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Homogeneous and Heterogeneous Catalytic (Dehydrogenative) Oxidation of Oleochemical 1,2-Diols to α -Hydroxyketones

Nam Duc Vu, Boris Guicheret, Nicolas Duguet,* Estelle Métay* and Marc Lemaire

The preparation of methyl oleate α -hydroxyketone from the corresponding 1,2-diol has been investigated with both homogeneous and heterogeneous systems. Homogeneous conditions using $\text{Pd}(\text{OAc})_2$ / neocuproine complex were first developed using oxygen as sole oxidant under mild conditions (MeOH, 50°C). Under these conditions, the conversion of diol reached 95% and the α -hydroxyketone was obtained with 97% selectivity. The access to α -hydroxyketone has also been studied by dehydrogenation using a range of heterogeneous catalysts under solvent-free conditions at high temperature (160–180°C). Dehydrogenation using activated Ru/C under vacuum gave the α -hydroxyketone with 93% conversion and 82% GC yield. The optimized conditions were applied to a range of oleochemical diols, including a vegetable oil derivative, to give the corresponding α -hydroxyketones with up to 74% isolated yields.

Introduction

Vegetable oils (triglycerides) are attractive renewable raw materials for the chemical industry.¹ Indeed, they are widely available (about 202 million tons in 2015)² and relatively inexpensive. For instance, they can be used as biofuel³ (biodiesel) but this application is subject of controversy and only pertinent when the price of fossil resources is high. To date, they can be best converted to valuable building blocks for a wide range of applications.⁴ Unsaturated oleochemicals are particularly interesting for the installation of a wide range of organic functions. On the one hand, unsaturated plant oils could be directly (co)-polymerized to give functional materials such as Linoleum and alkyd resins.⁵ Epoxidized plant oils could also be used for the formation of epoxy resins and their polyol-derived analogs for the formation of polyesters and polyurethanes. On the other hand, unsaturated fatty acid derivatives have been intensively studied for the introduction of a wide range of organic functions⁶ including aldehyde,⁷ epoxide,⁸ diol,⁹ ketone and diketone,¹⁰ carbonate,¹¹ among others.¹² Comparatively, there are only few studies related to the α -hydroxyketone function on fatty acid compounds. So far, these derivatives have been mainly used for the preparation of heterocyclic fatty compounds.¹³ More recently, our group has reported an original method for the cleavage of methyl oleate α -hydroxyketone.¹⁴ This method gives access to the corresponding aldehydes, *i.e.*, nonanal and methyl azelaaldehyde, that could be used as building-blocks for the preparation of surfactants¹⁵ and polymers.¹⁶ More importantly, the process occurs under non-oxidative conditions and could therefore constitute a safer alternative to reductive ozonolysis.¹⁷ In this context, the development of a scalable, economical and environmentally-friendly method for the preparation of fatty α -hydroxyketones is highly desirable. In early reports, oleic acid was directly used as starting material for the preparation of 9(10)-hydroxy-10(9)-oxo-stearic acid using “neutral” KMnO_4 (Scheme 1, path a).¹⁸ Apart from using a stoichiometric oxidant, these methods require high dilutions and gave low yields. However, a fine control of pH (phosphate buffer) could generate the desired α -hydroxyketone with 61% yield.^{18f} Inspired by the pioneer's

work of Cohen and Tsuji,¹⁹ Brousse and Lefort have prepared methyl 9(10)-hydroxy-10(9)-oxostearate by oxidative ring-opening of methyl 9,10-epoxystearate using DMSO as an oxidant in the presence of catalytic $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (Scheme 1, path b).²⁰ In their report, the α -hydroxyketone was obtained with 65% yield but we have observed that the method suffers from a lack of reproducibility.²¹ A similar procedure was applied to *cis*- and *trans*-9,10-epoxystearic acids but the reaction provided low yields.²² Furthermore, both methods generate dimethyl sulfide as malodorous and toxic gas, thus compromising the scale-up. Alternatively, 9,10-diketostearic acid, prepared by KMnO_4 oxidation of stearic acid,²³ could also serve as starting material for the generation of the α -hydroxyketone function (Scheme 1, path c).²⁴ Reduction of the α -dioxo-acid using zinc in acetic acid afforded the ketol-acid with up to 88% yield.^{18f} The mono-oxidation of *erythro*-9,10-dihydroxystearic acid has also been investigated using *N*-bromosuccinimide (NBS) as an oxidant (Scheme 1, path d). Under these conditions, the corresponding α -ketol-acid was obtained with 63% yield (based on recovery of starting material) with inevitable formation of the corresponding α -dioxo-acid, thus complicating the purification.^{18f} All these routes are of great interest to access fatty α -hydroxyketone derivatives, however, they usually imply the use of stoichiometric (toxic) reagents.

The mono-oxidation of (secondary) 1,2-diols to α -hydroxyketones represents a challenge in terms of chemoselectivity due to competing over-oxidation, dehydration and carbon-carbon cleavage reactions. Several stoichiometric methods have been reported based on silver carbonate on Celite (Fetizon reagent),²⁵ dioxiranes,²⁶ stannylene acetal oxidation,²⁷ $\text{NaBrO}_3/\text{NaHSO}_3$ ²⁸ and $\text{KBrO}_3/\text{KHSO}_4$ reagents.²⁹ However, most of these methods suffer from concomitant overoxidation, functional group incompatibilities, lack of selectivity, low yields as well as the generation of a large quantities of waste. Catalytic methods have also been reported based on Sn-Br_2 ,³⁰ boronic acid-dibromoisocyanuric acid (DBI),³¹ Ru-oxone,³² Cu-NBS³³ and Pd-benzoquinone systems.³⁴ However, these methods rely on oxidants that generate a lot of waste, and therefore, they are not compatible with green chemistry principles. Other systems based on homogeneous-Pd³⁴ and peroxotungstophosphate³⁵

are probably more promising as they use greener oxidants such as O₂ (or air) and H₂O₂, respectively. From an ecological point of view, the preparation of α -hydroxyketones by catalytic dehydrogenation of 1,2-diols is more advantageous as it generates only hydrogen as byproduct. To the best of our knowledge, there are only two reports for the

dehydrogenation of 1,2-diols using metallic Cu³⁶ or Ir-ReO_x/SiO₂³⁷ as heterogeneous catalysts. These systems require high temperatures (220-260°C) and have never been applied to challenging substrates such as vegetable oils derivatives.

Scheme 1. Preparative routes to α -hydroxyketone from oleic acid and methyl oleate.

In this context, we have developed two methodologies to prepare α -hydroxyketones from fatty 1,2-diols using both catalytic homogeneous-palladium and heterogeneous-ruthenium systems (Scheme 2). High selectivities ($\approx 90\%$) towards the formation of the desired α -hydroketone function were achieved under solvent-free conditions.

Scheme 2. Catalytic preparation of α -hydroxyketone from fatty acid-derived 1,2-diols.

Results and discussion

Homogeneous-palladium system.

Waymouth *et al.* have recently reported the selective oxidation of glycerol to dihydroxyacetone (DHA) using a Pd(OAc)₂/neocuproine complex³⁸ in the presence of benzoquinone as oxidant.^{34a} Inspired by this work, we have first attempted the selective monooxidation of methyl 9,10-dihydroxystearate under their optimized conditions [5 mol% Pd, 3 equiv benzoquinone, CH₃CN or DMSO, rt, 20°C]. However, no α -hydroxyketone has been detected probably due to the lack of solubility of the starting material. Thus, the reaction conditions have been reinvestigated and benzoquinone has been substituted by oxygen as a cleaner oxidant. Initially, the oxidation of methyl 9,10-dihydroxystearate has been carried out in a sealed tube using Pd-neocuproine catalytic system (4 mol%), oxygen (1 bar) in MeOH at 50°C for 3 hours (Table 1). Under these conditions, the conversion reached 54% and the selectivity towards the formation of α -hydroxyketone **2** (1:1 mixture of regioisomers) attained 91% (Table 1, entry 1). The concentration of starting material **1** was progressively increased and the best selectivity (93%) was obtained for 1.5 M (Table 1, entries 2-3). Realizing

that the pressure of oxygen gradually decreases as the reaction progresses, it was then carried out in a stainless steel reactor using a constant pressure of oxygen (3 bar). Gratifyingly, the conversion was complete after 3 hours and the selectivity was preserved around 90% (Table 1, entry 4). Moreover, an additional experiment has shown that the reaction is complete within 30 minutes (Table 1, entry 5). Similar results (99% conversion, 89% selectivity) were also obtained using only 2 mol% of catalyst, provided an extended reaction time (Table 1, entry 6). Finally, further decreasing the catalyst loading to 1 mol% did not allow reaching complete conversion (Table 1, entry 7).

Table 1. Catalytic oxidation of methyl 9,10-dihydroxystearate with Pd-neocuproine complex^a

Entry	[1] (mol.L ⁻¹)	Pd complex (mol%)	Time (h)	Conv. ^b (%)	Sel. 2 ^b (%)	Sel. 3 ^b (%)
1	0.5	4	3	54	91	5
2	1.5	4	3	58	93	1
3	3	4	3	77	90	2
4 ^c	1.5	4	3	> 99	90	10
5 ^c	1.5	4	0.5	> 99	90	10
6 ^c	1.5	2	1.5	99	89	8
7 ^c	1.5	1	1	67	93	2

^a Reaction conditions: 20-mL sealed tube, 3 mmol of **1**, Pd(OAc)₂ (4 mol%), neocuproine (4 mol%), O₂ (1 bar), MeOH (2-6 mL), 50°C, 3 hours. ^b Determined by GC. ^c Reaction carried out in a 30-mL stainless steel reactor using diol **1** (4 g, 12 mmol), O₂ (3 bar, 0.5 equiv), MeOH (8 mL).

The effect of the ligand's structure on the catalytic activity was next probed on the model reaction using previously optimized

conditions. No reaction was observed with pyridine-2,6-dicarboxylic acid. Strikingly, only neocuproine could efficiently catalyze the reaction as structurally-related ligands such as 3,4,7,8-tetramethyl-1,10-phenanthroline and 1,10-phenanthroline only returned starting material (Figure 1).

Figure 1. Ligands tested in the Pd-catalyzed monooxidation of 1,2-diols.

According to Waymouth's work,³⁴ steric hindrance arising from the presence of two methyl groups in neocuproine would prevent the formation of a stable dimeric complex. An active monomeric Pd(II) complex would be favoured, allowing the coordination of 1,2-diol, and leading to the formation of the desired α -hydroxyketone. In contrast, the use of other phenanthroline ligands leads to more stable complexes that are unable to catalyze this transformation, at least, under the conditions used. Finally, the presence of neocuproine was found essential for catalytic activity as the reaction proceeds very slowly (6% conversion) without ligand.

Various oxidants were next screened for the monooxidation of 1,2-diol **1** under the previously optimized conditions (Table 2). Under an air flow at atmospheric pressure, the conversion only reached 48% (Table 2, entry 1). However, the conversion increased to 58 and 92% using 0.5 and 1 equivalent of O₂, respectively (Table 2, entries 2-3). Satisfyingly, the selectivity towards **2** still remained around 90%. Excellent results (95% conversion and 99% selectivity) were obtained with benzoquinone (1 equiv) as an oxidant. Moreover, the conversion can be further improved to > 99% using 2 equivalents but the selectivity dropped to 70% due to overoxidation to diketone **3** (Table 2, entries 4-5). Despite that excellent results could be attained with this oxidant, this procedure generates hydroquinone as a by-product which represents a lot of waste to eliminate or to recycle. Hydrogen peroxide was also found an adequate oxidant to promote the formation of α -hydroxyketone **2** with a satisfying 83% conversion and 91% selectivity (Table 2, entry 6). Contrary to benzoquinone, increasing the amount of oxidant did not affect the selectivity but led to a poor 26% conversion (Table 2, entry 7). This result has been attributed to the ability of H₂O₂ to oxidize the methyl groups of neocuproine, affecting the structural integrity of the ligand and thus decreasing the reaction rate of reaction.

Table 2. Screening of oxidants.^a

Entry	Oxidant	Equiv.	Conv. ^b (%)	Sel. 2 ^b (%)	Sel. 3 ^b (%)
1	air	excess	48	92	4
2	O ₂ (1 bar)	0.5	58	92	1
3 ^c	O ₂ (1 bar)	1	92	89	6
4	benzoquinone	1	95	99	1
5	benzoquinone	2	> 99	70	30
6	H ₂ O ₂	1	83	91	3
7	H ₂ O ₂	2	26	85	1

^a Reaction conditions: 20-mL sealed tube, 3 mmol of **1**, Pd(OAc)₂ (2 mol%), neocuproine (2 mol%), MeOH (2 mL), 50°C, 3 hours. ^b Determined by GC. ^c 1.5 mmol of **1**.

From these results, oxygen was conserved as the most desirable oxidant from an atom-economy point of view since it only generates water as by-product. Another strategy to improve the selectivity towards the formation of **2** has been investigated using an exogenous acid (Table 3). Indeed, it is assumed from previous reports^{34,38,39} that a monocationic Pd(II)-hydride complex is generated after the release of the α -hydroxyketone. Moreover, this Pd(II)-hydride could form a Pd(0)-neocuproine complex by the loss of a proton. Insertion of molecular oxygen into either Pd(II)-hydride or Pd(0)-neocuproine complexes should yield Pd(II)-hydroperoxo⁴⁰ or Pd(II)-peroxo⁴¹ complexes, respectively. Addition of acetic acid onto these species should reform the active monomeric Pd(II) complex, thus maintaining the catalytic performances of the system.⁴¹ Based on these mechanistic considerations, we hypothesized that acetic acid could have a beneficial effect on both the conversion and the selectivity. Treatment of diol **1** with a catalytic amount of acetic acid (3 mol%) under the optimized conditions led a slight improvement of the selectivity to 92% (Table 3, entries 1-2).

Table 3. Aerobic Pd-catalyzed oxidation of 1,2-diol in the presence of AcOH.^a

Entry	AcOH loading (mol%)	Time (h)	Conv. ^b (%)	Sel. 2 ^b (%)	Sel. 3 ^b (%)
1	-	1.5	99	89	8
2	3	1	> 99	92	6
3	4.5	1.5	> 99	90	8
4	6	1.5	95	97	3
5	12	1.5	74	96	3
6	12	3	94	94	3

^a Reaction conditions: 30-mL stainless steel reactor, 12 mmol of **1**, Pd(OAc)₂ (2 mol%), neocuproine (2 mol%), O₂ (3 bar), MeOH (8 mL), 50°C. ^b Determined by GC.

The scope of the reaction was then investigated (Table 4). Treatment of diol **1** under optimized conditions gave α -hydroxyketone **2** with 80% isolated yield after purification by column chromatography (Table 4, entry 1). Diol **4** derived from *tert*-butyl oleate gave similar results and α -hydroxyketone **8** was obtained with 78% yield (Table 4, entry 2). Symmetrical diols **5** and **6** were next considered. These starting materials could be prepared from the corresponding alkenes formed by self-metathesis of methyl oleate,⁴² however, other synthetic

Table 4. Scope of the catalytic oxidation of fatty acid-derived 1,2-diols to α -hydroxyketones.^a

Entry	1,2-Diol	Conv. ^b (%)	Alpha-hydroxyketone	Isolated Yield ^c (%)	Selectivity ^b (%)		
1		1	95		2	80	97 (3% DK)
2		4	99		8	78	80 (14% DK)
3		5	99		9	84	90 (9% DK)
4		6	75		10	61	92 (no DK)
5		7	99		11	72	74 (12% DK)

^a Reaction conditions: 30-mL stainless steel reactor, 12 mmol of 1,2-diol, Pd(OAc)₂ (2 mol%), neocuproine (2 mol%), AcOH (6 mol%), O₂ (3 bar), MeOH (8 mL), 50°C, 1.5 hour. ^b Conversion and selectivity were determined by ¹H NMR. ^c Isolated yield after purification by column chromatography. DK = 1,2-diketone.

Although exhibiting excellent performances, the Pd-neocuproine complex has the inherent drawbacks of homogeneous systems, that are short-term stability and limited recyclability. In this context, the development of a complementary methodology using a heterogeneous catalytic system is highly desirable. Moreover, such robust systems are

particularly adequate to prepare α -hydroketones by catalytic dehydrogenation of 1,2-diols, that is usually requiring elevated temperatures. First, a range of commercially available heterogeneous catalysts was screened at 160°C under solvent-free conditions (Table 5).

Table 5. Screening of heterogeneous catalysts.^a

Entry	Catalyst	Loading (mol%)	Conv. ^b (%)	Sel. 2 ^b (%)
1	5%-Pd/SiO ₂	2.5	0	-
2	5%-Pd/Al ₂ O ₃	2.5	0	-
3	10%-Pd/BaSO ₄	2.5	0	-
4	5%-Pt/SiO ₂	2.5	0	-
5	5%-Ru/C	2.5	20	35
6	5%-Ru/Al ₂ O ₃	2.5	45	29
7	5%-Ru(OH) _x /Al ₂ O ₃	2.5	50	60
8	10%-Ru(OH) _x /Al ₂ O ₃	5	62	64
9	Al ₂ O ₃	5	-	-

^a Reaction conditions: 20-mL sealed tube, argon atmosphere, 3 mmol of **1**. ^b Determined by GC.

Supported palladium catalysts gave no conversion while platinum on silica gave poor results (Table 5, entries 1-4). On the contrary, all ruthenium-based catalysts were found to be active for the dehydrogenation of **1** but with important disparities regarding the nature of the support. Both Ru/C and Ru/Al₂O₃ gave moderate selectivities but better conversion was obtained with Al₂O₃ (Table 5, entries 5-6). The replacement of Ru/Al₂O₃ by Ru(OH)_x/Al₂O₃ – Mizuno's catalyst – gave 50% conversion and 60% selectivity and improved results could be obtained with a higher catalyst loading (Table 5, entries 7-8). Finally, control experiment with Al₂O₃ gave poor results, indicating the important role of Ru species in the dehydrogenation process (Table 5, entry 9). This initial screening has been carried out in sealed tube in order to select a suitable catalyst for the dehydrogenation process. However, the conversions are limited, probably due to the fact that hydrogen generated from the dehydrogenation process remains in the tube, thus preventing to shift the equilibrium towards the formation of the alpha-hydroxyketone. In order to circumvent this problem, hydrogen scavengers such as 1-octene or 4-vinylanisole were used. However, the results could not be improved and partial polymerization of scavengers was observed at high temperature. Consequently, another strategy to shift the equilibrium has been envisioned by removing hydrogen under vacuum (Table 6). Thus, diol **1** was heated at 170°C in the presence of 10%-Ru(OH)_x/Al₂O₃ (5 mol%) and hydrogen was removed at 5 mbar. Gratifyingly, the conversion increased to 78% and the selectivity reached 90% (Table 6, entry 1). Increasing the temperature to 180°C improved the conversion to 91% but the selectivity dropped to 75% (Table 6, entry 2). An excellent 99% selectivity was obtained with 5%-Ru/Al₂O₃ but the conversion plateaued at 70% and could not be improved with a prolonged time (Table 6, entry 3). Using 5%-Ru/C gave 80% conversion and 94% selectivity towards the formation of **2** (Table 6, entry 4). These results were encouraging, however, a mass loss of about 10% was noticed for all these experiments.

Table 6. Dehydrogenation of diol **1** under vacuum^a

Reaction scheme showing the conversion of diol **1** to a mixture of isomers **2** and **12** using a metal *M* on a support under solvent-free conditions at temperature *T* (°C) and vacuum = 5 mbar.

Entry	Catalyst	Loading (mol%)	Conditions	Conv. ^b (%)	Sel. 2 ^b (%)	Mass balance (%)
1	10%-Ru(OH) _x /Al ₂ O ₃	5	170°C, 8 h	78	90	8
2	10%-Ru(OH) _x /Al ₂ O ₃	5	180°C, 8 h	91	75	10
3	5%-Ru/Al ₂ O ₃	5	170°C, 8 h	70	99	10
4	5%-Ru/C	5	170°C, 8h	80	94	10

^a Reaction conditions: 30-mL Schlenk flask fitted with a condenser, 12 mmol of **1**.

^b Determined by GC.

This phenomenon has been attributed to the evaporation of the monoketone **12** produced by dehydration under these reaction conditions. In order to avoid such inconvenience, the vacuum pressure was progressively increased and it was found that applying a vacuum of 100 mbar led to similar results but without any mass loss. Therefore, the efficiency of the dehydrogenation process was re-investigated under these conditions (Figure 2). For that purpose, only commercially available Ru/Al₂O₃ and Ru/C catalysts were considered and a temperature of 175°C has been selected as a compromise to maintain high conversion and selectivity.

Figure 2. Dehydrogenation with unactivated or activated catalysts.

Unactivated Ru/Al₂O₃ gave 79% conversion of diol **1** and 70% GC yield after 11 h at 175°C (Figure 2, dark blue and red curves). Interestingly, almost no activity was detected during the first four hours. Intrigued by this observation, Ru/Al₂O₃ was activated under an atmospheric hydrogen pressure for 1 h at 175°C. Using this activated catalyst, the dehydrogenation process was much faster. However, the conversion could not exceed 70% after 6 hours and the GC yield only attained 62% (Figure 2, green and purple curves). Activated Ru/C gave an even better activity with 93% conversion and 82% GC yield

after only 4 h (Figure 2, light blue and orange curves). These results show that activation under hydrogen is essential for the catalytic activity but does not affect the selectivity. Indeed, the selectivity was maintained to 88-89% whatever the catalyst. The scope of the dehydrogenation of fatty acid-derived 1,2-diols was then investigated under the optimized conditions [activated Ru/C (5 mol%), solvent-free, vacuum of 100 mbar, 175°C, 3 hours] (Table 7). These starting materials were prepared from the corresponding alkenes through a two-step epoxidation / ring-opening sequence, unless otherwise stated.⁴³ Diols **1**, **13-14** obtained from methyl, *n*-butyl and 2-ethylhexyl oleate gave good conversions (71-91%) and good selectivities (87-92%) and the corresponding α -hydroxyketones **2**, **17-18** were obtained with 56-67% isolated yields (Table 7, entries 1-3). Diol **4** obtained from *tert*-butyl oleate was also subjected to the dehydrogenation conditions. Full conversion was obtained but no desired product was detected (Table 7, entry 4). Only diol **19** and its corresponding α -hydroxyketone **20**, lacking the *tert*-butyl group, were detected by GC. We hypothesized that Ru/C is acidic enough to promote de-*tert*-butylation under these conditions. Indeed, this process, usually catalysed by a wide range of acids,⁴⁵ could be accelerated under vacuum with the removal of *iso*-butene. In order to prevent de-*tert*-butylation, diol **4** was treated with activated Ru/Al₂O₃ to give the desired α -hydroxyketone **8** with 28% isolated yield (Table 7, entry 5). Dehydrogenation of diols **5** and **6** gave 93-94% conversion and 79-76% GC yield (Table 7, entries 6-7). The corresponding α -hydroxyketones **9-10** were recovered with 74 and 57% isolated yield, respectively. The protocol was then extended to diols from other fatty acid methyl esters. Diol **7** derived from methyl erucate gave 85% conversion and α -hydroxyketone **11** was obtained with 46% isolated yield (Table 7, entry 8). Diol **15** derived from 12-*O*-acetyl methyl ricinoleate was also subjected to dehydrogenation. Despite a complete conversion, only traces of the desired α -hydroxyketone were detected by GC. Conversely, tetrahydrofurans **21a** and **21b** were isolated with 60% yield and obtained as a 2:1 inseparable mixture of diastereomers (Table 7, entry 9).⁴⁶ These compounds are supposedly formed by acid-catalysed 1,4-migration of the acetyl group followed by dehydrative intramolecular cyclisation. A similar product (with free hydroxy group) has been reported by Werner during the preparation of carbonate from epoxidized methyl ricinoleate, thus supporting this hypothesis.^{11c} The replacement of Ru/C by Ru/Al₂O₃ for the dehydrogenation of diol **15** did not allow the preparation of the desired α -hydroxyketone. Finally, in order to push forward this methodology, tris(diol) **16**, prepared from high oleic sunflower oil, was subjected to the dehydrogenation conditions (Table 7, entry 10). The corresponding tris(α -hydroxyketone) **22** was produced with a moderate 42% yield (determined by ¹H NMR). This result demonstrates that the

method is also applicable to challenging substrates such as vegetable oil derivatives.

The recyclability of the heterogeneous Ru/C catalyst has been assessed using 1,2-diol **1** as model substrate using our standard conditions [activated 5wt%Ru/C (5 mol%), solvent-free, 175°C, 3 hours under a vacuum of 100 mbar] (Figure 3).

Figure 3. Recycling of the heterogeneous Ru/C catalyst. Conversion (%) of 1,2-diol **1** (black) and selectivity (%) of α -hydroxyketone **2** (gray).

The first run was carried out using freshly activated Ru/C and gave 90% conversion of diol **1** and 88% selectivity for the α -hydroxyketone **2**. These results are very close from those previously obtained (Table 7, entry 1) showing the good reproducibility of the method. After reaction, the catalyst was filtered, washed thoroughly (EtOAc), dried at 120°C under vacuum and re-activated under hydrogen.⁴⁷ Under these conditions, the conversion reached 70% and similar results were obtained for the next runs. Gratifyingly, the selectivity remained constant around 88-89% for all runs. The loss in conversion between runs 1 and 2 suggests some Ru leaching, however, it seems quite unlikely because the filtrate has no significant catalytic activity. A more reasonable explanation is the change in the oxidation degree of the Ru/C catalyst as recently shown in a recent work on a commercial Ru/C catalyst.⁴⁸ Further studies will be carried out to understand the activation/deactivation processes and the results will be reported in due course.

Table 7. Scope of the dehydrogenation of fatty acid-derived diols to alpha-hydroxyketones.^a

Entry	Diol		Conv. ^b (%)	Alpha-hydroxyketone		GC Yield ^b (%)	Selectivity ^b (%)
1		1	91		2	79 (67)	87
2		13	75		17	69 (65)	92
3		14	71		18	63 (56)	89
4		4	99		19, 20	-	-
5 ^c		4	40		8	35 (28)	88
6		5	93		9	79 (74)	85
7		6	94		10	76 (57)	81
8		7	85		11	69 (46)	81
9		15	> 99		21a, 21b	(60)	-
10 ^{d,e}		16	50		22	42 (nd)	84

^a Reaction conditions: 20-mL Schlenk flask, Ru/C was activated under atmospheric hydrogen pressure for 1 h at 175°C, 3 mmol of diol. ^b Determined by GC. ^c Activated Ru/Al₂O₃ was used. ^d Conversion and yield were determined by ¹H NMR. ^e The reaction was carried out in 6 hours.

Conclusions

In conclusion, we have developed two complementary methods for the preparation of α -hydroxyketones derived from fatty acids. The monooxidation of methyl oleate-derived diol using homogeneous $\text{Pd}(\text{OAc})_2$ / neocuproine complex gave the corresponding α -hydroxyketone with up to 97% selectivity under mild conditions (MeOH, 50°C). The access to alpha-hydroketone has also been investigated by dehydrogenation

using heterogeneous ruthenium-based catalysts under solvent-free conditions at 175°C. It has been shown that activated Ru/C was the most active catalyst for this transformation and working under vacuum is essential to reach high conversion and selectivity. In addition, the catalyst was found to be recyclable over 5 runs without loss of selectivity. Finally, the optimized conditions were applied to a range of oleochemical 1,2-diols to give the corresponding α -hydroxyketones with up to 74% isolated yields. These original

fatty acid derivatives could be further functionalized or cleaved to the corresponding acids or aldehydes.

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Experimental

Typical procedure for the preparation of α -hydroxyketones using homogeneous Pd(OAc)₂ / neocuproine complex:

In 30-mL steel reactor, methyl 9,10-dihydroxyoctadecanoate **1** (4 g, 12 mmol), Pd(OAc)₂ (54 mg, 0.24 mmol, 2 mol% in Pd), neocuproine (50 mg, 0.24 mmol, 2 mol%) were successively introduced in MeOH (8 mL) under stirring. The mixture was stirring at room temperature in a few minutes until the medium became more homogeneous. Next, glacial acetic acid (43 mg, 0.72 mmol, 6 mol%) was added to the solution before closing the apparatus. Oxygen (3 bar) was charged in the reactor, then the reaction was heated at 50°C (oil bath) for 1.5 hour. The reaction mixture was cooled down to 25°C by stream of water before adding EtOAc (20 mL). The suspension was filtered and the filtrate was evaporated under reduced pressure to give a green oil (3.97 g). The crude product was purified by column chromatography on silica gel (CH₂Cl₂/EtOAc, 100:0 → 95:5) to give the α -hydroxyketone **2** (3.20 g, 80%) as white solid. See Supporting Information for the full characterization of the compound.

Typical procedure for the preparation of α -hydroxyketones using heterogeneous Ru/C:

In a Schlenk flash, methyl 9,10-dihydroxyoctadecanoate **1** (0.92 g, 2.8 mmol) and activated 5%-Ru/C (0.26 g, 5 mol% in Ru) were introduced. Then, argon was filled inside the equipment. The outline of apparatus was connected with evaporator system to control the vacuum pressure at 100 mbar. The reaction was heated at 175°C (oil bath) for 3 hours. After cooling to room temperature, EtOAc (2 x 20 mL) was added in the mixture then the resulting slurry was filtered through millipore system (pore 0.1 μ m). The filtrate was evaporated under reduced pressure to give the crude product (0.89 g). The residue was purified by column chromatography on silica gel (CH₂Cl₂/EtOAc, 100:0 → 95:5) to give the α -hydroxyketone **2** (0.61 g, 67%) as white solid.

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