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Boris Guicheret, Eric Alberto da Silva, Regis Philippe, Alain Favre-Reguillon, Laurent Vanoye, et al.. Aerobic Oxidative Cleavage of Vicinal Diol Fatty Esters by a Supported Ruthenium Hydroxide Catalyst. ACS Sustainable Chemistry & Engineering, 2020, 8 (35), pp.13167-13175. 10.1021/acssuschemeng.0c01265 . hal-03041041

HAL Id: hal-03041041

<https://hal.science/hal-03041041>

Submitted on 4 Dec 2020

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Aerobic Oxidative Cleavage of Vicinal-Diol Fatty Esters by Supported Ruthenium Hydroxide Catalyst

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KEYWORDS: Oxidative cleavage – Heterogeneous ruthenium catalyst - Oxygen – azelaic acid - pelargonic acid- Dihydroxystearic acid - Mechanism.

ABSTRACT: Oxidative cleavage of fatty acids and fatty acid derivatives can be used to obtain mono- and dicarboxylic acids which are valuable building blocks in different industries.

Although ozonolysis has been industrially developed, there is a need to replace ozone with a more benign oxidant. An alternative process for the oxidative cleavage of dihydroxystearic acid methyl ester **6b** using oxygen as oxidant and a heterogeneous ruthenium catalyst ($\text{Ru(OH)}_x/\gamma\text{-Al}_2\text{O}_3$) was studied. Detailed investigations of the formation of intermediates and by-products as a function of time led us to improve the experimental conditions. **1b** was oxidized into the corresponding pelargonic acid **2a** and azelaic acid **3a** with a yield of 85% and 80% respectively in a batch reactor with a biphasic organic-aqueous system under 5 bar of oxygen. The reactivities of the different intermediates studied independently under the same experimental conditions, enabled us to propose a parallel mechanism for the oxidative cleavage of diol **6b**. The recyclability of the catalyst was also studied. Even if Ru traces could be found in the aqueous phase, the observed drop in activity after 4 runs could be explained by adsorption of by-products at the surface of the catalyst. The activity could be recovered after washing the catalyst with 0.1 M NaOH under sonication.

Introduction

In the chemical industry, products obtained through oxidation reactions represent a huge market. A large panel of compounds can be synthesized and used as such or as intermediates in the preparation of organic chemicals, perfumes, cosmetics, or pharmaceutical products.¹ The research activities concerning new selective oxidation processes having low environmental and safety impacts are of prominent importance regarding a growing demand of these added-value compounds in combination with growing concerns regarding existing and new regulations. To minimize both the safety risks and the amount of waste produced, the development of process

using safe and sustainable oxidant/catalyst packages is highly requested. Thanks to their abundance, availability, diversity, and biodegradability, vegetable oils offer a large number of potential applications.²⁻³ Modifications can be performed on the carboxyl group as well as on the alkyl chain. Oxidation methods are widely used to transform unsaturated fatty acids into useful building blocks for the synthesis of monomers that have countless applications in the textile and automobile industries.⁴ The transformation of alkenes through an oxidation process also leads to the production of a large panel of compounds (epoxides, diols, aldehydes, etc...).^{1,5}

The products of oxidative cleavage of oleic acid **1a** are pelargonic **2** and azelaic acids **3** (Figure 1). Azelaic acid **3** is industrially used in the manufacture of polyamides, laminates, adhesives, plasticizers, and hydraulic fluids. Pelargonic acid **2**, which is the co-product of the process, finds applications as herbicide, fungicide, and also used in the manufacture of lubricants and plasticizers.

From oleic acid **1a**, the direct access to carboxylic acids is industrially carried out by ozonolysis (Figure 1).⁶⁻⁷ Though this transformation is highly efficient from an atom economy point of view, it presents some disadvantages, such as the risk linked to explosive intermediates (ozone and ozonides **4**) and high-electricity consumption for the ozone production.^{4,8} Therefore, new methods with alternative oxidants are in high demand. Molecular oxygen and hydrogen peroxide combined with efficient catalytic systems are considered the most suitable for the oxidative cleavage of unsaturated fatty acids.⁵

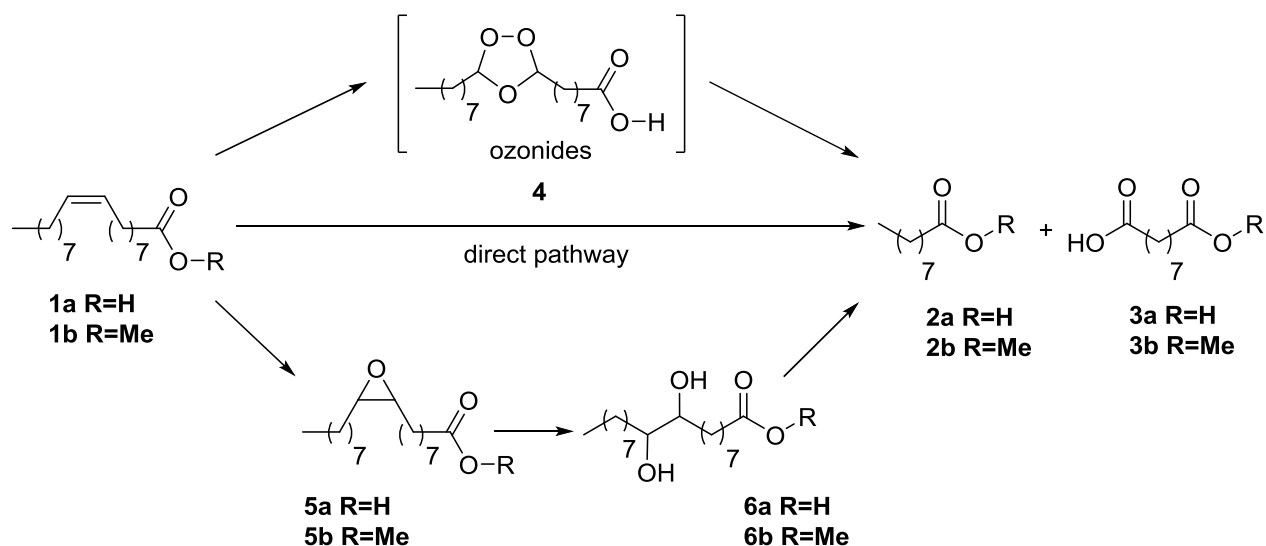


Figure 1. Oxidative cleavage of oleic acid **1a** or methyl oleate **1b**

The direct cleavage of methyl oleate **1a** with H_2O_2 as an oxidant was investigated extensively using tungsten-based catalysts (Figure 1). When polyoxotungstates is associated with hydrogen peroxide, yields of **2a** and **3a** close to 80% were obtained.⁹⁻¹¹ Results obtained with tungsten oxide nanoparticles¹² or supported tungsten oxide has been reported.¹³ In 2013, Behr et al.¹⁴ have proposed efficient homogeneous Ru-catalyzed oxidative cleavage of **1b** using H_2O_2 as oxidant given **3b** with a yield of 86%.

An indirect pathway was also studied (Figure 1) where the diol **6** is the key product *via* epoxidation of the double bond followed by a ring-opening reaction. This reaction sequence is often used without isolation of the intermediately formed epoxides **5**.⁵ To our knowledge, Novamont is the only company to operate the indirect pathway at an industrial scale. The epoxidation step of **1b** or triglycerides is performed using an $\text{H}_2\text{WO}_4/\text{H}_2\text{O}_2$ catalytic system while $\text{Co}(\text{OAc})_2/\text{air}$ was used for the oxidative cleavage of **6**.^{4,15}

The oxidative cleavage of **6** has also been studied by several authors. Kulik *et al.* have described the oxidative cleavage of **6a**.¹⁶⁻¹⁷ Reactions were performed under oxygen as oxidant and with a gold catalyst supported on alumina in basic aqueous media giving high yields of **2a** and **3a**. Our group has patented an efficient “metal-free” oxidative cleavage of **6a** using NaOCl as an oxidant.¹⁸ Unfortunately, at a pilot-scale, the formation of chlorinated by-products has constituted a serious limitation for industrial development.¹⁹ An alternative pathway was developed consisting of a two consecutive steps procedure of dehydrogenation of **6b** with Ni/SiO₂ catalyst forming α -hydroxy ketones followed by the oxidative cleavage with H₂O₂-HCOOH.²⁰

Catalytic systems based on Ru have been widely studied and are well-known to catalyze the oxidative cleavage of unsaturated fatty acids but strong oxidants like NaIO₄ are generally required.^{1, 3} Behr *et al* have shown that Ru complexes using H₂O₂ as oxidant can effectively cleave **1b** into the corresponding carboxylic acid.¹⁴ Furthermore, among numerous support metal catalysts reported for the oxidation, Ru catalysts, and in particular Ru(OH)_x/ γ -Al₂O₃ catalyst (Mizuno catalyst) are reported to have good catalytic activities for the aerobic oxidation of alcohols.²¹⁻²² In this report, this catalyst was evaluated for the aerobic cleavage of **6b**. A detailed investigation of the operating conditions, their influences on the formation of intermediates and by-products were performed.

Experimental

Sources of chemicals are listed in Supporting Information. **6a** (75% purity) was obtained from AVRIL Group, purified to 95% by recrystallization in EtOAc/MeOH mixture converted to **6b** by esterification in MeOH using Amberlyst 15 as catalyst.²⁰

The Ru(OH)_x/γ-Al₂O₃ catalyst was prepared according to Mizuno et al.²³ Powder γ-Al₂O₃ (20.0 g) calcined at 550°C for 3 h was stirred with 600 mL of an aqueous solution of RuCl₃ (20 mM) at room temperature. After 15 min, the pH of the solution was adjusted to 13.2 by addition of an aqueous solution of NaOH (1 M) and the resulting slurry was stirred for 24 h at room temperature. The solid was then filtered off, washed with a large amount of water (18.0 MΩ.cm), and dried under vacuum at 100 °C overnight to afford 21 g of Ru(OH)_x/γ-Al₂O₃ as a dark green powder.

Safety

It is worth mentioning that in the case of oxidation reactions, fuel, oxidant, and energy are present at the same time in the batch reactor. Thus, the safety of the process should receive explicit attention. The reactions must be supervised by well-trained personnel in a batch reactor dedicated to reactions under oxygen. In the case of a runaway, the pressure must be relieved via adequate relief devices to a safe location. The presence of water in the gas phase in most of our reactions is an additional safety factor.

General procedure for aerobic oxidative cleavage by supported ruthenium hydroxide catalyst

The reactions were performed in a 300 mL thermo-regulated stainless steel autoclave (Parr instrument) with a mechanical stirring system. A total volume of 120 mL of the mixture of **6b**, catalyst, and solvent were placed in the batch reactor. The reactor was purged with argon and heated to the required temperature. At $t = 0$, the partial pressure of oxygen in the reactor is fixed

to 5 bar. The oxygen pressure inside the reactor was kept constant during the reaction and oxygen consumption can be followed as a function of time. At the end of the reaction, the reactor was cooled, and then purged with argon. The reaction mixture was collected in a beaker and the batch reactor was washed with ethyl acetate. The ruthenium catalyst was filtered through Millipore filter 0.1 μm . Organic layers were separated from water and water was extracted two times by 100 mL of ethyl acetate. Organic phases were dried over MgSO_4 and add in a 500 mL volumetric flask containing 402 mg of eicosan. The volume of the volumetric flask was adjusted using ethyl acetate and the organic phase was analyzed by gas chromatography.

Results and discussion

The aerobic oxidation of **6b** was first attempted under neat conditions in a batch reactor using air as oxidant and $\text{Ru}(\text{OH})_x/\gamma\text{-Al}_2\text{O}_3$ as the catalyst. 30 bar of air was introduced in the reactor at the reaction mixture was heated at 130°C for 5 h. Gas chromatography analysis shows the full conversion of the starting material. The reaction mixture was cooled and then diluted with MeOH, filtrated over celite and then 5 wt% of Amberlyst 15 was added as a catalyst for esterification. After 12 h at reflux, 20% of the corresponding esters **2b** and **3b** could be obtained after purification. These encouraging results have prompted us to further study this reaction under oxygen. Reactions will be performed at a constant O_2 pressure of 5 bar, and the oxygen consumption as a function of time could be followed. To increase safety, water was added as a diluent and the concentration of **6b** was decreased to 33 g/L. The reaction was performed at 130°C for 5 h under 5 bar of O_2 and the results are shown in Figure 2.

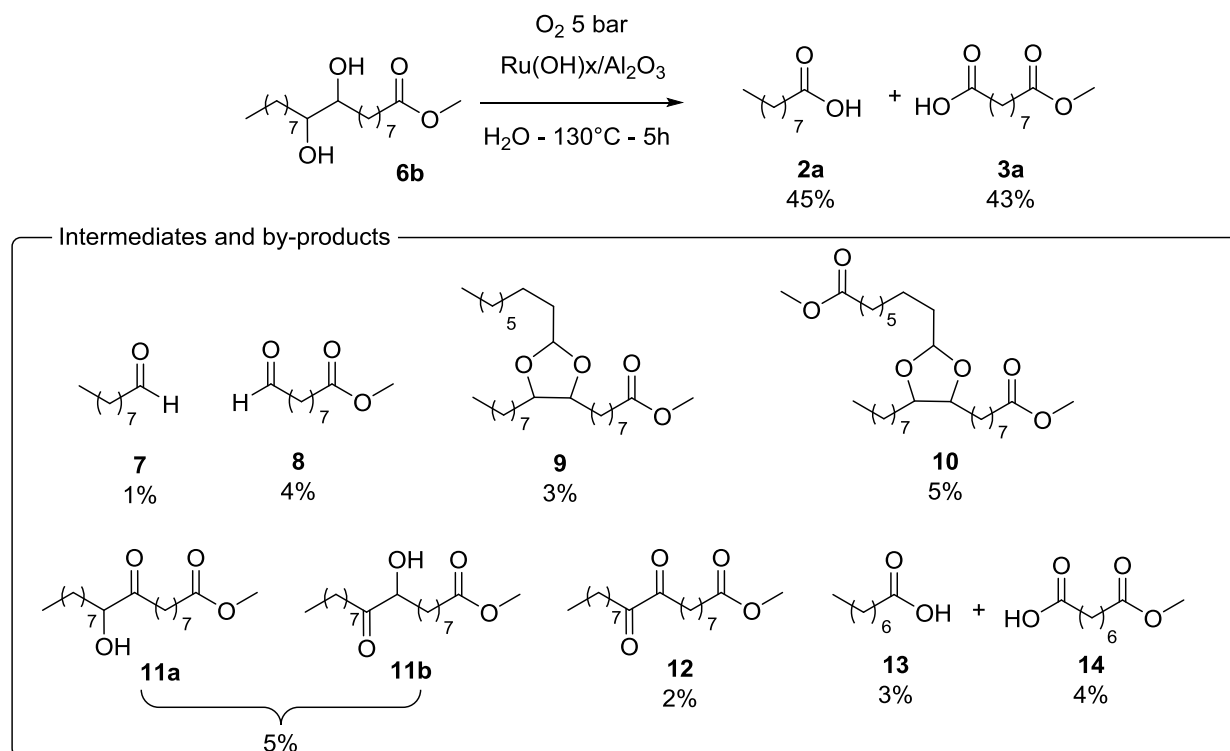


Figure 2. Oxidative cleavage of **6b** by $\text{Ru(OH)}_x/\gamma\text{-Al}_2\text{O}_3$ catalyst (6 mol%) using O_2 as oxidant. $[\mathbf{6b}] = 33\text{g/L}$ in H_2O , 130°C , $\text{Ru(OH)}_x/\gamma\text{-Al}_2\text{O}_3$ (4 mol%), O_2 5 bar, 5h. Yields are determined by GC after calibration with eicosan as an external standard.

After 5 hours, **6b** was completely converted and 45% of **2a** and 43% of **3a** were obtained. Several intermediates or by-products could be also identified by GC and GC/MS (Figure 2). The structure of the products was confirmed by comparison with authentic products previously synthesized.²⁰ The latter are used for calibration using eicosan as an external standard (see Supporting Information). Aldehydes **7** and **8** could be identified and quantified. These products could be considered as the first intermediates of the cleavage of **6b** (*vide supra*). These aldehydes could also react with the starting materials, even in the presence of water, to form ketals **9** and **10**. The formation of these heavy by-products has already been mentioned in the literature.^{4, 15}

Two other products that could be considered as the first intermediates of the cleavage of **6b** (*vide supra*) could be also identified, *i.e.* α -hydroxy ketone **11a** and **11b**. We were not able to separate both isomers, and thereafter, we will only discuss the two regioisomers **11**. **11** could also be oxidized into α -diketone **12** under our conditions. **11** and/or **12** could be then cleaved into **2a** and **3a** (*vide supra*). By-products cleavage obtained after the loss of carbon, *i.e.* octanoic acid **13** and then mono methyl ester of suberic acid **14** (*i.e.* 8-methoxy-8-oxooctanoic acid), could also be precisely quantified. Under those conditions, a carbon balance of 79% could be calculated. The evolution of the concentration of possible intermediates **7**, **8**, **11**, and **12** as well as by-products **9**, **10**, **13**, and **14** as a function of time could give us important information on the mechanism of this reaction and was thus studied.

Study of the evolution of the concentration of identified compounds as a function of time

Then, the concentration of the identified products formed (Figure 2) as a function of time was studied. The results are summarized in two graphs (Figure 3). After 20 minutes at 130°C, the conversion of **6b** was close to 30% and cleavage compounds **2a** and **3b** were obtained with a yield of 13% and 5% respectively (Figure 3a). Aldehydes **7** and **8** were the major intermediate products with a yield of 20% and 11% respectively (Figure 3b) along with 5% of ketals **9** and **10**. The carbon balance was up to 98% taking into account the presence of less than 2% of α -hydroxy ketones **11**, diketone **12** as well as **13** and **14** (Figure 3b). The maximum concentration of aldehydes **7** and **8** was reached after 30 min and then slowly decreased until the end of the experiment. The maximum yield of aldehydes **7** and **8** also corresponds to a sharp decrease in the mass balance, from up to 98% down to 84% at 60 min. The presence of C8 derivatives, compounds **13** and **14**, with the loss of one carbon from the starting materials, were also detected at this point. After that, the mass balance slowly decreases to 79% (Figure 3 a). The yield of

cleavage compounds **2a** and **3b** increase steadily until the yields of 45 and 43 % respectively were reached. After 60 min, the concentration of α -hydroxy ketones **11** slowly decreased as a function of time, reaching a yield of 5% after 240 min. The yield of **11** α -diketone **12**, *i.e.* 2%, was almost stable during the experiment.

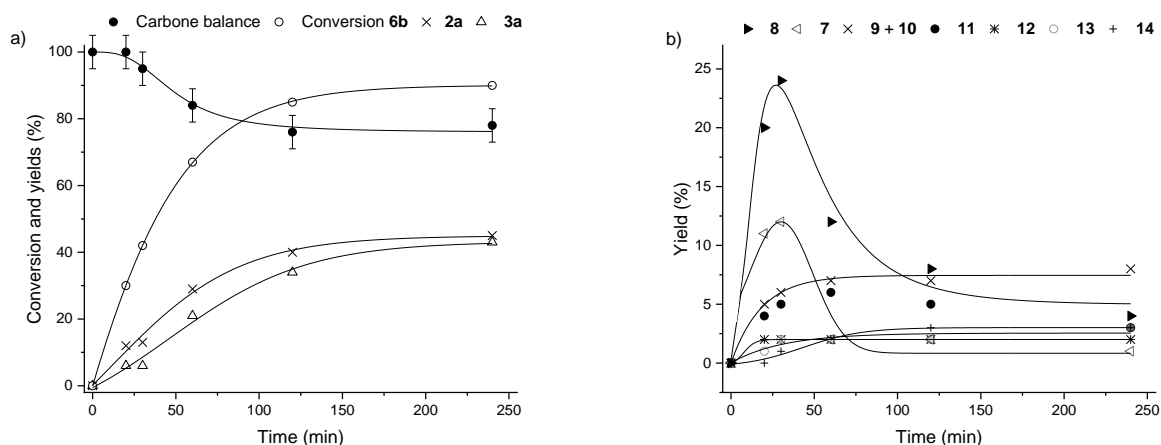


Figure 3. Evolution of the conversion of **6b**, carbon balance, and yield of the products identified in figure 2 as a function of time during the oxidative cleavage of **6b** by $\text{Ru}(\text{OH})_x/\gamma\text{-Al}_2\text{O}_3$ catalyst (6 mol%) using O_2 as oxidant. [**6b**]=33g/L in H_2O , 130°C , O_2 5 bar. Yields are determined by GC after calibration with eicosan as an external standard.

The same experiment was performed at 150°C (see Supporting Information) and gave the same profile of product formation but in a shorter time. These experiments demonstrated that the first intermediates of the cleavage of **6b** are aldehydes **7** and **8**, but α -hydroxy ketones **11** and α -diketone **12** were also detected. To clarify the mechanism, the reactivity of the different molecules identified (Figure 3) has been independently studied under the same conditions.

Reactivity of α -hydroxy ketones **11**

The reactivity of α -hydroxy ketones **11a** and **11b** was studied under the same experimental conditions (Figure 4). The synthesis of 1:1 mixture of regioisomers **11** has been previously described from **6b** heterogeneous nickel catalyst.²⁰

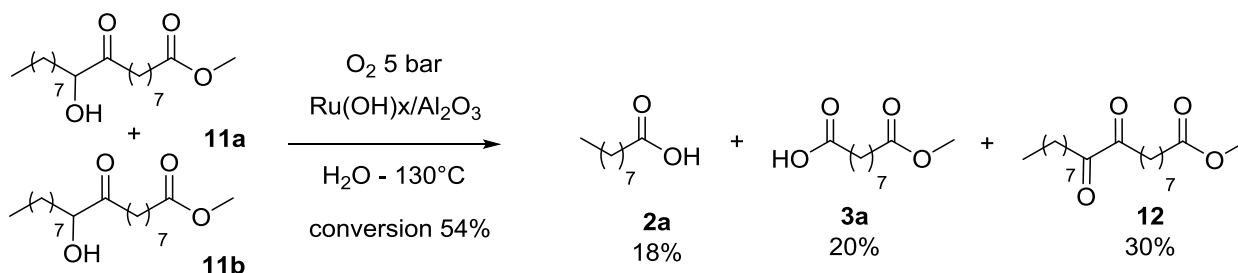


Figure 4: Oxidative cleavage of **11a** and **11b** by $Ru(OH)_x/\gamma-Al_2O_3$ catalyst (6 mol%) using O_2 as oxidant. $[11]=33g/L$ in H_2O , $130^\circ C$, O_2 5 bar, time 5h. Yields are determined by GC after calibration with eicosan as an external standard.

After 12 h, a conversion of 54 % was obtained, clearly indicating that α -hydroxy ketones **11** are less reactive than the starting material **6b**. Despite this, cleavage products **2a** and **3a** could be obtained with yields of 18% and 20% respectively. But, under those conditions, the major product was the diketone **12** with a yield of 30%. The other by-products listed in Figure 2 were not present. From this experiment, one can conclude that α -hydroxy ketones **11** were slowly cleaved into desired products **2a** and **3a** during oxidative cleavage of **6b**.

Reactivity of aldehydes **7** and **8**

As already mentioned, aldehydes **7** and **8** could be considered as the first intermediates formed during the oxidative cleavage of **6b** (vide supra). The reactivity of commercially available aldehyde **7** was first evaluated under similar experimental conditions (Figure 5).

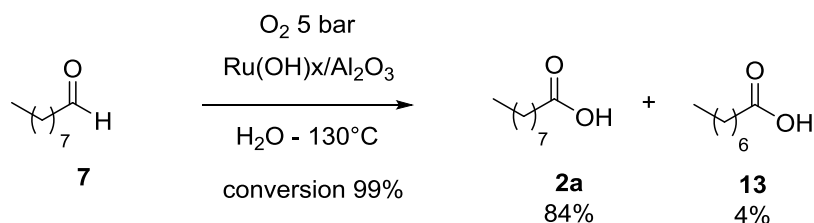


Figure 5: Oxidative cleavage of **7** by Ru(OH)_x/γ-Al₂O₃ catalyst (6 mol%) using O₂ as oxidant. [7]=33g/L in H₂O, 130°C, O₂ 5 bar, time 5h. Yields are determined by GC after calibration with eicosan as an external standard.

The total conversion of **7** was achieved under those conditions (Figure 5). A yield of 84% of pelargonic acid **2a** was obtained with 4% of octanoic acid **13**, clearly demonstrated that under those conditions the intermediates aldehydes are easily oxidized into the corresponding carboxylic acids. We have already demonstrated that aldehydes into carboxylic acid could be oxidized under oxygen even without catalyst via the formation of an acyl radical **15** (Figure 6).²⁴ The latter reacts with oxygen forming a radical peracid **16** subsequently converted by reaction with **7** into a new acyl radical **14** and peracid **17**. We have recently shown that **17** is easily transformed into the corresponding carboxylic acid **2a**.²⁵ There has been speculation on the mechanism of formation products with one carbon less than expected but the only hypothesis (*i.e.* isomerization) was ruled out.^{11, 26} We could explain the formation of the small amount of

octanoic acid **13** (with the loss of one carbon from **7**) by a loss of CO₂ from radical peracid **16** or loss of CO from radical acyl **15** due to oxygen starvation in the reaction mixture.²⁷⁻²⁸ Oxygenated species **19** obtained by reaction of carbon radical **18** with oxygen or by decarboxylation of **16** could be oxidized into **13** under the experimental condition (Ru catalyst, 130°C, O₂).

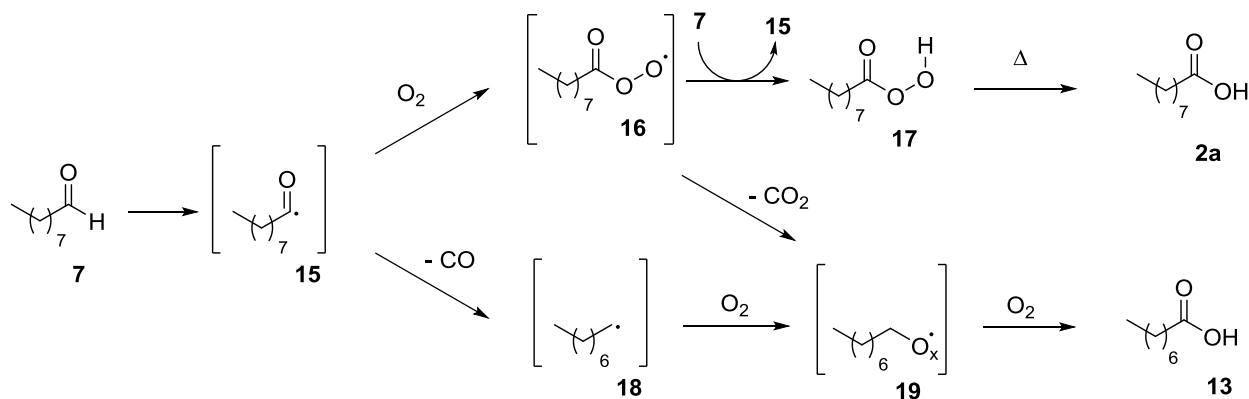


Figure 6: Proposed aerobic oxidation pathway of products with one carbon less than expected (*i.e.* compounds **13** from aldehyde **7**) (adapted from^{25, 27-28})

A mixture of aldehydes **7** and **8** (60/40) was synthesized according to the work of Lemaire *et al*²⁹ and was oxidized under similar experimental conditions. At 150°C, the total conversion of a mixture of aldehydes **7** and **8**²⁹ was obtained in less than 30 min (Figure 7). The corresponding carboxylic acids were obtained, *i.e.* **2a** and **3a** with a yield of 79%. Less than 5% of products resulting from the loss of one carbon, *i.e.* octanoic acid **13** and monomethyl ester of adipic acid **14** was obtained.

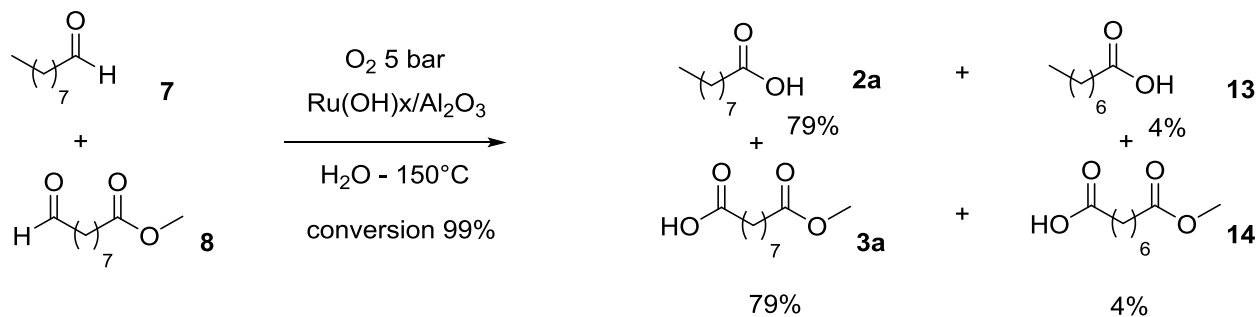


Figure 7: Aerobic oxidation of aldehydes **7** and **8** (60/40) by $\text{Ru(OH)}_x/\gamma\text{-Al}_2\text{O}_3$ catalyst (6 mol%) using O_2 as oxidant. $[\mathbf{7}+\mathbf{8}]=33\text{g/L}$ in H_2O , 150°C , O_2 5 bar, time 30 min. Yields are determined by GC after calibration with eicosan as an external standard.

Oxidative cleavage of fatty diol in water/diluent system

Formation of compounds **13** and **14** could be explained by oxygen starvation in the reaction mixture.²⁷⁻²⁸ In order, to limit the formation of such by-products, another diluent showing a better solubility for oxygen could be used. Furthermore, it has also been demonstrated that the presence of alcohol functionality has a strong impact on the reactivity of aldehyde towards oxidation.³⁰ We believed that oxidation of aldehyde could be improved by dilution. The dilution could also decrease the formation of ketals (Figure 3). However, safety issues should be also considered. We decided to first study the oxidative cleavage of **6b** in the CO_2 /water mixture.

In a batch reactor, 4g of **6b** in 120 mL of water were mixed with the ruthenium catalyst (6 mol%). 5 bar of oxygen and 45 bar of CO_2 were then added and the reactor was heated at 150°C (Table 1, entry 1). After 2 hours, the total conversion was obtained and improvement of the yield of **2a** and **3a** up to 67% were determined compared to 45% yield without CO_2 (Figure 2). The carbon balance was comparable to previous experiments. It should be noticed that under those

conditions, the CO₂ was not supercritical. A reaction was performed without water (Table 1, entry 2). 5 bar of oxygen and 51 bar of CO₂ were added in the batch reactor containing 4g of **6b** and 500 mg of the ruthenium catalyst (4 mol%). The reactor was heated to 150°C for 2h. Under those conditions, the final pressure inside the reactor reaches 120 bar but we were pleased to see that the yield of **2a** and **3a** remains very high, around 70% (Table 1, entry 2). Under these conditions, the products are obtained directly without extraction steps.

Table 1: Oxidative cleavage of **6b** by Ru(OH)_x/γ-Al₂O₃ (6 mol%) using O₂ as the oxidant in a water/CO₂ mixture ^{b)} or in CO₂ ^{c)}

		GC yield (%) ^{a)}						
Entry	P CO ₂ ini. (bar)	P final (bar)	Conv.	Carbon balance	2a	3a	13	14
1 ^{b)}	45	80	> 99	75	66	67	6	6
2 ^{c)}	51	120	>99	73	68	67	5	5

^{a)} Yields are determined by GC after calibration with eicosane as an external standard.

^{b)} [**6b**]=33g/L in H₂O, initial P O₂=5 bar.

^{c)} The reaction was performed without water; 4g of **6b** neat, initial P O₂ 5 bar.

Dodecane was then used as diluent instead of CO₂. **6b** was dissolved in 12mL of dodecane and then 108 mL of water was added. The reaction was performed under the same conditions, *i.e.* 150°C, 5 bar of oxygen. The presence of dodecane strongly improved the carbon balance, from

70 % to 90% (Table 2, entry 1). The yields of **3a** and **3b** were up to 80%. The numbers of by-products were limited, below 10%. Only traces of aldehydes **7** and **8** (less than 2%) and α -hydroxy ketones **11** and diketone **12**, 2% and 5% respectively, could be quantified. This result could be explained by a higher solubility of oxygen in the reactive phase (diluent and **6b**) compared to neat **6b** dispersed in water (Figure 4). The increase of the dodecane/water ratio was then studied (Table 2, entries 2 and 3). A decrease of the dodecane/water ratio at constant dodecane volume has a limited impact on carbon balance showing that, as expected, the reaction occurs in the organic phase. The reaction was also performed at 170°C. Similar yields are obtained in a shorter time (See supporting information).

Table 2: Oxidative cleavage of **6b** by $\text{Ru(OH)}_x/\gamma\text{-Al}_2\text{O}_3$ (6 mol%) using O_2 as the oxidant in a dodecane/water mixture ^{a)}

GC yield (%) ^{b)}							
Entry	Vol. (mL)C ₁₂ H ₂₆ / H ₂ O	Conv.	Carbon balance	2a	3a	13	14
1	12/108	> 99	90	81	79	6	6
2	12/60	> 99	93	86	83	4	6
3	12/20	> 99	95	85	80	8	7

^{a)} **6b** 4 g (12.1 mmol), dodecane 12 mL, H₂O 108, 60 or 20 mL, $\text{Ru(OH)}_x/\gamma\text{-Al}_2\text{O}_3$ catalyst (6 mol%), O_2 5 bar.

^{b)} Yields are determined by GC after calibration with eicosane as an external standard.

Catalyst recycling

The recycling of the catalyst was then studied. Four runs were consecutively performed with the same catalyst with a lower Ru content (2 mol% vs 6 mol%) and at a higher temperature (170°C vs 130°C) with 5 bar of oxygen and a mixture of dodecane/water (12/108). At the end of the reaction, the reaction mixture was filtrated. The catalyst was washed with ethyl acetate and then with water. The catalyst was then reused for another oxidative cleavage of **6b** under the same conditions. Figure 8 shows the oxygen consumption rate as a function of time. When the temperature of the reaction mixture reaches the setpoint temperature (*i.e.* 170°C), O₂ was added to the reactor. Liquid-phase oxidation reactions proceed with a free-radical mechanism. These reactions are characterized by an induction period followed by a rapid reaction phase. During the induction period, initiation reactions gradually increase the free-radical concentration until propagation becomes a dominant process. This phenomenon could be observed in Figure 8. After O₂ was added in the reactor (time=0), the oxygen consumption rate was marginal until a strong increase after ~ 15 min was observed. Under those conditions, the total conversion was obtained for the first run after 40 min. From run 1 to run 4, the induction period gradually increases as well as the decrease in the rate of O₂ consumption (Figure 8). Run 4 was stopped after 35 min. ICP-OES analysis of aqueous phase filtrated at 90°C after the 4th run shows that a small amount of ruthenium was leached (< 0.03 w% of initial Ru). The catalyst was filtrated and washed with ethyl acetate and then with water. The catalyst was then added to a 0.1M solution of NaOH under sonication. The catalyst was then filtrated and washed with water until neutral. The alkaline solution was acidified to pH 2 using HCl 1M and extracted with EtOAc. The organic phase was analyzed by GC and **3a** was identified as a major product. This could explain the slightly lower yield generally observed for **3a** compared to **2a** (Figure 2). Absorption of **3a** as

well as other compounds on the surface of the catalyst could also explain the increase of the induction period as well as the decrease of the rate of O₂ consumption (Figure 8). The regenerated catalyst was then used in a fifth experiment (Figure 8, run 5) and we were pleased to see that the activity was recovered, an indication that the small leaching of Ru is not entirely responsible for the decrease of the activity as a function of reuse.

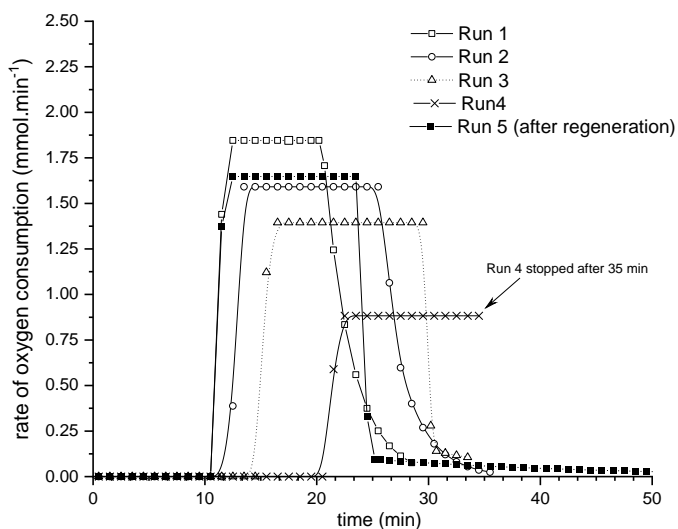


Figure 8. Evolution of oxygen consumption rate as a function of time for five successive runs during the oxidative cleavage of **6b** by Ru(OH)_x/γ-Al₂O₃ catalyst (2 mol%) using O₂ as oxidant. [**6b**]=33g/L in dodecane/H₂O (12 mL/108 mL), 170°C, O₂ 5 bar.

Comparison to current technologies of oxidative cleavage fatty acids and derivatives

The comparison between the known processes is made in Table 3. Even if appropriate metrics of sustainability for the comparison between industrial and lab-scale processes are difficult to determine, some key characteristics can be highlighted.

Table 3: Comparison to current technologies of oxidative cleavage fatty acids and derivatives

Technology	Atom economy	safety	Major drawbacks	Ref.
Ozonolysis ^{a)}	+++	---	Explosive intermediates	6-7
Co(OAc) ₂ /air in H ₂ O ^{b)}	+	+	Homogenous catalysis	15
Ru/C and then thiazolium salts	-	+	Two steps from vicinal diols	29, 31
NaOCl aq ^{b)}	+	++	Chlorinated by-products	18
Au/Al ₂ O ₃ /O ₂ , NaOH in water ^{b)}	--	+	Presence of base in excess	17
Ru(OH) _x /γ-Al ₂ O ₃ /O ₂ in H ₂ O-tetradecane ^{b)}	+	-	High temperature	This study

a) from unsaturated fatty acid

b) from vicinal diol. The latter could be obtained by dihydroxylation of unsaturated fatty acid by H₂WO₄/H₂O₂.¹⁵

If the major advantage of ozonolysis is atom economy, the presence of explosives intermediates makes this process sensitive to operate even if it's practiced by two major companies in China and USA.⁴ Novamont has proposed a two-step alternative process in which the cleavage of the diol is performed with homogeneous cobalt catalyst in water using air as oxidant.¹⁵ Lab-scale processes have been proposed but the presence of an excess of base¹⁷, chlorinated by-products¹⁸ or multi-steps processes^{29, 31} (Table 3) limits their practical use. Our process deals with the replacement of a homogenous catalytic system¹⁵ by heterogeneous catalysis without an added

base. The recyclability of the heterogeneous catalytic system was demonstrated. In batch, water was added to the system as an additional safety factor. A continuous water-free process is currently under optimization in our laboratories in order to reinforce the safety and productivity of the process as already demonstrated for the oxidation of alcohols.²¹

Pathway discussion

Through the study of the reactivity of the intermediates **7**, **8**, **11**, and **12** identified during the oxidative cleavage of **6b**, a competitive pathway for the oxidative cleavage of vicinal-diol fatty esters by heterogeneous ruthenium hydroxide catalyst in the presence of oxygen could be proposed (Figure 9). Unlike Köckritz *et al.*¹⁶⁻¹⁷ and Cavani *et al.*³² that use respectively gold and homogeneous ruthenium catalyst, the α -hydroxy ketones **11** and diketone **12** are not the main intermediates during the cleavage of **6b**. In our case, α -hydroxy ketone **11** and diketone **12** are much less produced than intermediates aldehydes **7** and **8**, and their transformation into the corresponding carboxylic acids **2a** and **3a** is much slower than aldehydes **7** and **8**. In contrast, the cleavage of **6b** into the corresponding aldehydes **7** and **8** is favored. However, a competition between the formation of ketals **9** and **10** with the starting product and oxidation to the corresponding carboxylic acids **2a** and **3a** could be noticed. The yield could be increased by using a diluent like dodecane. The use of dodecane has two distinct advantages: a) increasing the oxygen solubility in the liquid phase (compare the oxidation of **6b** in water, (Figure 3, yield 45%) vs the oxidation of **6b** in water/dodecane mixture (Table 2, entries 2 and 3, yield > 80%) and b) dilution the organic phase to decrease the formation of ketals by-products **9** and **10**. From these experiments, the pathway of the cleavage of **6b** by $Ry(OH)_x$ could be proposed (Figure 9).

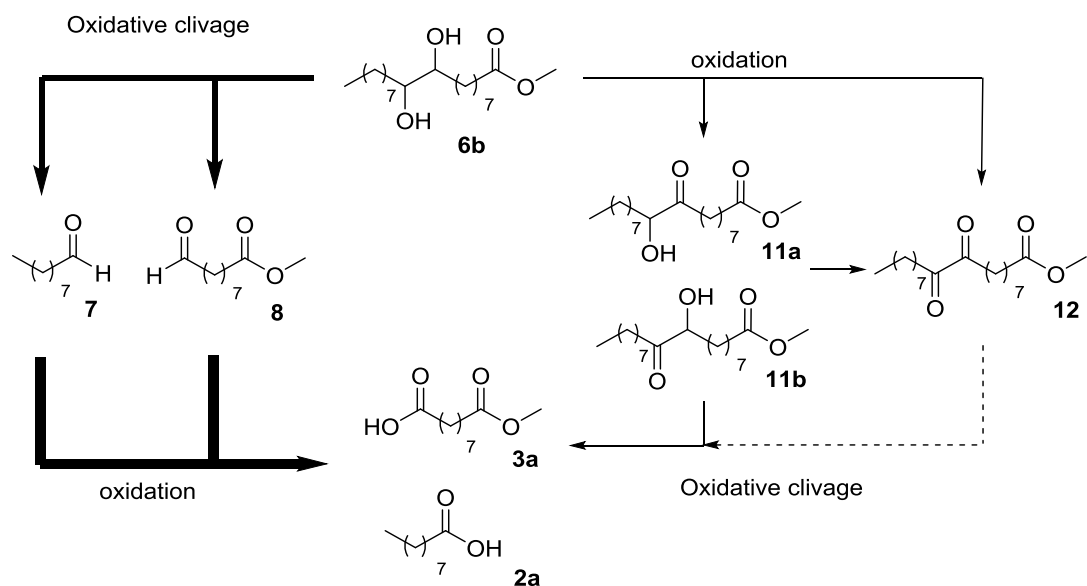


Figure 9. Potential parallel mechanism pathway of oxidative cleavage of **6b** by $\text{Ru}((\text{OH})_x/\gamma\text{-Al}_2\text{O}_3)$ using O_2 as oxidant. The width of the arrows is an indication of the relative reaction rate.

We could also propose a mechanism for the oxidative cleavage of vicinal diol by $\text{Ru}((\text{OH})_x/\gamma\text{-Al}_2\text{O}_3)$ (Figure 10).²¹ The diol **A** is absorbed on the surface of the catalyst **B** forming **C**. Rearrangement of **C** lead to the formation of two aldehydes **D₁** and **D₂** and metal hydride **E**. The catalyst **B** is regenerated by reaction with O_2 via **F**, generating hydrogen peroxide that is decomposed into water under the experimental conditions used ($T > 130^\circ\text{C}$) or could be used as a radical initiator for the aerobic oxidation of aldehydes **D₁** and **D₂** leading to the desired carboxylic acids **G₁** and **G₂**.

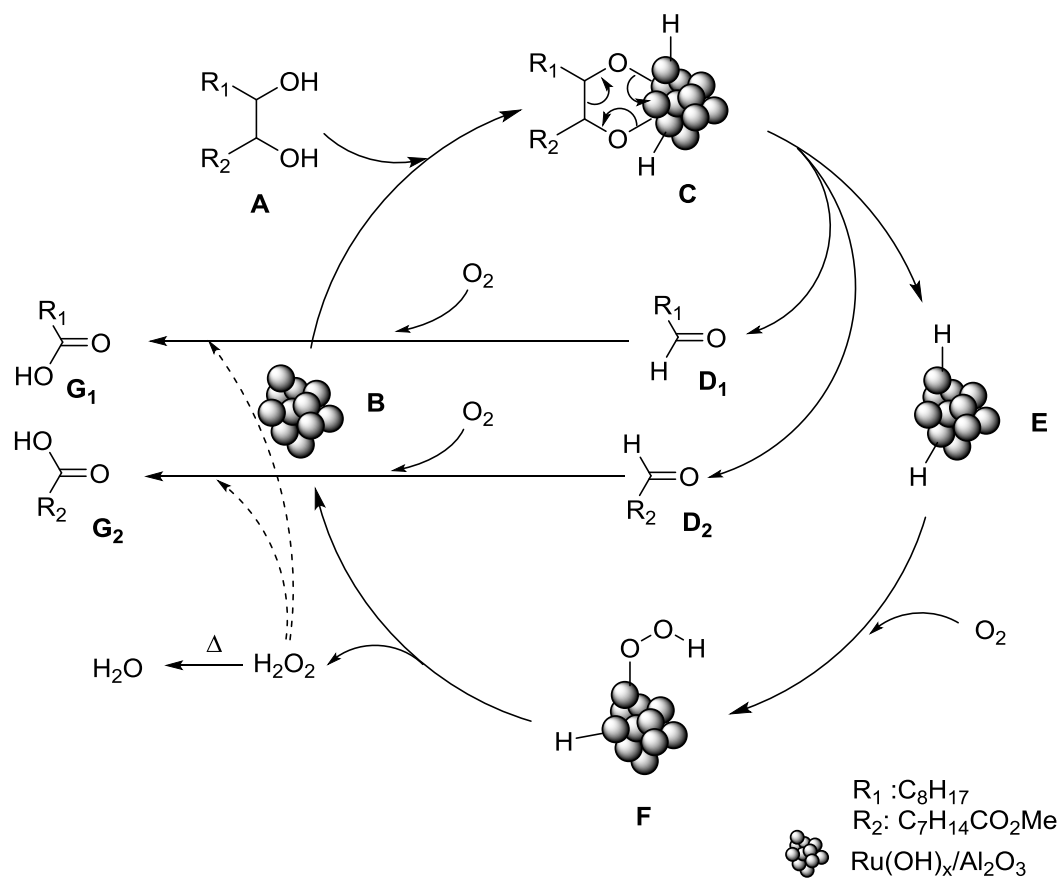


Figure 10: Proposed mechanism for the oxidative cleavage of vicinal diol by $Ru(OH)_x/\gamma-Al_2O_3$ using O_2 as oxidant

Conclusions

Aerobic oxidative cleavage of vicinal-diol fatty esters **6b** by supported ruthenium hydroxide catalyst in neat conditions using air as oxidant gave a low yield of pelargonic acid **2a** and azelaic acid **3a** (20%). The yield is increased to 45% when air is replaced by oxygen, but for safety reasons, this requires the addition of water to the reactor. Despite the use of water, by-products from acetalization reactions are still observed, *i.e.* **9** and **10**. The use of CO₂ allows the formation of the desired acids **2a** and **3a** with a yield of 70%. However, the best results, 80% yield, are obtained with a biphasic system (water/dodecane) with a mass balance higher than 90%. A detailed study of the reactivity of the intermediates and by-products has enabled us to propose a mechanism for the oxidative cleavage of diol by Ru(OH)_x/γ-Al₂O₃ using O₂ as oxidant. The recycling of the catalyst was also studied. Low leaching of Ru was detected but the observed deactivation could be explained by the absorption of carboxylic acids (*i.e.* products of the reaction: azelaic acid, ...). Cleaning the catalyst with a 0.1M solution of NaOH under sonication enables the recovery of most of the catalytic activity.

ASSOCIATED CONTENT

Supporting Information. The following files are available free of charge.

Experimental procedures, characterization data of products, NMR spectra for key compounds, calibration curves.

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ACKNOWLEDGMENT

The authors thank the French National Agency for financial support through a Ph.D. grant to

B.G. (ANR-13-CDII-0001-COUPOX).

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