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# A highly efficient, green and recoverable catalytic system for the epoxidation of fatty esters and biodiesel with H<sub>2</sub>O<sub>2</sub>

Miriam De Torres<sup>a,1</sup>, Isabel W.C.E. Arends<sup>b,2</sup>, José A. Mayoral<sup>c,3</sup>, Elisabet Pires<sup>a,1</sup>, Gonzalo Jiménez-Osés<sup>a,d,\*</sup>

<sup>a</sup> Departamento de Química Orgánica, Instituto de Ciencia de Materiales de Aragón, Facultad de Ciencias, Universidad de Zaragoza-CSIC, Pedro Cerbuna, 12, E-50009 Zaragoza, Spain <sup>b</sup> Laboratory for Biocatalysis and Organic Chemistry, Delft University of Technology, Julianalaan 13, 2628 BL Delft, Netherlands

<sup>c</sup> Instituto Universitario de Catálisis Homogénea, Facultad de Ciencias, Universidad de Zaragoza, Pedro Cerbuna, 12, E-50009 Zaragoza, Spain

<sup>d</sup> Department of Chemistry and Biochemistry, University of California, Los Angeles, California, 607 Charles E. Young Drive East, 90095, Los Angeles, CA, United States

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### ABSTRACT

A highly efficient and green strategy for the epoxidation of fatty esters, combining a green oxidant (aqueous hydrogen peroxide) and a recyclable catalyst (a seleninic acid derivative) is presented. The possibility of integrating renewable solvents derived from glycerol in the productive cycle of biodiesel commodities is also explored. Fluorinated solvents (both commercial and glycerol-derived) play a double key role on this methodology: on the one hand, they strongly accelerate epoxidation reaction with respect to common non-fluorinated solvents and, on the other hand, some of them allow catalyst recycling. Mono- and polyunsaturated fatty esters, as well as soy biodiesel have been epoxidized with excellent yields and selectivities towards epoxide under the optimal conditions and with minimum catalyst loads.

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# 1. Introduction

In the last decade great interest has been focused in the development of new efficient processes for the functionalization of fatty acids through oxidation reactions [1]. This interest has been prompted by the need of reaching renewable chemicals in order to satisfy society demands for a greener chemistry. In this way, epoxidation of fatty acids derivatives is one of the most promising reactions to achieve the synthesis of a large variety of interesting products such as hydroxyethers, hydroxyesters, diols, *etc.* To this aim, the use of hydrogen peroxide  $(H_2O_2)$  for selective epoxidations is highly desirable because it is cheap, it has a high content in active oxygen, and it is clean, since the only byproduct formed is water [2]. The use of  $H_2O_2$  as oxidant often requires an efficient catalytic process in order to achieve high conversions and

E-mail addresses: I.W.C.E.Arends@tudelft.nl (I.W.C.E. Arends), mayoral@unizar.es (J.A. Mayoral), epires@unizar.es (E. Pires),

gjimenez@chem.ucla.edu (G. Jiménez-Osés).

selectivities, because of the poorer reactivity of  $H_2O_2$  compared to other classic epoxidizing reagents such as organic peracids, peroxyesters or persulfates. Many catalytic systems based on different metals have been reported for the epoxidation of a wide range of alkenes using hydrogen peroxide [3].

With respect to fatty acid derivatives epoxidation, several examples using the classical conditions based on peroxy acids generated *in situ* from carboxylic acids (typically formic or acetic acids) as active oxygen carriers,  $H_2O_2$  as oxygen donor and strong mineral acids ( $H_2SO_4$ ,  $HNO_3$ ,  $H_3PO_3$ ) as catalysts have been reported [4]. Inorganic and organometallic catalysts based on tungsten [5], rhenium and manganese [6] have also been used. The heterogeneous version of the epoxidation reaction with  $H_2O_2$  on fatty derivatives has also been explored using amorphous  $SiO_2/Ti$  [7] and methyl-trioxorhenium on niobia catalysts [8], ion exchange resins [9], and sol–gel aluminas [10]. In the past years, the enzimatically promoted epoxidation of vegetable oils and fatty acids is gaining increasing interest [11].

Aryl diselenides [12] and their oxidized counterparts, *i.e.* aryl seleninic [13] and peroxyseleninic acids [14] have been described as highly efficient oxygen transfer catalysts for different processes, principally the epoxidation of olefins. Heterogenized versions of these catalysts have been also described [15]. On the other hand, the so-called "booster effect" of fluorinated alcohols, which has been beautifully described by the groups of Neumann and co-workers

<sup>\*</sup> Corresponding author at: Department of Chemistry and Biochemistry, University of California, Los Angeles, California, 607 Charles E. Young Drive East, 90095, Los Angeles, CA, United States. Tel.: +1 310 2060515; fax: +1 310 2061843.

<sup>&</sup>lt;sup>1</sup> Tel.: +34 976762271; fax: +34 976762077.

<sup>&</sup>lt;sup>2</sup> Tel.: +31 15 2784423; fax: +31 15 2784700.

<sup>&</sup>lt;sup>3</sup> Tel.: +34 976762077; fax: +34 976762077.

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[16], van Vliet et al. [17] and Berkessel et al. [18], allows the use of  $H_2O_2$  in the absence of a catalyst to epoxidize different types of alkenes, although usually at the expense of longer reaction times and higher temperatures. These studies have demonstrated the activation of  $H_2O_2$  in fluorinated solvents towards oxidation reactions increasing reaction rates up to five times.

The combination of both aryl diselenides as catalysts and fluorinated solvents has raised a powerful methodology, developed by Sheldon and co-workers, for the epoxidation of cyclic and acyclic alkenes and the oxidation of carbonyl compounds, with very high turnover numbers and selectivities under different mono-, bi-, and even triphasic conditions [19]. Our aim was to test the applicability of this methodology, and eventually to improve it, to efficiently epoxidize fatty esters and biodiesel, in competition with the existing common methodologies.

In this sense, an important shortcoming of many of these epoxidation methods is, however, that catalysts are not readily available and that some of them are expensive to prepare and potentially toxic. Thus, greenness and economy of the catalytic reactions can be further improved by catalyst recycling, which is usually accomplished by using solid heterogeneous catalysts. However, the use of classical heterogeneous catalysts (for instance, based on titanium) together with aqueous hydrogen peroxide often results in extensive epoxide hydrolysis, and many efforts have been devoted to the synthesis of heterogeneous solid catalysts with hydrophobic properties [20]. A possible alternative would be the use of homogeneous catalysis in a liquid phase allowing easy separation of reagents and products by distillation from the catalytic phase, which would be subsequently recycled for further reactions. This strategy has been described for other reactions in the case of ionic liquids [21]. In a previous work, we described the homogeneously catalyzed epoxidation reaction of cyclooctene, using aqueous hydrogen peroxide as oxidant and a diphenyl diselenide as catalyst precursor in a wide range of solvents [22]. Although classically this catalytic system had been dominated by the use of dichloromethane (DCM) and 2,2,2-trifluoroethanol (TFE) [12b,19], it was found that some glycerol-derived solvents are as good as TFE in some cases and better than DCM in others, the best ones being those containing short fluorinated chains. These glycerol-derived solvents, which present some attractive advantages, such as being renewable, presumably low toxic, low volatile, and possessing tunable physico-chemical properties [23], have ultimately allowed the recycling of the catalytic phase thorough the selective evaporation of volatile reaction products, i.e. cyclohexene oxide [24]. However, one important drawback of this attractive strategy is being limited to volatile reagents and products, which is not the case of unsaturated fatty derivatives as oleates and linoleates.

In this paper, we overcome this limitation and take advantage of using a green oxidant (hydrogen peroxide) and a highly active homogeneous catalyst (namely bis[3,5-bis(trifluoromethyl)diphenyl] diselenide) [14a,e] in combination with fluorinated alcohols as solvents or co-solvents, to selectively epoxidize fatty methyl esters and their mixtures as presented in biodiesel (Scheme 1). The use of adequate amounts of fluorinated alcohols is of key importance to both accelerate the reaction and to prepare recyclable catalytic liquid phases.

## 2. Experimental

## 2.1. Non-catalyzed reactions

Methyl oleate (1 mmol, 297 mg) and eicosane (internal standard, 0.15 mmol, 40 mg) were dissolved in 1 mL of the corresponding fluorinated alcohol.



Solvent = EtOH, <sup>i</sup>PrOH, <sup>t</sup>BuOH, CH<sub>2</sub>Cl<sub>2</sub>, TFE, HFIP,



**Scheme 1.** Catalytic epoxidation of unsaturated fatty methyl esters with arylseleninic acid-hydrogen peroxide system in several common and glycerol-derived solvents (fluorinated and no-fluorinated).

Then, hydrogen peroxide (60% in water, 2 mmol, 0.1 mL) was added and the mixture was heated at reflux or 90 °C (in highboiling point GlyF). Reactions were monitored by taking samples at regular times. Those samples were dissolved in tetrahydrofuran; some manganese dioxide was added to quench the excess of hydrogen peroxide in the sample. Samples were dried over anhydrous MgSO<sub>4</sub> and analyzed by GC. Glycerol-based solvents were obtained by ring-opening of epichlorohydrin with the corresponding alkoxide (sodium ethoxide) or alcohol (TFE) in alcoholic media [23] and subsequent purification by vacuum distillation.

## 2.2. Se-catalyzed reactions

The general procedure for the epoxidation of fatty acid methyl esters was carried out at 25 °C, using the following conditions: 0.1-1.0 mol% per mol<sup>4</sup> of unsaturation of bis[3,5-bis(trifluoro-methyl)diphenyl] diselenide [14a,e], was dissolved in 1 mL of solvent. Next, hydrogen peroxide (60% in water, 2 mol per mole of unsaturation) was added. When the solution became colorless, eicosane (internal standard, 0.15 mmol, 40 mg) was added followed by 1 mmol of the olefin. The reaction was monitored by GC as described above.

For biodiesel epoxidation, the nature and proportion of unsaturated methyl esters was considered (typically, 50% of methyl oleate, 30% of methyl linoleic and 5% of methyl linolenate in soy biodiesel). Once the total unsaturation grade is calculated (1.45 mmol/300 mg in our biodiesel samples), the epoxidation reaction is carried out under the same conditions described above.

## 2.3. Recycling experiments

Bis[3,5-bis(trifluoro-methyl)diphenyl] diselenide (0.01 mol, 5.8 mg) was dissolved in 5 mL of TFE. Next, hydrogen peroxide (60% in water, 1,1 mmol, 0.06 mL per cycle) was added. When the solution became colorless, eicosane (internal standard, 0.15 mmol, 40 mg per cycle) was added followed by methyl oleate (1 mmol, 297 mg per cycle). The reaction was monitored by GC as described

<sup>&</sup>lt;sup>4</sup> Although the optimum catalyst load is 0.1 mol% when HFIP is used as a solvent, the use of 1 mmol% is strongly recommended in order to maintain reasonable reaction times along the successive reaction cycles.

above. When the reaction was complete, the products and internal standard were extracted with isooctane  $(3 \times 3 \text{ mL}, \text{ upper layer})$ , dried over anhydrous MgSO<sub>4</sub>, filtered and evaporated under reduced pressure. Then more hydrogen peroxide and eicosane were added to the remaining residue (solvent and catalyst). After a few minutes more olefin (1 mmol, 297 mg) was added. When the last reaction cycle is complete, the catalyst is completely removed by entrapment in 4 Å molecular sieves powder and filtration.

# 3. Results and discussion

## 3.1. Non-catalyzed epoxidation

Given the remarkable effects of fluorinated alcohols, as mentioned in the Introduction, and inspired on previous works in which TFE, 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) [16-18] and 1,3-bis(2,2,2-trifluoroethoxy)-2-propanol (GlyF) [22] were successfully used as activating solvents in the absence of catalysts for the epoxidation of diverse olefins with H<sub>2</sub>O<sub>2</sub>, we first assayed the direct epoxidation of methyl oleate with H<sub>2</sub>O<sub>2</sub>. An initial screening of common alkyl and fluoroalkyl alcohols was carried out to determine the most suitable solvent in terms of rate, conversion of alkene and selectivity towards the corresponding oxide. Apart from the commercially available solvents, glycerol-derived symmetric ethers such us 1,3-diethoxypropan-2-ol and GlyF were first prepared and purified following a protocol previously reported by our group [23]. DCM was selected as a non-alcoholic probe, which in turn is widely used in the environmentally harmful epoxidation of alkenes with organic perbenzoic acids like *m*-chloroperbenzoic acid (MCPBA). In this initial survey, an excess of H<sub>2</sub>O<sub>2</sub> (60% in water) was employed (2 equiv). Under these conditions, the reaction at room temperature did not progress at all or was too slow for being analyzed, so the reaction temperature was raised up to reflux conditions for all solvents and up to 90 °C for GlyF. When commercial non-fluorinated alcohols (EtOH, <sup>*i*</sup>PrOH, <sup>*t*</sup>BuOH) were used as solvents in the absence of Se catalyst (1), no detectable amount of epoxide was obtained after prolonged heating, which revealed their much worse properties as hydrogen peroxide activators. Conversely, HFIP was revealed as the most convenient solvent for this process, cleanly leading to 76% yield of cis-epoxide in 2 h and to a full completion of the reaction in 5 h. TFE exhibited slower reaction rates, yielding only 24% yield in 4.5 h and being necessary 28 h of heating at reflux to reach 71% yield of epoxide in the same cis configuration. It must be noted that the reflux temperature of HFIP (59 °C) is lower than that of TFE (77–80 °C), so the outstanding accelerating properties of the former are corroborated. The crude mixtures obtained using these commercial fluorinated alcohols as solvents were very clean under the standard conditions (1 mmol of methyl oleate, 2 mmol of  $H_2O_2$  and 1 mL of solvent). In an attempt to reduce reaction times with TFE, an excess of 4 equiv. of H<sub>2</sub>O<sub>2</sub> was used, which slightly increased epoxide yield at short reaction times (38% versus 24% after 4.5 h) but, in turn, did not allowed to reach full conversion of methyl oleate. Worse still, significant amount of the corresponding 1,2-diol (43%) and traces of the 1,2-(trifluoroethoxy)alcohol were generated at the expense of reducing the global yield of epoxide (30%) through side ringopening reactions, after 20 h of stirring under reflux (80% conv). These results, together with those obtained in the recycling assays (vide infra) show that long reaction times, more than a large excess of water in the reaction mixture, seriously affect the selectivity of the epoxidation reaction and should be, as far as possible, avoided.

For this reason, the use of GlyF under non-catalytic conditions was revealed to be problematic, due to the poor selectivity achieved towards epoxidation. With this solvent, nearly all the starting material is consumed after prolonged heating at reflux, but time and



**Fig. 1.** Solvent effects in the Se-catalyzed epoxidation of methyl oleate. Reaction conditions: 1 mmol methyl oleate, 2 eq.  $H_2O_2$ , 1 mol% catalyst **1**, 1 mL solvent, room temperature. Yields determined by GC.

temperature-dependent products distribution were observed. The corresponding allyl alcohols, 1,2-diol and 1,2-hidroxyethers resulting from allylic oxidation and the ring-opening reactions of the oxirane with water and GlyF, respectively, were identified among these products. Apart from these expected side reactions, which have been observed before under similar conditions [16a,22], the rather complex mixture of products obtained could be related to the thermal decomposition of  $H_2O_2$ , which seems to quickly take place at temperatures above 90 °C (i.e., no reaction occurred at 80 °C). Evidence pointing to a radical-mediated epoxidation resulting from the thermal homolytic cleavage of hydrogen peroxide is that variable amounts of *cis* and *trans* epoxides were obtained [25]. Noteworthy, a major proportion of the *trans* epoxide<sup>5</sup> was obtained even at low conversion values (40% conv at 22 h, 2:1 trans/cis ratio) when the non-catalyzed epoxidation reaction was conducted under the same conditions but using the non-fluorinated analogue of GlyF (1,3-diethoxypropan-2-ol) as a solvent. In this case, much lower conversions and a similar complex mixture were obtained. These results, together with those described for the Se-catalyzed reaction (vide infra), clearly discards this compound as a suitable solvent to perform the epoxidation of unsaturated fatty esters, despite is renewable character.

### 3.2. Se-catalyzed epoxidation

After demonstrating the different accelerating properties of the solvents in the control reactions described above, we thoroughly assayed the selenium-catalyzed epoxidation of fatty acid derivatives, the main objective of our study. Initially, the amount of catalyst precursor **1** was fixed to 1 mol% (*i.e.*, 2 mol% of the catalytically active species, Scheme 1), and the excess of  $H_2O_2$  (60% in water) employed was again fixed to 2 equiv. The same solvents used in the non-catalytic tests were employed. Reactions were carried out at room temperature and under concentrated conditions, namely 1 mL of solvent and 1 mmol of substrate (methyl oleate). As could be confirmed by GC and <sup>1</sup>H NMR analysis of the crude mixtures, a complete selectivity towards the corresponding *cis* epoxide was obtained in all cases. The results of this study are summarized in Fig. 1. As can be seen on these plots, and according to previous reports [16–18] and the control results described above, the

<sup>&</sup>lt;sup>5</sup> The epoxide in *trans* configuration was selectively obtained, characterized in parallel by applying the same Se-catalyzed oxidation protocol using methyl elaidate ((*E*)-methyl octadec-9-enoate as starting material.

epoxidation reaction was greatly accelerated in the presence of fluorinated alcohols, being the maximum final turnover frequencies (TOF<sub>F</sub>, measured when the substrate was totally consumed) achieved with HFIP(TOF<sub>F</sub> = 588 h<sup>-1</sup>) and TFE(TOF<sub>F</sub> = 67 h<sup>-1</sup>). It must be emphasized that this acceleration cannot be attributed to a significant contribution of the non-catalyzed epoxidation reaction pathway, given the much slower reaction rates described in the precedent section, even at higher reaction temperatures. Acceleration by solvent must be therefore connected to the catalyst action.

Noteworthy, using a fluorinated glycerol-derived solvent such as 1,3-bis(2,2,2-trifluoroethoxy)-2-propanol (GlyF,  $TOF_F = 16 h^{-1}$ ), despite bearing rather separated fluorine and hydroxyl groups, allows to perform the selective epoxidation of fatty esters with excellent yields in a short time and with limited wastes. This strategy allows to efficiently integrate all the materials derived from the production of biodiesel, that is, the fatty methyl esters and glycerol, into the same process, which would contribute to improve the productive cycle of a biorefinery. With respect to non-fluorinated solvents, only DCM allows an acceptable reactivity (TOF =  $12 h^{-1}$ ), in good agreement with previous reports [22]. On the other side, all non-fluorinated alcohols showed low conversions at short times, being necessary at least 24 h to reach only a 75% yield under the best conditions (<sup>i</sup>PrOH). Thus, glycerol-derived 1,3-diethoxypropan-2ol, albeit being more environmentally and economically convenient than its fluorinated analogue (GlyF), is not suitable to perform the epoxidation of unsaturated fatty compounds, in view of the slow reaction rates and low yields obtained.

At this early stage of the study it was also noticed that, according to recent observations [26], the time required to preactivate the catalyst, *i.e.* to oxidize the diselenide (pale yellow) to the seleninic acid (colorless) in the presence of H<sub>2</sub>O<sub>2</sub>, correlated with the global reaction time (from 15 min of preactivation in <sup>i</sup>PrOH to 5 min in TFE to 20 s in HFIP). The advantage of fluoroalcohols in similar Se-catalyzed reactions has been attributed to their polar but non-basic, non-oxidisable and water-miscible character, which avoids mass transfer limitations and reduces epoxide solvolysis rate [12b]. Furthermore, the results described herein demonstrate that the accelerating properties of fluoroalcohols also play a key role in the H<sub>2</sub>O<sub>2</sub>-promoted activation (and regeneration) of the catalyst. However, this activation was not strong enough to promote the regeneration of MCPBA with H<sub>2</sub>O<sub>2</sub> (which commonly require strongly acidic catalysts and/or solvents [27]) in TFE as solvent under the same conditions, precluding the use of catalytic amounts MCPBA in a similar manner.

The scope of this non-optimized selenium-catalyzed epoxidation protocol was quickly evaluated by performing the same reaction using methyl linoleate and soybean biodiesel as substrates and industrially affordable TFE. The amount of hydrogen peroxide was carefully adjusted depending on the number of unsaturations and the nature and proportion of the unsaturated compounds (see Section 2). These experiments revealed that the epoxidation of methyl oleate and the first double bond of poly-unsaturated fatty esters were rather fast because of the greater concentration of hydrogen peroxide at short reaction times ( $\sim$ 30 min). On contrary, the complete epoxidation of the second double bond of methyl linoleate took place much more slowly (2-2.5 h), when at least one equiv. of H<sub>2</sub>O<sub>2</sub> had been consumed, and the formation of related ring-opening diols was observed at long reaction times (3.5-4 h). Therefore, it was shown that this selenium/fluoroalcohol-based methodology can be successfully applied for the epoxidation of both pure and mixtures of mono- and polyunsaturated compounds under very mild and sustainable conditions.

Once the best solvents to perform de epoxidation of methyl oleate were found (TFE and HFIP), an optimization of the catalyst load was done in order to improve the economy of the process. In this sense, the reduction in the amount of catalyst from 1% to

Table 1

Optimization of the reaction conditions for the epoxidation of methyl oleate with  $H_2O_2$  using diselenide 1 as catalyst at room temperature.

Entry	Solvent	$H_2O_2$ (equiv.)	Catalyst (mol%)	Yield <sup>a</sup>	Time
1	TFE	2.0	1.0	>99%	1.5 h
2	TFE	2.0	0.5	>99%	2 h
3	HFIP	2.0	1.0	>99%	10 min
4	HFIP	2.0	0.5	>99%	15 min
5	HFIP	2.0	0.25	>99%	15 min
6	HFIP	2.0	0.1	>99%	20 min
7	TFE	1.1	1.0	87%	1.5 h
8	HFIP	1.1	1.0	93%	10 min

<sup>a</sup> Determined by GC.

0.5% slightly increased the total reaction time in TFE from 1.5 to 2 h (Table 1, entries 1 and 2). More impressive was the significant tenfold reduction of the catalyst load that could be accomplished when carrying out the reaction in HFIP, in which with only 0.1 mol% of **1** the epoxidation of methyl oleate was completed in 25 min (Table 1, entries 3–6).

Despite its outstanding accelerating capacity, the high price of HFIP can be a serious drawback to perform the reaction in a costeffective manner at an industrial scale. For this reason, we assayed the use of decreasing volumes of HFIP as a cosolvent in the presence of its non-fluorinated and inexpensive analogue (<sup>i</sup>PrOH). Catalyst 1 (1 mol%) and 1 mL of total volume with variable proportions of <sup>i</sup>PrOH and HFIP were used. As can be seen (Table 2, entries 1–3), a reasonable catalytic activity can be maintained with 50% (v/v)of HFIP, although longer reaction times are required to complete the reaction. The same trend is observed with glycerol-derived 1,3diethoxypropan-2-ol, albeit its flourinated analogye (GlyF) shows a superior performance (Table 2, entries 4 and 5), in good agreement with the results described above. Presumably, hydroxylated alkyl cosolvents could interfere within the hydrogen bonding network created by HFIP around hydrogen peroxide [18], so we decided to repeat these experiments but with other widely used non-alcoholic solvents such us *n*-hexane, toluene, ethyl acetate, tetrahydrofuran and tert-butyl methyl ether. (Table 2, entries 6-16) According to this hypothesis, a good correlation between hydrogen donor/acceptor capabilities of each solvent/cosolvent and their accelerating properties was observed. Non-polar hydrocarbon solvents (*n*-hexane, toluene) were the best co-solvents in terms of reactivity, followed

Table 2 Solvent mixtures for the epoxidation of methyl oleate with  $H_2O_2$  using diselenide 1 as catalyst.<sup>a</sup>

Solvent	Yield <sup>b</sup> (time)
HFIP/ <sup>i</sup> PrOH (1:1)	61% (30 min), 97% (3 h)
HFIP/ <sup>i</sup> PrOH (1:3)	55% (3 h), >99% (23 h)
HFIP/ <sup>i</sup> PrOH (1:9)	39% (3 h), 88% (23 h)
HFIP/1,3-diethoxypropan-2-ol (1:1)	49% (30 min)
HFIP/GlyF(1:1)	91% (30 min)
HFIP/n-hexane (1:1)	97% (15 min)
HFIP/n-hexane (1:3)	95% (15 min)
HFIP/n-hexane (1:9)	98% (1.5 h)
HFIP/toluene (1:1)	97% (15 min)
HFIP/toluene (1:3)	94% (15 min)
HFIP/toluene (1:9)	57% (15 min), 92% (1 h)
HFIP/ethyl acetate (1:1)	56% (30 min), 79% (1 h)
HFIP/ethyl acetate (1:3)	78% (5 h)
HFIP/ethyl acetate (1:9)	35% (3 h), 83% (23 h)
HFIP/THF (1:1)	27% (30 min)
HFIP/ <sup>t</sup> BuOMe (1:1)	48% (30 min)
	Solvent      HFIP/ <sup>i</sup> PrOH (1:1)      HFIP/ <sup>i</sup> PrOH (1:3)      HFIP/ <sup>i</sup> PrOH (1:9)      HFIP/1,3-diethoxypropan-2-ol (1:1)      HFIP/1,3-diethoxypropan-2-ol (1:1)      HFIP/GlyF (1:1)      HFIP/n-hexane (1:1)      HFIP/n-hexane (1:3)      HFIP/toluene (1:1)      HFIP/toluene (1:3)      HFIP/toluene (1:3)      HFIP/toluene (1:3)      HFIP/toluene (1:3)      HFIP/toluene (1:3)      HFIP/thyl acetate (1:3)      HFIP/ethyl acetate (1:9)      HFIP/ThF (1:1)      HFIP/ <sup>I</sup> BuOMe (1:1)

 $^a$  Reaction conditions: 1 mmol methyl oleate, 2 equiv. H\_2O\_2, 1 mol% catalyst 1, 1 mL solvent, room temperature.

<sup>b</sup> Determined by GC.



**Fig. 2.** Catalyst recovery experiments. Method A: 1 mmol methyl oleate, 2 equiv.  $H_2O_2$ , 1 mol% catalyst 1, 1 mL TFE, room temperature. Method B: 1 mmol methyl oleate, 2 equiv.  $H_2O_2$ , 1 mol% catalyst 1, 5 mL TFE, room temperature. Method C: 1 mmol methyl oleate, 2 equiv.  $H_2O_2$ , 1 mol% catalyst 1, 5 mL TFE, room temperature. Extractions were performed with isooctane (3 × 3 mL). Yields determined on the crude mixture after extraction and evaporation.

by hydrogen bond acceptors (ethers<sup>6</sup> and esters) and hydrogen bond donors/acceptors (alcohols).

As found thorough these studies, excellent epoxide yields in relatively short times and in the presence of non-toxic and inexpensive solvents, together with small amounts of HFIP, can be obtained.

It must be noted that, with 10% (v/v) HFIP solvent mixtures, only 0.95 mmol of this fluoroalcohol per mole of substrate is required to notably accelerate the epoxidation reaction, which is an excellent compromise between efficiency and economy. These unprecedented results reveal a true catalytic role of such fluorinated solvents, and expand the scope of these derivatives to be used in industry in a sustainable manner.

As a final step, the excess of hydrogen peroxide was optimized. Excellent yields of epoxide (87–93%) with total *cis*-selectivity were obtained using 1.1 equiv of  $H_2O_2$  in TFE and HFIP, respectively under the same conditions (Table 1, entries 7–8).

This allowed to significantly reduce the amount of water generated as byproduct, which was of capital importance to achieve a good catalyst recoverability, as will be described later on.

#### 3.3. Catalyst recycling experiments

Once the best reaction conditions for the epoxidation of fatty methyl esters were found, we focused our attention on recycling and/or reusing the catalyst. To this aim, we found that some common and inexpensive alkanes were practically immiscible with the reaction mixture in TFE. This allowed to take advantage of the highly hydrophobic character of the fatty reaction products, in order to isolate them by extraction with these alkanes. As demonstrated by preliminary assays, isooctane (2,2,4-trimethylpentane) showed superior extracting properties than hexanes and was the solvent of choice for this process, in which the catalyst remains 'inmobilized' in the fluoroalcoholic phase, ready to be used for additional reaction cycles after recharging with more substrate and oxidant. However, it was found that the standard protocol based on substrate concentrations of 1 M in TFE could not be repeated more than four times due to the accumulation of water on the catalytic phase and the appearance of insolubility and mass transfer problems associated to it (Fig. 2, Method A). The negative effect of the increasing amount of water formed along the oxidation cycles

has been reported on previous studies [26]. This problem could be partially overcome by diluting methyl oleate fivefold in TFE, at an expense of a more prolonged reaction time (2h) to reach full conversion. The increase of reaction volume (5 mL) also facilitated the extractive workup, so that this operation could be optimized to achieve a global >99% yield of isolated epoxide after  $3 \times 3 \text{ mL}$ extractions with isooctane. As represented in Fig. 2 (Method B), the same catalytic phase could be reused up to five times although an increasing loss of activity due to the accumulation of water is observed. For this reason, the amount of H<sub>2</sub>O<sub>2</sub> was first reduced from 2 eq. to 1.1 eq., as described before (Table 1, entries 7 and 8). Additionally, the common strategy of adding a strong drying agent like 4 Å molecular sieves (200 mg per mmol of substrate) to remove water from the reaction phase after the extraction of products with isooctane, resulted in a complete loss of activity after filtering and washing the solid with TFE.<sup>7</sup> This issue was due to the complete entrapment of the catalyst in the solid, as demonstrated by Selenium analysis of the recovered molecular sieves. On contrary, the same treatment using optimized amounts of anhydrous MgSO<sub>4</sub> after the fourth reaction cycle (400 mg per mmol of substrate) allowed to restore the initial catalytic activity (Fig. 2, Method C). With this optimized recovering protocol, the catalytic phase could be reused up to seven times without significant loss of activity or cis stereoselectivity. A final treatment of the fluorous phase with molecular sieves allows the complete removal of the catalyst for its safe disposal. In summary, an important conclusion drawn from these recoverability assays, is that water does not deactivate Se/fluoroalcohols catalytic systems irreversibly; instead, an indirect and reversible decrease on the reaction rate due to solubility and mass transfer issues is produced.

# 4. Conclusions

A highly efficient and green strategy for the epoxidation of fatty esters, combining a green oxidant (aqueous hydrogen peroxide) and a recyclable catalyst (a seleninic acid derivative) has been explored. The possibility of integrating renewable solvents derived from glycerol in the productive cycle of biodiesel commodities is also tested. Fluorinated solvents (both commercial and glycerolderived) play a key double role on this methodology: on the one hand, they strongly accelerate epoxidation reaction with respect to common non-fluorinated solvents and, on the other hand, some of them allow the easy catalyst recycling by extraction of the reaction products with inexpensive alkane solvents like hexanes and isooctane, and subsequent reuse of the fluorinated catalytic phase. The activating properties of certain fluorinated solvents (TFE and especially HFIP) towards hydrogen peroxide are so strong that the epoxidation of fatty derivatives can be accomplished even in the absence of a catalyst, albeit at the expense of a longer reaction times and higher temperatures. A negative effect of water accumulation has been observed, although it does not result in irreversible catalyst deactivation and can be overcome by the use of an inexpensive desiccant. Great optimization efforts have been done to achieve an environmentally friendly and sustainable protocol. In summary, mono- and polyunsaturated fatty, as well as soy biodiesel have been epoxidized with excellent yields and selectivities towards epoxide under the optimal conditions with minimum catalyst loads (0.1–1% mmol) and the possibility of reusing the catalytic system up to seven reaction cycles.

<sup>&</sup>lt;sup>6</sup> As solvent grade tetrahydrofuran was used, the presence of water traces could be the cause of the observed poor performance.

<sup>&</sup>lt;sup>7</sup> While activated molecular sieves powder fully disrupted the catalytic activity of **1**, beads did not show any beneficial effect and the reaction proceeded as in the absence of the desiccant.

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# References

- [1] A. Kockritz, A. Martin, Eur. J. Lipid Sci. Technol. 110 (2008) 812-824.
- [2] I. Arends, R.A. Sheldon, Top. Catal. 19 (2002) 133–141.
  [3] (a) G. Grigoropoulou, J.H. Clark, J.A. Elings, Green Chem. 5 (2003) 1–7; (b) D.E. De Vos, B.F. Sels, P.A. Jacobs, Adv. Synth. Catal. 345 (2003) 457-473;
- (c) D.E. De Vos, B.F. Sels, P.A. Jacobs, Adv. Catal, 46 (2001) 1-87. [4] (a) V.V. Goud, A.V. Patwardhan, N.C. Pradhan, Bioresour. Technol. 97 (2006)
  - 1365-1371 (b) S. Dinda, A.V. Patwardhan, V.V. Goud, N.C. Pradhan, Bioresour, Technol, 99 (2008) 3737-3744;
  - (c) V.V. Goud, S. Dinda, A.V. Patwardhan, N.C. Pradhan, Asia-Pac. J. Chem. Eng. 5 (2010) 346-354.
  - E. Poli, J.M. Clacens, J. Barrault, Y. Pouilloux, Catal. Today 140 (2009) 19-22.
- [6] G.D. Du, A. Tekin, E.G. Hammond, L.K. Woo, J. Am. Oil Chem. Soc. 81 (2004) 477-480
- [7] A. Campanella, M.A. Baltanas, M.C. Capel-Sanchez, J.M. Campos-Martin, J.L.G. Fierro, Green Chem. 6 (2004) 330-334.
- [8] A.O. Bouh, J.H. Espenson, J. Mol. Catal. A: Chem. 200 (2003) 43-47.
- (a) R. Mungroo, N.C. Pradhan, V.V. Goud, A.K. Dalai, J. Am. Oil Chem. Soc. 85 [9] (2008) 887-896;
- (b) S. Sinadinovic-Fiser, M. Jankovic, Z.S. Petrovic, J. Am. Oil Chem. Soc. 78 (2001) 725-731.
- [10] J. Sepulveda, S. Teixeira, U. Schuchardt, Appl. Catal., A 318 (2007) 213-217.
- [11] (a) C. Orellana-Coca, U. Tornvall, D. Adlercreutz, B. Mattiasson, R. Hatti-Kaul, Biocatal. Biotransform. 23 (2005) 431-437;
  - (b) C. Orellana-Coca, S. Camocho, D. Adlercreutz, B. Mattiasson, R. Hatti-Kaul, Eur. J. Lipid Sci. Technol. 107 (2005) 864-870;
  - (c) C. Orellana-Coca, J.M. Billakanti, B. Mattiasson, R. Hatti-Kaul, J. Mol. Catal. B: Enzym. 44 (2007) 133-137;
  - (d) U. Tornvall, C. Orellana-Coca, R. Hatti-Kaul, D. Adlercreutz, Enzyme Microb. Technol. 40 (2007) 447-451;
- (e) M.R.G. Klaas, S. Warwel, J. Am. Oil Chem. Soc. 73 (1996) 1453-1457. [12] (a) J. Mlochowski, M. Brzaszcz, M. Giurg, J. Palus, H. Wojtowicz, Eur. J. Org. Chem. (2003) 4329-4339;

B.C.M. Fernes, Brink, M.C.A. (b) G.J. ten van Vliet. Arends, R.A. Sheldon, J. Perkin Trans. Chem. Soc., 1 (2001) 224-228.

[13] (a) S.B. Said, J. Skarzewski, J. Mlochowski, Synth. Commun. 22 (1992) 1851-1862;

- (b) A.G. Kutateladze, J.L. Kice, T.G. Kutateladze, N.S. Zefirov, J. Org. Chem. 58 (1993) 995-996;
- (c) L.G. Faehl, J.L. Kice, J. Org. Chem. 44 (1979) 2357-2361;
- (d) T. Hori, K.B. Sharpless, J. Org. Chem. 43 (1978) 1689-1697;
- (e) J.L. Kice, T.W.S. Lee, J. Am. Ceram. Soc. 100 (1978) 5094-5102.
- [14] (a) L. Syper, J. Mlochowski, Tetrahedron 43 (1987) 207-213; (b) H.J. Reich, F. Chow, S.L. Peake, Synthesis (1978) 299-301;
  - (c) L. Syper, Synthesis (1989) 167-172;
  - (d) L. Syper, Tetrahedron 43 (1987) 2853-2871;
  - (e) L. Syper, J. Mlochowski, Synthesis (1984) 747-751.
- [15] (a) R.T. Taylor, L.A. Flood, J. Org. Chem. 48 (1983) 5160-5164; (b) B. Betzemeier, F. Lhermitte, P. Knochel, Synlett (1999) 489-491; (c) H. Wojtowicz, G. Soroko, J. Mlochowski, Synth. Commun. 38 (2008) 2000-2010;
  - (d) D. Crich, Y.K. Zou, Org. Lett. 6 (2004) 775-777;
  - (e) D. Crich, Y.K. Zou, J. Org. Chem. 70 (2005) 3309-3311.
- [16] (a) K. Neimann, R. Neumann, Org. Lett. 2 (2000) 2861-2863; (b) S.P. de Visser, J. Kaneti, R. Neumann, S. Shaik, J. Org. Chem. 68 (2003) 2903-2912.
- [17] M.C.A. van Vliet, I. Arends, R.A. Sheldon, Synlett (2001) 248-250.
- [18] (a) A. Berkessel, J.A. Adrio, Adv. Synth. Catal. 346 (2004) 275-280;
- (b) A. Berkessel, J.A. Adrio, J. Am. Ceram. Soc. 128 (2006) 13412-13420; (c) A. Berkessel, J.A. Adrio, D. Huettenhain, J.M. Neudorfl, J. Am. Ceram. Soc. 128 (2006) 8421-8426.
- [19] (a) G.J. ten Brink, J.M. Vis, I. Arends, R.A. Sheldon, J. Org. Chem. 66 (2001) 2429-2433;

(b) G.J. ten Brink, J.M. Vis, I. Arends, R.A. Sheldon, Tetrahedron 58 (2002) 3977-3983.

[20] (a) See, for instance T. Blasco, M.A. Camblor, A. Corma, P. Esteve, J.M. Guil, A. Martinez, J.A. Perdigon-Melon, S. Valencia, J. Phys. Chem. B 102 (1998) 75-88; (b) J.M. Fraile, J.I. Garcia, J.A. Mayoral, E. Vispe, J. Catal. 189 (2000) 40-51; (c) J.M. Fraile, J.I. Garcia, J.A. Mayoral, E. Vispe, J. Catal. 204 (2001) 146-156; (d) J.M. Fraile, J.I. Garcia, J.A. Mayoral, E. Vispe, D.R. Brown, M. Naderi, Chem. Commun. (2001) 1510–1511; (e) J.M. Fraile, J.I. Garcia, J.A. Mayoral, E. Vispe, Appl. Catal., A 245 (2003) 363-376;

(f) J.A. Fraile, J.I. Garcia, J.A. Mayoral, E. Vispe, Appl. Catal., A 276 (2004) 113-122; (g) M. Guidotti, C. Pirovano, N. Ravasio, B. Lazaro, J.M. Fraile, J.A. Mayoral, B. Coq, A. Galarneau, Green Chem. 11 (2009) 1421-1427.

- [21] J. Dupont, R.F. de Souza, P.A.Z. Suarez, Chem. Rev. 102 (2002) 3667-3691, and references cited therein.
- [22] H. Garcia-Marin, J.C. van der Toorn, J.A. Mayoral, J.I. Garcia, I. Arends, Green Chem. 11 (2009) 1605-1609.
- [23] J.I. Garcia, H. Garcia-Marin, J.A. Mayoral, P. Perez, Green Chem. 12 (2010) 426-434.
- [24] H. Garcia-Marin, J.C. van der Toorn, J.A. Mayoral, J.I. Garcia, I. Arends, J. Mol. Catal, A 334 (2011) 83-88.
- [25] M. De Torres, G. Jimenez-Osés, J.A. Mayoral, E. Pires, Bioresour. Technol. 102 (2011) 2590-2594.
- [26] J.C. van der Toorn, G. Kemperman, R.A. Sheldon, I. Arends, J. Org. Chem. 74 (2009) 3085-3089.
- [27] L.S. Silbert, D. Swern, E. Siegel, J. Org. Chem. 27 (1962) 1336-1342.