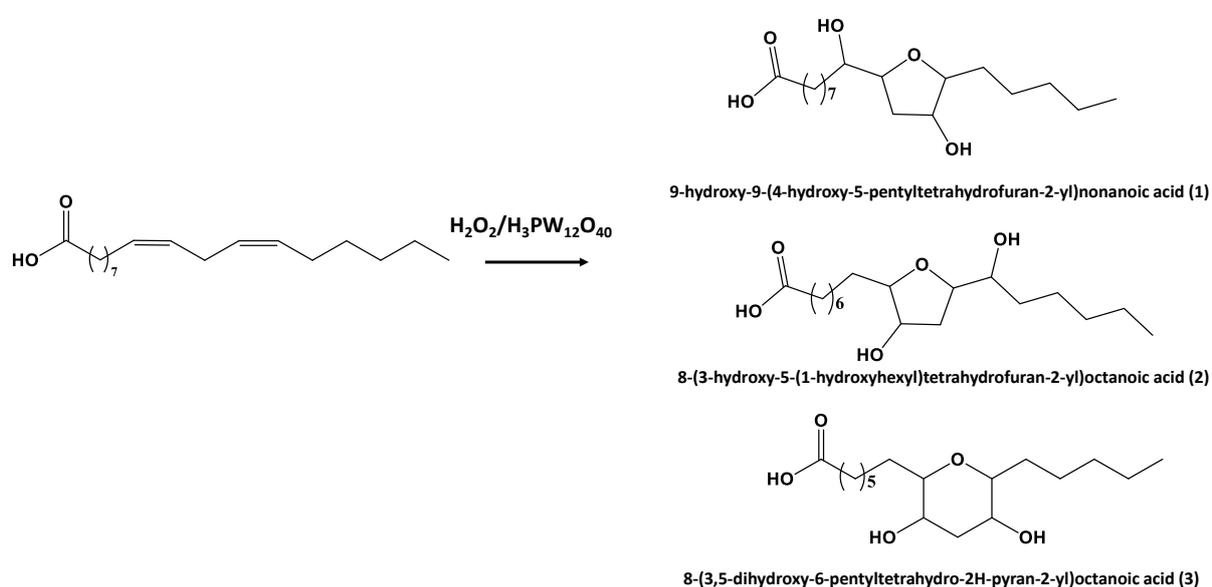
Travis et al. [11] investigated the oxidative cyclization of methyl linoleate and methyl arachidonate in a reaction medium containing tetrahydrofuran (THF), water and perchloric acid (HClO₄). Furanic isomers (five-membered ring) were formed (Scheme 1) through a cascade epoxidation/hydrolysis reaction (30% yield).



Scheme 1. Formation of 2,3,5-THF-tri-substituted diols from arachidonic acid [19].

In another study, several oxidant systems (KMnO₄, OsO₄, RuCl₃) were studied for the oxidative cyclisation of fatty acids (arachidonic acid) and fatty acid esters (methyl linoleate) [12]. These oxidants led to low yields of furanic isomers (30%) due to a competitive secondary oxidation reactions (fatty acid fragmentation). In addition, the oxidants used can be toxic, expensive and corrosive. Another interesting oxidant is hydrogen peroxide since the only by-product formed during the H₂O₂ based oxidation reaction is water. In the literature, the hydroxylation of unsaturated fatty acids using H₂O₂ as oxidant was generally performed using tungsten catalytic systems based for examples on tungstic, phosphotungstic or pertungstic acids [13–15]. The main drawbacks of these approaches were the need for high concentrations of hydrogen peroxide (up to 70%) and the use of a phase transfer agent. Another important challenge for successful hydroxylation reactions is the control of the selectivity toward the desired product, since several molecules can be obtained such as epoxides, diols or compounds resulting from the oxidative cleavage [16-18].

Herein, we report the selective oxidative cyclization (hydroxylation/cyclization) of linoleic acid to tetrahydrofuran (**1** and **2**) and tetrahydro-2H-pyran (**3**) derivatives in the presence of hydrogen peroxide and phosphotungstic acid as depicted on Scheme 2. The experimental conditions were optimized in order to obtain a high yield in cyclic isomers. A heterogeneous form of $H_3PW_{12}O_{40}$ was synthesized ($Cs_{2,3}H_{0,7}PW_{12}O_{40}$), and the recyclability of this catalytic system was studied. To the best of our knowledge, this is the first time that these cyclic compounds were obtained with high yield (99%) from fatty acids with an atom economical and safe oxidant, in absence of a phase transfer agent.



Scheme 2. Conversion of linoleic acid to substituted THF and Tetrahydro-2H-pyran.

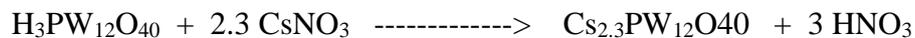
2. Experimental part

2.1. Materials and methods

Hydrogen peroxide (30 wt.%) purchased from Acros-Organics was the oxidant used for all reactions. Linoleic acid was purchased from Sigma Aldrich with a purity of 99% (Figure S1) and phosphotungstic acid $H_3PW_{12}O_{40}$ from Sigma-Aldrich, was used as an acid catalyst.

2.2. Synthesis of $Cs_{2,3}H_{0,7}PW_{12}O_{40}$ catalyst

The heterogeneous catalyst was synthesized by the exchange of 2.3 protons of H₃PW₁₂O₄₀ by 2.3 Cs atoms from cesium nitrate according to the study of Gharib *et al.* (Scheme 3) [19].



Scheme 3. Synthesis reaction of Cs_{2.3}H_{0.7}PW₁₂O₄₀.

To this aim, phosphotungstic acid (1.0 mmol, 2.9 g) was introduced to 15 ml of deionized water in a 50 ml flask under magnetic stirring for 10 min at room temperature. An aqueous solution of cesium nitrate (2.5 mmol, 0.49 g in 4 ml deionized water) was added drop by drop to the solution. A stirring was maintained for 24 h at room temperature. The white catalyst was recovered by filtration. The catalysts was washed several times with deionized water before being drying in an oven at 60 °C for 16 h. The specific surface area was measured by N₂ adsorption–desorption isotherms and was 123 m².g⁻¹ accordingly to the literature [20]. The pore volume was 0.103 cm³/g and the pore size measured by BJH was 8.9 nm. The acid sites of this catalyst was measured by NH₃ TPD in the literature and was reported to be 161 μLmol g⁻¹ [21].

2.3. Catalytic tests

In a 50 ml round flask, linoleic acid (1.5 mmol, 420 mg) was introduced with an amount of aqueous hydrogen peroxide (30 wt.%, 1.5- 3.5 eq., 0.23-0.54 ml) to a specified amount of phosphotungstic acid (21-63 mg). The reaction medium was subsequently heated under reflux and kept under vigorous agitation. After reaction, ethyl acetate (40 ml) was added to the reaction medium in order to solubilize and extract the organic phase. The organic phase was subsequently recovered and dried by adding sodium sulphate. After a filtration, the ethyl acetate was evaporated using a rotary evaporator. Before gas chromatography (GC) analysis, the sample was diluted using 1 ml of pyridine and silylated by adding hexamethyldisilazane (1 ml) and chlorotrimethylsilylamine (1 ml). Sorbitol (2 mg) used as external standard was added to the sample before analysis.

2.4. Analyses

In our study, the analysis and quantification of linoleic acid and formed products were performed using a Varian 3900 gas chromatograph. The latter is equipped with a split/splitless injection port, a flame ionization detector (FID) and a BP5 column (30 m × 0.32 mm × 1 μm) composed of a mixture of 5% phenyl and 95% dimethyl polysiloxane.

Linoleic acid conversion and products yields were calculated based on calibration curves and using the following equations:

$$\text{Conversion (\%)} = \frac{A_{\text{linoleic acid}}^i/A_{\text{sorbitol}} - A_{\text{linoleic acid}}^t/A_{\text{sorbitol}}}{A_{\text{linoleic acid}}^i/A_{\text{sorbitol}}} \times 100$$

$$\text{Yield (\%)} = \frac{\text{mol. of products at } t}{\text{mol of linoleic acid at } t = 0} \times 100$$

Where $A_{\text{linoleic acid}}^i$ and $A_{\text{linoleic acid}}^t$ represent the values of the area of linoleic acid chromatographic peaks respectively at the initial time (time zero) and time of control (similarly for A_{product}^i and A_{product}^t). A_{sorbitol} is the area of the external standard.

The yields of reactive products were measured using ^1H NMR spectroscopy recorded on a 400 MHz Bruker Avance DPX spectrometers for 9,12-diepoxy stearic acid and by GC analysis for the substituted THF and tetrahydro-2H-pyran derivatives. To this end, these products were synthesized from linoleic acid with a purity of 99% and used for calibration. The nature of the cyclic compounds were confirmed by ^1H NMR (Figure S2) and by mass spectrometry analysis using a Bruker Impact HD (Q-TOF) (Figure S3). Despite our efforts, we could not separate the three cyclic compounds by GC analysis, due to their similar polarity. Thus, a global yield of the three cyclic compounds was reported.

3. Results and discussion

In a first set of experiments, the oxidative cyclization of linoleic acid (1.5 mmol) was performed in the presence of 15 wt.% of $\text{H}_3\text{PW}_{12}\text{O}_{40}$ and 3.5 equivalents of H_2O_2 (30 wt. %) at 80 °C. After 2 h of reaction, a total conversion of linoleic acid was observed with the formation of two 5-membered ring cyclic ethers (**1** and **2**) and one 6-membered ring one (**3**) with a total yield of 50% (Figure 1, Scheme 2).

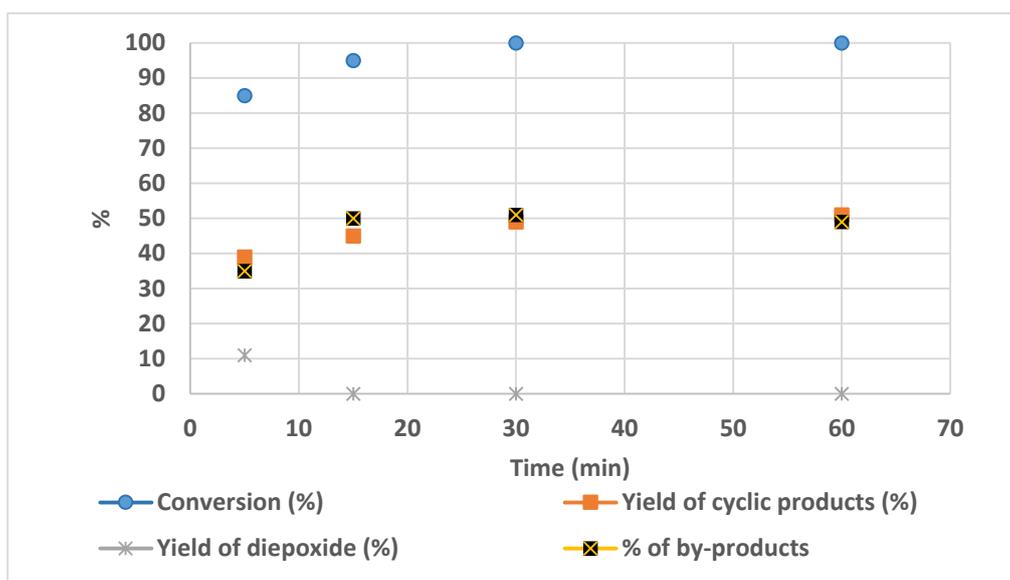


Figure 1. Kinetic profile of the conversion of linoleic acid (1.5 mmol) as a function of time in the presence of 3.5 equivalents of H_2O_2 and 15 wt.% of $\text{H}_3\text{PW}_{12}\text{O}_{40}$ at 80 °C.

Cyclic products were analyzed by ^1H NMR and MS analysis. The cyclic compounds were therefore synthesized by hydroxylating 1.5 mmol of linoleic acid in the presence of 15 wt.% of phosphotungstic acid and 2.5 equivalents of H_2O_2 at 80 °C for 30 min of reaction. The purity of the synthesized products were measured using ^1H NMR spectroscopy and mass spectrometry as shown in Figures 2 and 3 **respectively**. On Figure 2, all the peaks correspond to the cyclic compounds and the non identified impurities present in linoleic acid as shown on Figure S1.

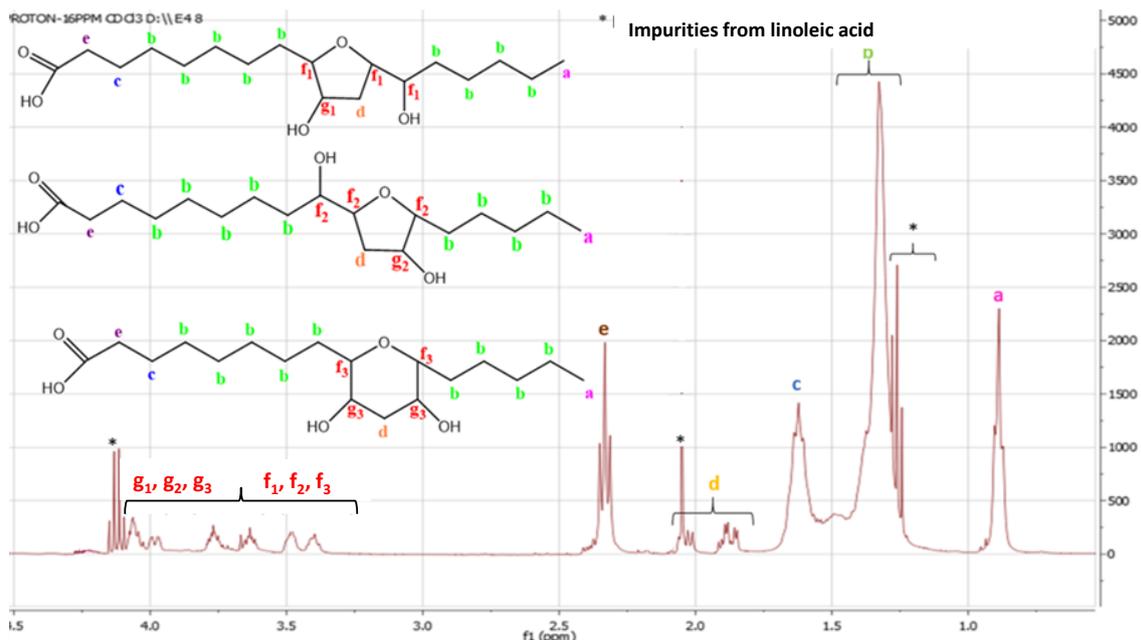


Figure 2. ^1H NMR of the produced cyclic compounds.

There is one peak that corresponds to the cyclic compounds with a m/z of 353 with a Na adduct. Another peak at m/z of 683 was observed corresponding to two diols sur to the high concentration of products used (Figure 3).

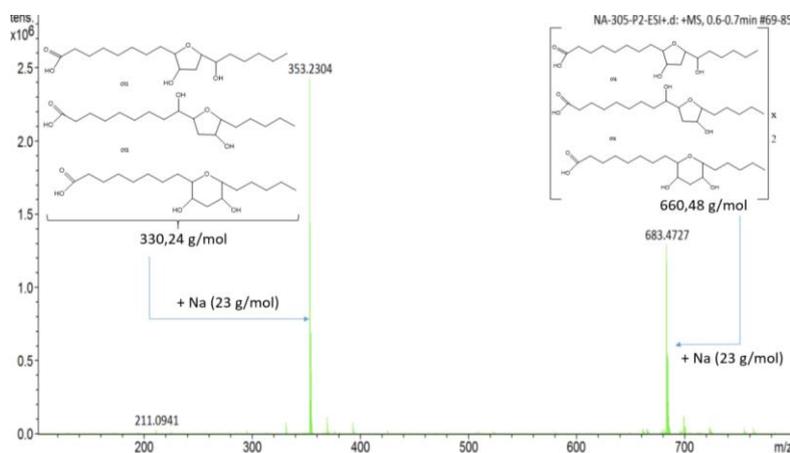


Figure 3. Mass spectrometry of the produced cyclic compounds.

To confirm that we these compounds are formed, ^{13}C NMR analysis was performed and we obtained the following spectra that corroborate cyclic compounds are formed (Figure 4).

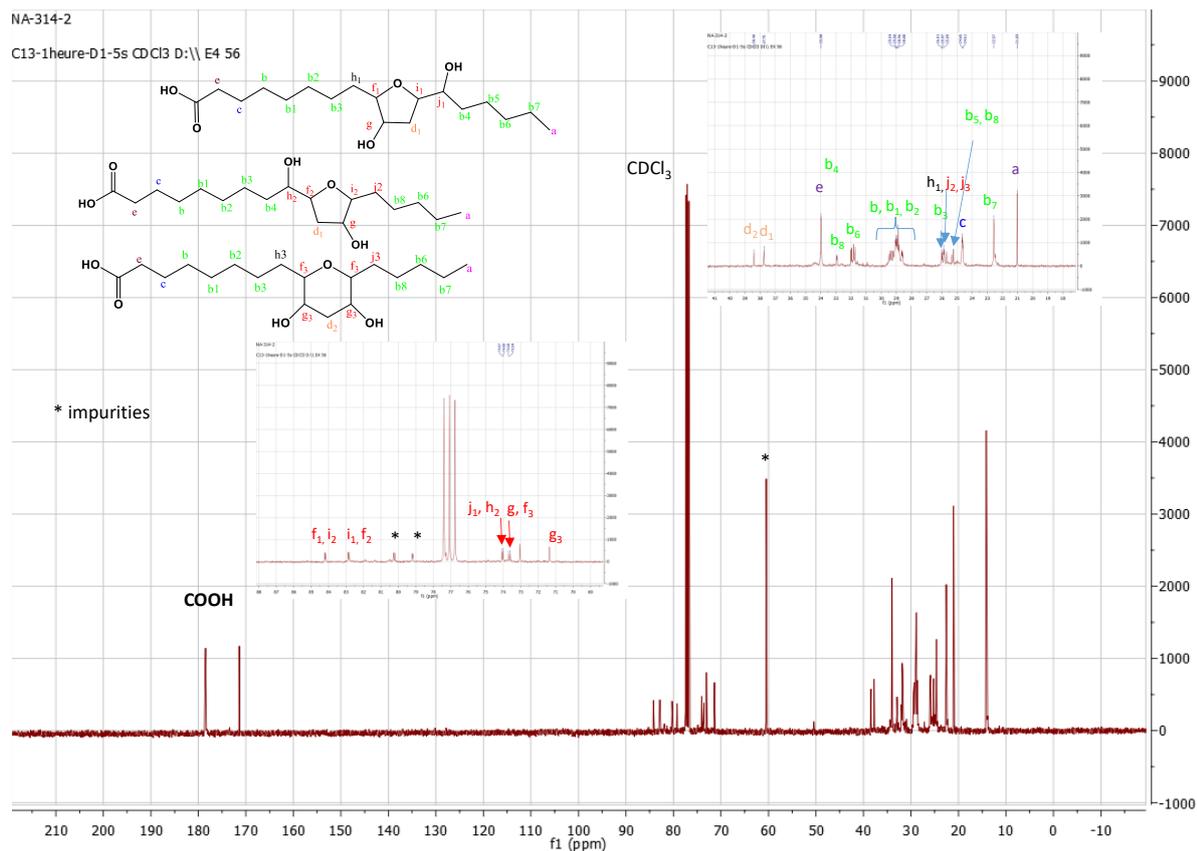


Figure 4. ¹³C NMR of products obtained.

The chemical shifts were attributed using prediction and the peaks are split due to the presence of diastereoisomers. A 2D-HSQC NMR analysis was also performed and confirm that cyclic compounds were formed as depicted on Figure 5.

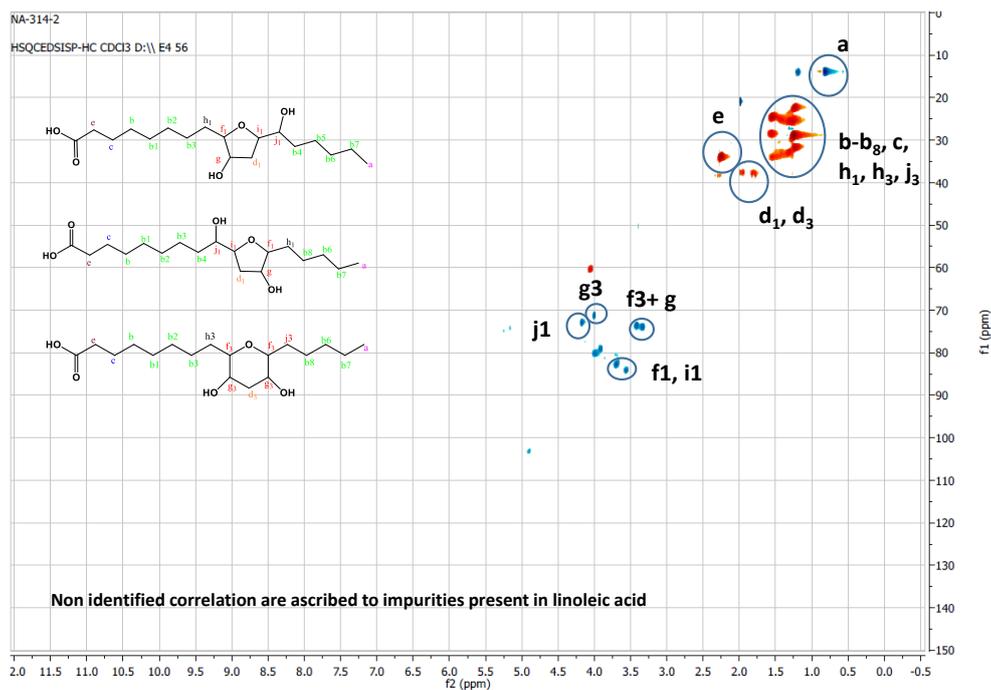


Figure 5. 2D HSQC NMR of products obtained.

Based on these analysis, the products were purified and they were analyzed by GC (Figure 6)

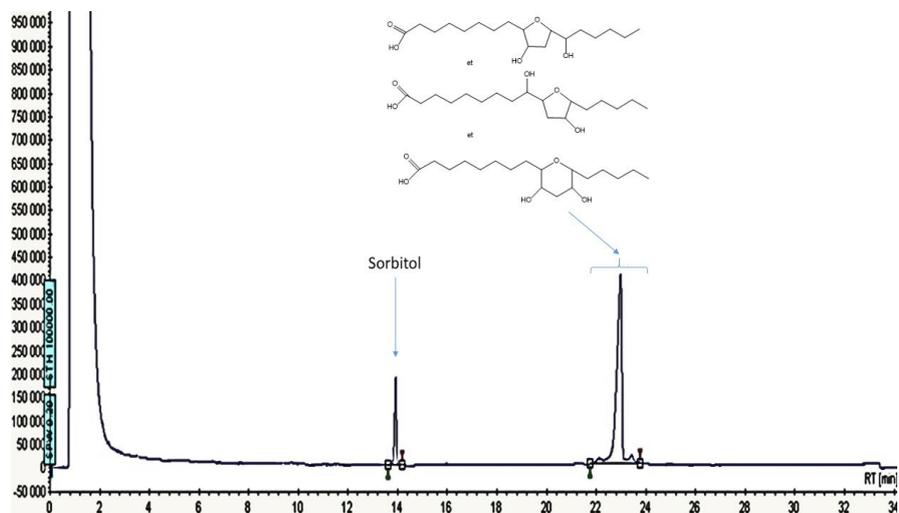
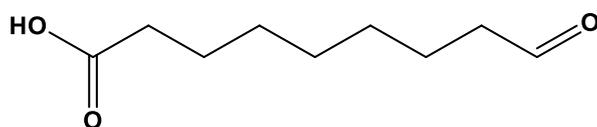


Figure 6. Chromatogram of the three cyclic isomers (sorbitol: internal standard)

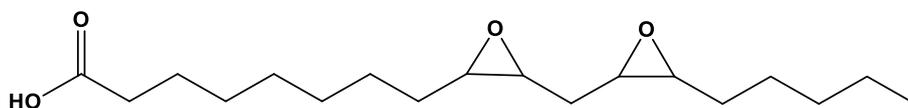
A calibration was made (Figures S2 and S3) and all the yields provided are GC yields. Unfortunately we were not in a position to separate them by GC and quantify them individually. For the intermediate, 9,12-diépoxysearic acid was identified and quantified. Other products were also detected. Despite our effort to analyze these by-products, we were only able to

identify one of them by mass spectroscopy analysis (Figure S4). A m/z of 195 was observed corresponding to the molecular weight of 9-oxononanoic acid and a sodium adduct (Scheme 4).



Scheme 4. Product resulting from the fragmentation of cyclic isomer: 1: 9-oxononanoic acid.

A kinetic profile was also carried out (Figure 1). After 5 min of reaction, 85% of linoleic acid was converted to the three cyclic compounds with a total yield of 39% and 46% of selectivity. Another product was formed corresponding to 9,12-diepoxy stearic acid with a yield of 11% (Scheme 5). By-products were also observed as reported on Figure 1. In all the presented results the missing percentage in yield is due to the formation of unidentified products.



Scheme 5. Structure of 9,12-diepoxy stearic acid.

After 15 min of reaction, the conversion of linoleic acid increased slightly to 95%. In parallel, the yield of cyclic compounds increased from 39% to 45%, while the yield of 9,12-diepoxy stearic acid decreased from 11% to 0%. A total conversion and a maximum yield in the cyclic compounds of 50% (50% selectivity) were observed after 30 min of reaction. The decrease in the yield of 9,12-diepoxy stearic acid from 11% to 0% can be due to its conversion to cyclic compounds or to its decomposition. Upon prolonged reaction time, the cyclic compounds selectivity did not change that can be due to the stability of the active species or to the lack of hydrogen peroxide in the reaction media. Additional studies were performed in order

to improve yield and selectivity in cyclic isomers and also to determine if 9,12-diepoxy stearic acid is an intermediate in this reaction.

3.1. Influence of the amount of hydrogen peroxide

The first parameter studied was the amount of H₂O₂. The reaction was performed using similar conditions as before with different loading of H₂O₂: 1.5 eq., 2.5 eq. and 3.5 eq. (Table 1). A decrease in the quantity of hydrogen peroxide from 3.5 to 2.5 eq. led to an increase of the yield of cyclic isomers. Thus, after 15 min of reaction, 75% of cyclic isomers and 15% of 9,12-diepoxy stearic acid were formed for 90% conversion of linoleic acid against 50% of cyclic compounds after 30 min in the presence of 3.5 eq. of H₂O₂. In the presence of 2.5 eq. of H₂O₂, a total conversion was achieved after 30 min of reaction and 2% yield of 9,12-diepoxy stearic acid with 98% of cyclic compounds were observed. With the increase of the reaction time from 15 min to 30 min, the selectivity to the desired cyclic compounds increased from 55% to 98% due to a decrease of 9,12-diepoxy stearic acid yield on the benefit of the cyclic compounds showing that 9,12-diepoxy stearic acid is a potential intermediate in the oxidative cleavage of linoleic acid. Moreover, an amount of 2.5 eq. of H₂O₂ prevented secondary reactions from happening and thus led to a maximum yield of 98% in cyclic isomers. However, upon prolonged reaction time (60 min), the cyclic isomers yield decreased due to their decomposition. By-products were also present throughout the reaction in the presence of 3,5 equivalents of H₂O₂ may be due to either (1) the presence of an excess of H₂O₂ which, after oxidizing the entire catalyst into active species, begins to oxidize unstable cyclic isomers into by-products, or (2) the potential degradation of the active species WO(O₂)₂ that is produced from H₃PW₁₂O₄₀ in the presence of H₂O₂, as reported in the literature [23–25]. Hence, in the literature, it is well known that the stability of polyoxometalates in the presence of an aqueous solution of hydrogen peroxide can be an issue [22]. The degradation of cyclic isomers after 60 min in the presence

of 2.5 eq. of H₂O₂ may be rationalized by the decomposition of the reaction products by excess H₂O₂ or active catalytic species after complete substrate (linoleic acid) consumption.

Table 1. Influence of the amount of hydrogen peroxide in the oxidative cyclization of linoleic acid (1.5 mmol) in the presence of 15 wt.% of H₃PW₁₂O₄₀ at 80 °C.

H ₂ O ₂ (eq.)	Time (min)	Conv. (%)	Yield of cyclic comp. (%)	Yield of 9,12-diepoxy stearic acid (%)
1.5	60	60	39	21
	15	90	75	15
2.5	30	100	98	2
	60	100	60	0
3.5	60	100	51	0

In the presence of a lower amount of H₂O₂ equal to 1.5 equivalents, a maximum linoleic conversion of 60% was achieved after 60 min of reaction with the formation of maximum yields of 40 % of cyclic compounds and 20 % of 9,12-diepoxy stearic acid. This means that this amount of H₂O₂ was insufficient to fully convert linoleic acid and 9,12-diepoxy stearic acid into cyclic isomers. In summary, the use of 2.5 equivalents of H₂O₂ was optimal to achieve a total conversion of linoleic acid and a cyclic compounds yield of 98%, after 30 min of reaction, with 15 wt% catalyst.

3.2. Influence of catalyst amount

The influence of the amount of catalyst was subsequently optimized. To this aim, different amount of H₃PW₁₂O₄₀ were compared: 2 wt.%, 5 wt.% and 15 wt.% (Figure 2). The reaction was performed at 80 °C in a reactor containing 1.5 mmol of linoleic acid and 2.5 equivalents of H₂O₂. By reducing the amount of catalyst from 15 wt.% to 5 wt.%, the TOF increased from 1,658 to 5,570 h⁻¹. Similar results were observed but for a longer reaction time (60 min) to reach 98% of cyclic isomers yield along with 2% of 9,12-diepoxy stearic acid for a total conversion

of linoleic acid in the presence of 5 wt.% of $\text{H}_3\text{PW}_{12}\text{O}_{40}$ catalyst. In contrast, for longer reaction time (120 min), the cyclic compounds were stable and their yield remained constant (99%). In the presence of 5 wt.% catalyst, the amount of active species formed did not lead to the fragmentation of cyclic isomers after 60 min of reaction.

These results show that in the presence of a catalyst loading higher than 5 wt.%:

- (1) the oxidation of the initial form of the catalyst into active species by hydrogen peroxide takes longer time than that in the presence of 5 wt.%, which explains the decrease in TOF of the reaction. Once the entire catalyst is oxidized into active species, the latter (the active species) being more important than in the presence of 5 wt.% catalyst, the reaction rate increases and a total conversion is achieved for a shorter reaction time;
- (2) the excess of active species which still present in the reaction medium will subsequently fragment the cyclic reaction products.

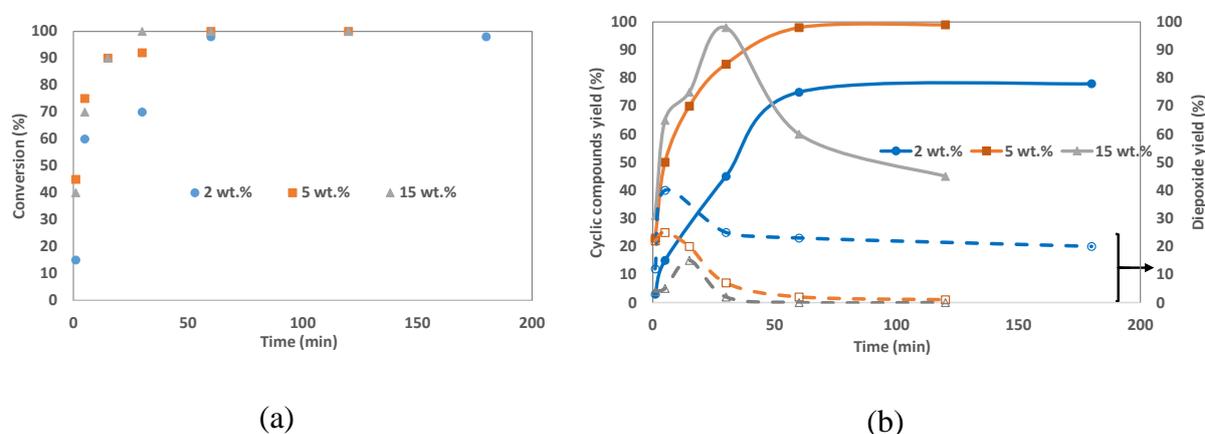


Figure 2. Influence of $\text{H}_3\text{PW}_{12}\text{O}_{40}$ catalyst loading on linoleic acid (1.5 mmol) oxidative cyclization in the presence of 2.5 eq. of H_2O_2 at 80 °C. a) conversion of linoleic acid; b) cyclic compounds yield (filled lines) and 9,12-diepoxystearic acid yield (dashed lines).

A further decrease of the catalyst loading from 5 wt.% to 2 wt.% led to a conversion of 98% after 1 h of reaction with a decrease in the TOF from $5,550 \text{ h}^{-1}$ to $4,658 \text{ h}^{-1}$. This amount

of catalyst is not sufficient to convert the entire reaction intermediate into cyclic isomers since the maximum yield in cyclic isomers formed is 75% after 60 min of reaction with 23% yield of 9,12-diepoxylinoleic acid. Upon prolonged reaction time, no change in the selectivity of the reaction was observed. It can be due to a decomposition of H₂O₂ at this temperature as shown below).

Therefore, an amount of 5 wt.% catalyst is optimal to convert selectively linoleic acid into cyclic compounds (98% yield) without any degradation of these products.

3.3. Influence of temperature

The influence of temperature was finally studied (Table 2). The kinetic study was performed using 1.5 mmol of linoleic acid in the presence of the optimal amounts of catalyst (5 wt.% of H₃PW₁₂O₄₀) and 2.5 eq. of H₂O₂.

Table 2. Influence of temperature on the oxidative cyclization of 1.5 mmol of linoleic acid, 5 wt.% of H₃PW₁₂O₄₀ and 2.5 eq. of H₂O₂.

T (°C)	Time (min)	Conv.(%)	Cyclic compounds Yield (%)	9,12-diepoxylinoleic acid Yield (%)
60 °C	5	60	26	14
	15	75	35	23
	30	95	79	0
	60	98	79	0
80 °C	5	75	50	25
	15	90	70	20
	30	92	85	7
	60	100	98	2
90 °C	5	66	40	26
	15	80	61	19
	30	85	75	10
	60	100	99	1

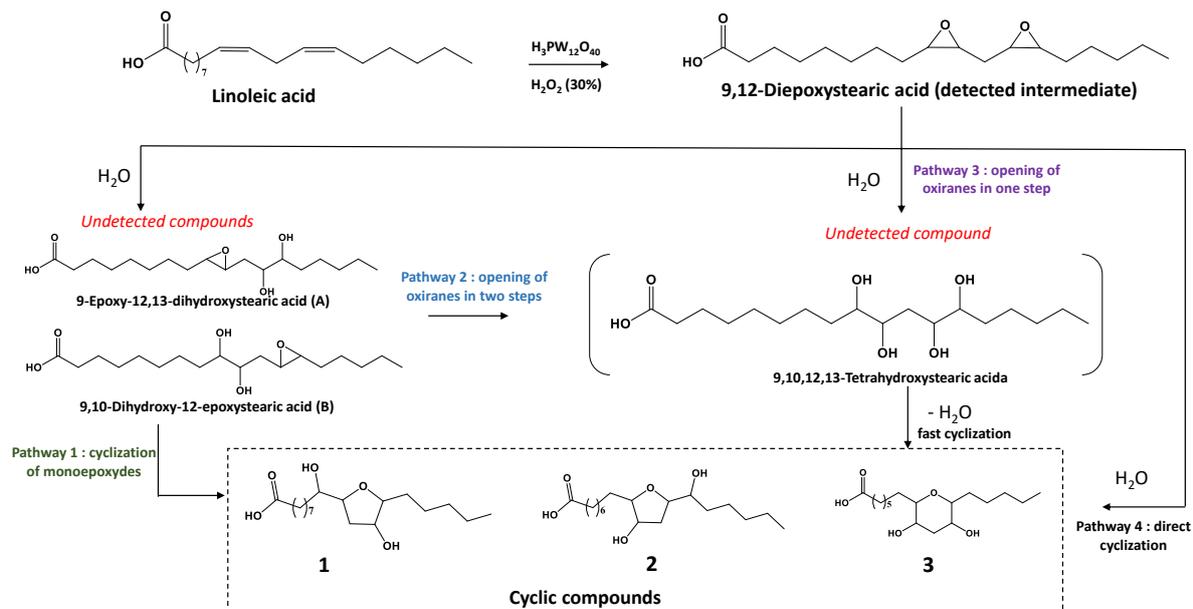
At 90 °C, similar results to those obtained at 80 °C were observed in terms of conversion and yields. A total conversion was achieved after 60 min of reaction with formation 99% yield of cyclic compounds and 1% of 9,12-diepoxy stearic acid.

However, by decreasing reaction temperature from 80 to 60 °C, degradation products are formed even at short reaction time. A maximum yield of 80% of cyclic compounds was achieved after 30 min of reaction for 95% conversion of linoleic acid. The presence of degradation product at 60 °C can be due to lack of catalytic activity to convert linoleic acid to cyclic compounds. Thus, a competition could take place between the activity of the active species and the hydrogen peroxide action to linoleic acid that will decompose linoleic acid. To confirm this hypothesis, a reaction was performed in the absence of catalyst and in the presence of 1.5 mmol of linoleic acid and 2.5 eq. of H₂O₂ at 60 °C. After 60 min of reaction, 20% of linoleic acid was converted into non identified products. This result confirms that a temperature of 60 °C is not high enough to completely oxidize linoleic acid. In conclusion, the highest cyclic compounds yields (98%) were obtained using 2.5 eq. of hydrogen peroxide in the presence of 5 wt.% of H₃PW₁₂O₄₀ after 1 h of reaction at 80 °C. Based on the effect of the temperature studied, the activation energy of this reaction was calculated based on the Arrhenius' law. The E_a was 187.2 kJ.mol⁻¹ based on Figure S5.

3.4. Reaction pathways

The oxidative cyclization of linoleic acid involves an epoxidation step of the two double bonds leading to the production of 9,12-diepoxy stearic acid as an intermediate as shown before. Then hydrolysis/dehydrative cyclization of the 9,12-diepoxy stearic acid occurred. One can mention that during all the experiments, no diol neither monoepoxide was detected. In the cyclization step, four pathways can occur (Scheme 6). 9,10,12,13-tetrahydroxy stearic acid can be formed either in a single step by the parallel opening of the two oxirane rings of 9,12-diepoxy stearic

acid or *via* two steps by the opening of an oxirane ring to form the compounds A or B shown in Scheme 4. In this case, the oxirane ring of each compound (A or B) will be then opened to form the 9,10,12,13-tetrahydroxystearic acid (pathway 1 in Scheme 6). However, the formation of the 3 cyclic compounds from the two compounds A and B can also be done on a direct cyclization (pathway 2 in Scheme 6) from the reaction of a -OH group of the compound A or B with the oxygen of the oxirane ring. None of the two compounds (A and B) was detected in all reactions. One of these pathway is the opening of the oxirane rings of the epoxides to form the 9,10,12,13-tetrahydroxystearic acid (pathway 3 in Scheme 6). The different cyclic isomers will therefore be formed as a result of the interaction between two different hydroxyl groups on the carbon atoms C9 and C12, C10 and C13 and C9 and C13 respectively to form the cyclic compounds 1, 2 and 3 (Scheme 2). On the other hand, 9,10,12,13-tetrahydroxystearic acid was not detected in the kinetic studies so its formation is probably followed by a very rapid interaction between the different hydroxyl groups. Another route is the direct cyclization of 9,12-diepoxystearic acid which could explain that no monoepoxide neither diol was detected (pathway 4, Scheme 6). However, as a consequence, it is complex to select one of these pathways for this reaction. Further studies need to be done to understand the reaction pathway.



Scheme 6. Reaction pathways of the formation of cyclic isomers from linoleic acid.

3.5. Synthesis of THF and Tetra-2H- pyrene derivatives in the presence of $\text{Cs}_{2,3}\text{H}_{0,7}\text{PW}_{12}\text{O}_{40}$

Since the homogeneous catalyst $\text{H}_3\text{PW}_{12}\text{O}_{40}$, was not recyclable, a heterogeneous catalyst was synthesized, $\text{Cs}_{2,3}\text{H}_{0,7}\text{PW}_{12}\text{O}_{40}$, to study the possibility to use a recyclable catalyst in the conversion of linoleic acid into cyclic compounds. The recycling of $\text{Cs}_{2,3}\text{H}_{0,7}\text{PW}_{12}\text{O}_{40}$ was therefore performed by filtration after reaction using the following conditions: 10 wt.% catalyst and 2.5 equivalents of H_2O_2 at 80 °C for 2 h reaction (Figure 3). Under these conditions 85% of linoleic acid was converted to 60 % of cyclic compounds and 25% of 9,12-diepoxy stearic acid.

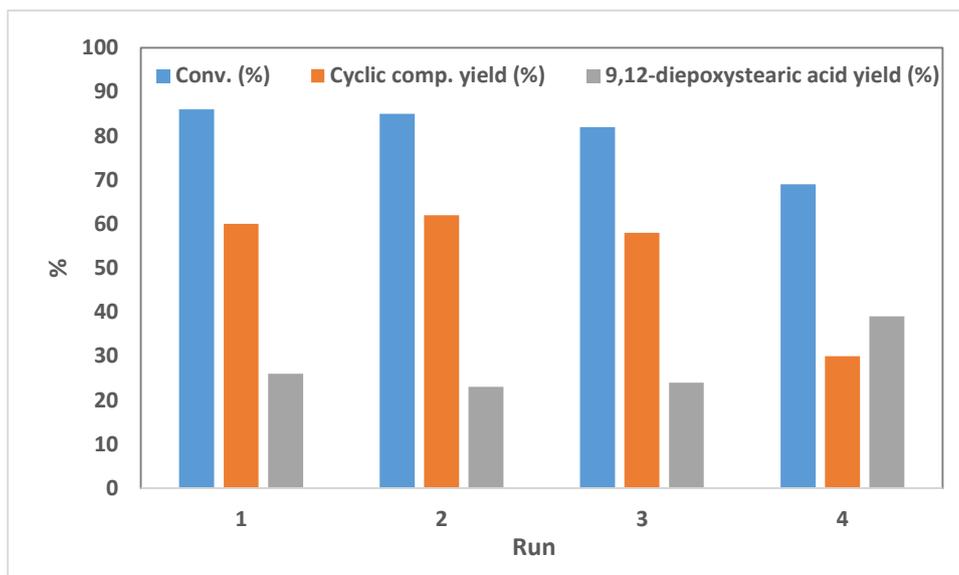


Figure 3. Recyclability of $\text{Cs}_{2,3}\text{H}_{0,7}\text{PW}_{12}\text{O}_{40}$ in the presence of 1.5 mmol of linoleic acid, 2.5 eq. of H_2O_2 and 10 wt. % $\text{Cs}_{2,3}\text{H}_{0,7}\text{PW}_{12}\text{O}_{40}$ at 80 °C for 2 h of reaction.

The results show that the heterogeneous catalyst could be recycled up to 3 times without significant loss in activity and selectivity. Similar conversions of linoleic acid (about 85%) and constant yields to cyclic isomers (about 60%) and 9,12-diepoxy stearic acid (about 25%) were observed. After the 4th cycle, the catalytic efficiency of the catalyst decreased, resulting in a decrease of linoleic conversion from 85% to 69% with the formation of 30% of cyclic isomers and 35% of 9,12-diepoxy stearic acid. This can be explained by a leaching of tungsten which are the active species as previously observed in our lab [26].

Conclusion

In this paper, the efficiency of the $\text{H}_3\text{PW}_{12}\text{O}_{40}/\text{H}_2\text{O}_2$ system was studied on the oxidative cyclization of linoleic acid to substituted THF and tetrahydro-2H-pyran. The reaction leads to the formation of three cyclic compounds that are bioactive molecules *via* a reaction pathway which involves 9,12-diepoxy stearic acid as a reaction intermediate. Under optimal conditions a total conversion was achieved after 60 min of reaction with a yield of 98% to cyclic isomers.

Compared to the different oxidants and catalytic systems used in the literature, the $\text{H}_3\text{PW}_{12}\text{O}_{40}/\text{H}_2\text{O}_2$ system resulted in higher cyclic compounds yields (98%) in the presence of a “greener” oxidant (H_2O_2 instead of NaIO_4) and in the absence of any phase transfer agent. Moreover, under optimal conditions the degradation of the cyclic compounds was avoided. A heterogeneous catalyst $\text{Cs}_{2,3}\text{H}_{0,7}\text{PW}_{12}\text{O}_{40}$ was synthesized and was recycled up to 3 times without significant loss of activity and yield.

Acknowledgements

The authors would like to thank the French Ministry of National Education, Higher Education and Research as well as the France-Canada Research Fund for the funding of the PhD grant of NA. The authors are also grateful to the Région Nouvelle Aquitaine for the funding of this project through the FR CNRS INCREASE 3707 (International Consortium on Eco-conception and Renewable Resources), the chair TECHNOGREEN and FEDER.

Formatting of funding sources

French Ministry of National Education, Higher Education and Research as well as the France-Canada Research Fund for the funding of the PhD grant of NA.

Région Nouvelle Aquitaine (FR CNRS INCREASE 3707, TECHNOGREEN, FEDER)

References

[1] A.S. Yusuff, O.D. Adeniyi, M.A. Olutoye U. G. Akpan, A Review on Application of Heterogeneous Catalyst in the Production of Biodiesel from Vegetable Oils. *J. Appl. Sci. Eng.* 4 (2007). <https://doi.org/10.33736/jaspe.432.2017>; A. Masudi, O. Muraza, Vegetable Oil to Biolubricants: Review on Advanced Porous Catalysts, *Energy Fuels* 32 (2018) 10295–10310. <https://doi.org/10.1021/acs.energyfuels.8b02017>; S. S. Sagiri, A. Anis, K. Pal, Review on Encapsulation of

- Vegetable Oils: Strategies, Preparation Methods, and Applications, *Polymer-Plastics Technology and Engineering* 55 (2016) 291–311. <https://doi.org/10.1080/03602559.2015.1050521>.
- [2] A. Corma, S. Iborra, A. Velty, Chemical Routes for the Transformation of Biomass into Chemicals, *Chem. Rev.* 107 (2007) 2411–2502. <https://doi.org/10.1021/cr050989d>
- [3] N. Biermann, W. Friedt, S. Lang, W. Luhs, G. Machpmuller et J.O. Metzger, New Syntheses with Oils and Fats as Renewable Raw Materials for the Chemical Industry, *Angew. Chem. Int. Ed Engl.* 39 (2000) 2206–2224. [https://doi.org/10.1002/1521-3773\(20000703\)39:13<2206::AID-ANIE2206>3.0.CO;2-P](https://doi.org/10.1002/1521-3773(20000703)39:13<2206::AID-ANIE2206>3.0.CO;2-P).
- [4] A. Köckritz et A. Martin, Synthesis of azelaic acid from vegetable oil-based feedstocks, *Eur. J. Lipid Sci. Technol.* 113 (2011) 83–91. <https://doi.org/10.1002/ejlt.201000117>.
- [5] C. J. Dutton, B. J. Banks, C. B. Cooper, Polyether Ionophores. *Nat. Prod. Rep.* 12 (1995) 165–181. <https://doi.org/10.1039/NP9951200165>.
- [6] L. Zeng, Q. Ye, N. H. Oberlies, G.; Shi, Z.-M. Gu, K. He, J. L. McLaughlin, Recent Advances in Annonaceous Acetogenins. *Nat. Prod. Rep.* 13 (1996) 275–306. <https://doi.org/10.1039/NP9961300275>.
- [7] L. Zeng, Y. Zhang, Q. Ye, G.-E. Shi, K. He, J. L. McLaughlin, 4-deoxyannonontacin and (2,4-*cis* and *trans*)-annonontacinone, new bioactive mono-tetrahydrofuran annonaceous acetogenins from *Goniothalamus giganteus*. *Bioorg. Med. Chem.* 5 (1997) 549–553. [https://doi.org/10.1016/S0968-0896\(96\)00268-4](https://doi.org/10.1016/S0968-0896(96)00268-4).
- [8] Q. Ye, L. Zeng, G.-E. Shi, D. Evert, J. L. McLaughlin, 4-Acetyl Annonacin and 4-Acetyl Xylomaticin: Two Novel Bioactive Mono-Tetrahydrofuran Annonaceous Acetogenins from *Asimina Longifolia* (Annonaceae). *Nat. Prod. Lett.* 8 (1996), 291–298. <https://doi.org/10.1080/10575639608044910>.
- [9] S. Etcheverry, S. Sarpaz, D. Fall, A. Laurens, A. Cave, Annoglucin, an acetogenin from *Annona glauca*. *Phytochemistry* 38 (1995) 1423–1426. [https://doi.org/10.1016/0031-9422\(94\)00820-J](https://doi.org/10.1016/0031-9422(94)00820-J).
- [10] G.-E. Shi, L. Zeng, K. He, Q. Ye, Z.-M. Gu, J. M. MacDougal, J. L. McLaughlin, Applying Mosher's Method to Acetogenins Bearing Vicinal Diols. The Absolute Configurations of Muricatetrocin C and Rollidecins A and B, New Bioactive Acetogenins from *RoUinia mucosa*. *Bioorg. Med. Chem.* (1996) 1281–1286. [https://doi.org/10.1016/0968-0896\(96\)00114-9](https://doi.org/10.1016/0968-0896(96)00114-9).
- [11] B. Travis, B. Borhan, Oxidative cyclization of 1,4-dienes to yield 2,3,5-trisubstituted tetrahydrofuran-diols. *Tetrahedron Letters* 42 (2001) 7741–7745. [https://doi.org/10.1016/S0040-4039\(01\)01609-4](https://doi.org/10.1016/S0040-4039(01)01609-4).

- [12] B. Borhan, J. Nourooz-Zadeh, T. Uematsu, B. D. Hammock, M. J. Kurth, Stereochemical aspects of cytosolic epoxide hydrolase hydration of methyl diepoxystearates. *Tetrahedron* 49 (1993) 2601–2612. [https://doi.org/10.1016/S0040-4020\(01\)86339-0](https://doi.org/10.1016/S0040-4020(01)86339-0).
- [13] T. M. Luong, H. Schriftman, D. Swern, Direct hydroxylation of fats and derivatives with a hydrogen peroxide tungstic acid system. *J. Am. Oil Chem. Soc.* 44 (1967) 316–320. <https://doi.org/10.1007/BF02635624>.
- [14] E. Poli, J. Barrault, N. Bion, J. M. Clacens, Selective epoxidation of unsaturated fatty esters over peroxophosphotungstic catalysts (POW) under solvent free conditions: Study of the POW catalyst's mechanism. *Catal. Today* 157 (2010) 371–377. <https://doi.org/10.1016/j.cattod.2010.02.005>.
- [15] E. Santacesaria, A. Sorrentino, F. Rainone, M. Di Serio, F. Speranza, Oxidative Cleavage of the Double Bond of Monoenic Fatty Chains in Two Steps: A New Promising Route to Azelaic Acid and Other Industrial Products. *Ind. Eng. Chem. Res.* 39 (2000) 2766–2771. <https://doi.org/10.1021/ie990920u>.
- [16] D. Dalmizrak, H. Göksu, M. S. Gültekin, A facile synthesis of vicinal cis-diols from olefins catalyzed by in situ generated Mn_xO_y nanoaggregates. *RSC Adv.* 5 (2015) 20751–20755. <https://doi.org/10.1039/C5RA01646K>.
- [17] A. Enferadi Kerenkan, F. Béland, T.-O. Do, Chemically catalyzed oxidative cleavage of unsaturated fatty acids and their derivatives into valuable products for industrial applications: a review and perspective. *Catal. Sci. Technol.* 6 (2016) 971–987. <https://doi.org/10.1039/C5CY01118C>.
- [18] D. Vidal, G. Olivo, M. Costas, Controlling Selectivity in Aliphatic C–H Oxidation through Supramolecular Recognition. *Chem. Eur. J.* 24 (2018) 5042–5054. <https://doi.org/10.1002/chem.201704852>.
- [19] A. Gharib, M. Jahangir, M. Roshani, N. Noroozi Pesyan, J. Scheeren, Synthesis of (*S*)-(-)-Propranolol by Using $Cs_{2.5}H_{0.5}PW_{12}O_{40}$ Nanocatalyst as Green, Eco-Friendly, Reusable, and Recyclable Catalyst. *Synth. React. Inorg. M.* 45 (2015) 350–355. <https://doi.org/10.1080/15533174.2013.832323>.
- [20] A. S. Dias, S. Lima, M. Pillinger, A. A. Valente, Acidic cesium salts of 12-tungstophosphoric acid as catalysts for the dehydration of xylose into furfural. *Carbohydrate Research* 341 (2006) 2946–2953. [doi:10.1016/j.carres.2006.10.013](https://doi.org/10.1016/j.carres.2006.10.013)
- [21] T. Okuhara, T. Nishimura, H. Watanabe, M. J. Misono, Insoluble heteropoly compounds as highly active catalysts for liquid-phase reactions. *J. Mol. Catal.* 74 (1992) 247–256. [https://doi.org/10.1016/0304-5102\(92\)80242-9](https://doi.org/10.1016/0304-5102(92)80242-9)

- [21] L. I. Kuznetsova, R. I. Maksimovskaya, M. A. Fedotov, K. I. Matveev, Peroxo complexes of phosphotungstic heteropoly acid. *Russ Chem Bull* 32 (1983) 666–670. <https://doi.org/10.1007/BF00953453>.
- [23] L. Carlos de la Garza, K. De Oliveira Vigier, G. Chatel, A. Moores, Amphiphilic dipyridinium-phosphotungstate as an efficient and recyclable catalyst for triphasic fatty ester epoxidation and oxidative cleavage with hydrogen peroxide. *Green Chem.* 19 (2017) 2855–2862. <https://doi.org/10.1039/C7GC00298J>.
- [24] J.-E. Bäckvall, *Modern Oxidation Methods*, Wiley-VCH Verlag GmbH & Co. KGaA, 2004. DOI:10.1002/3527603689
- [26] PhD thesis of Nahla Araji, *Procédé éco-compatible d'oxydation catalytique de molécules biosourcées insaturées (furfural, esters ou acides gras insaturés)*, 2018.