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Additional Information

Solid-Catalyzed Esterification Reaction of Long-Chain Acids and Alcohols in Fixed-Bed Reactors at Pilot Plant Scale.

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Abstract: The esterification reaction of long-chain acids and alcohols is carried out in both academia and industry with soluble strong acids such as phosphoric or methanesulfonic acid, since the lower diffusion and higher steric hindrance of the long-chain reactants compared to small derivatives (such as methanol or ethanol) severely hampers a smooth esterification on catalytic solids. In order to design an efficient industrial process for the esterification reaction of long-chain acids and alcohols, under flow conditions, solid catalysts are of interest. Here we show that the esterification of different fatty acids with 2-ethyl hexyl alcohol proceeds in very high yields and selectivity when carried out with organic solid acids both in batch and in flow processes, enabling the use of fixed-bed reactors to perform the esterification reaction. To evaluate the process under real industrial conditions, experiments at multi-kilogram scale in pilot plant tubular reactors were carried out, confirming the feasibility of the ton-scale production of long-chain esters over solid catalysts in a continuous process.

Keywords: esterification • catalysis • solid acid • fatty acid • ethyl hexyl alcohol • in-flow reactions • pilot plant scale

1 Introduction

The simplest method to obtain esters is the reaction of an alcohol with a carboxylic acid, called Fischer esterification. From an industrial point of view, the most common catalysts

to carry out the esterification reaction are very strong soluble acids, such as phosphoric, sulfuric, methanesulfonic and *p*-toluenesulfonic acid. Despite the high catalytic activity of these homogeneous catalysts, they are not optimal for an efficient industrial process since the volume production is limited by the batch reactor size and reaction time, which includes product separation and washings. Besides, soluble catalysts are not recoverable, cause tank corrosion and the appearance of by-products due to unwanted side reactions, such as alcohol dehydration and ether formation [1–5].

Long-chain esters, in both the acidic and alcoholic part of the molecule, are of recognized industrial interest. These compounds are widely used as surfactants, vehicles for digital inks, dispersants and lubricants, among other applications [6]. They are synthesized in thousands of tons per year using sulfuric-type acid or phosphoric acid catalysts in solution, in batch processes, which requires a subsequent neutralization and huge amounts of water for washing the organic product, apart from the corrosive processes associated with acids and strong bases in solution [7]. In this regard, solid acids could be a suitable solution to circumvent these problems. Indeed, solid acid catalysts have already been reported for some esterification reactions, including exchange resins, zeolites, sulfated zirconia and niobic acid, among others [8–10]. However, previous works make generally use of methanol or ethanol as alcohol reactants, and also relatively short fatty acids, up to 12 carbons, and mainly for the production of biodiesel [11–15]. It is difficult to find in the open literature esterification reactions of fatty acids of more than 12 carbons with alcohols other than methanol or ethanol, even with homogeneous catalysts [16–22].

In view of all the considerations above, we decided to study the esterification reaction of long-chain fatty acids with 2-ethyl hexyl alcohol (2-EHA, 8 carbon atoms) catalyzed by solid acids. This approach will allow to get the commercially valuable esters in an efficient, sustainable and economical way [23,24]. Despite the esterification of acids can be viewed as an amortized reaction with little room for improvement, new catalysts have appeared in the last years that point towards new directions [25–30]. Solid catalysts allow to perform the esterification reaction on fixed-bed reactors, which offer numerous advantages over the batch reactors used so far. These advantages include better selectivity, productivity and eliminating catalyst separation costs. Besides, solid catalysts also enable a continuous production, better process control, easy automation and reduced operating costs [31–33]. Indeed, in-flow processes are gaining interest for the synthesis of a diversity of organic compounds [34–42].

Figure 1 shows the reactions to be studied here. Different long-chain acids will be employed, from octanoic to stearic acid, and 2-EHA was chosen as the long-chain alcohol model since the corresponding esters have excellent lubricating properties with application in different industries. The aim of the study is to design a potential industrial process, preferentially in-flow and at pilot plant scale, to manufacture the desired esters.

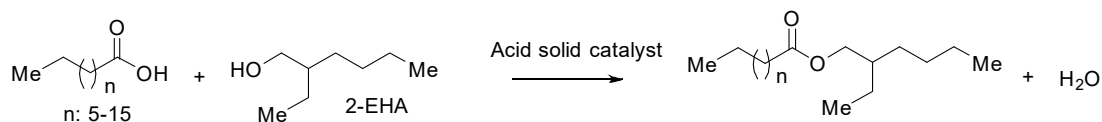


Figure 1. Esterification reactions studied here with solid catalysts.

2. Experimental.

2.1. General

Reagents and solvents were obtained from either Zschimmer & Schwarz Co. or Sigma Aldrich Co., and were used without further purification otherwise indicated. Gas chromatographic analyses were performed in a Bruker instrument equipped with a 25 m capillary column of 1% phenylmethylsilicone. GC-MS experiments were performed in a Shimadzu instrumentation with the same column and analysis conditions. ^1H and ^{13}C NMR were recorded in a Bruker 300 MHz instrument using the appropriate solvent containing TMS as an internal standard. For that, aliquots of 50 mg (i.e. coconut oil acid mixture) were dissolved in 0.6 ml of deuterated chloroform and analyzed by a 300 Mz ^1H -NMR instrument. IR spectra of the liquids were recorded on a Thermo Nicolet iS10 by impregnating the windows with a dichloromethane solution of the compound and leaving to evaporate before analysis. For that, aliquots of 50 mg were dissolved in 1 ml of dichloromethane and analyzed after leaving to evaporate the solvent. For reaction samples, the same solution of the NMR analysis was analyzed by IR. Acid value determinations were performed with KOH ethanolic solution 0.1 M with phenolphthalein as an indicator.

2.2 Synthesis of starting materials and catalysts.

PAFR synthesis. A mixture of a 2.0 M aqueous solution of *para*-phenol sulfonic acid (14.5 mL; 29.0 mmol), and 37% aqueous solution of formaldehyde (14.3 mL; 145 mmol) was stirred in a 300 mL flask with a reflux condenser at 120 °C (oil bath temperature) for 6 h under refluxing conditions. The flask was gradually cooled down to room temperature

over 12 h, to give a pale brownish gel. The obtained gel material was washed with methanol and acetone, and then was dried under reduced pressure.

Preparation of acidic solids from lignin. In a 250 ml round-bottomed flask, 10 g of lignin is dissolved in 100 ml of sulfuric acid, under continuous magnetic stirring and the mixture is heated to 150 °C for 5 h. The obtained solid is then vacuum filtered and washed with distilled water. Finally, the product is dried under vacuum or air at 100 °C for at least one night.

Drying of Amberlyst-16 on an oven. 25 grams of Amberlyst-16 are dried on a stove at 100 °C for 24 h, obtaining at the end 12 g of Amberlyst-16.

Drying of Amberlyst-16 in the reactor. The reactor is fed with 15 g of commercial Amberlyst-16 and dried with an air stream at 90 °C for 2 h. Next, about 5 g of wet Amberlyst-16 are introduced and dried following the same procedure. In the end, about 10 g of dried Amberlyst-16 already introduced into the reactor are obtained.

Preparation of the reaction mixture for aliphatic chain acids greater than 8 carbons. 10 moles of lauric acid are dissolved in 10 moles of 1-ethyl-2-hexanol at 80 °C. This mixture is used in the subsequent reaction feeding the reactor at that temperature so that the acid does not solidify again.

Coconut oil hydrolysis. 100 g of coconut oil and 100 ml KOH 1 M in ethanol were refluxed for 1 h. The mixture was extracted with *n*-hexane and concentrated to obtain the coconut fatty acid as a white solid mixed with glycerol.

2.3 Reaction procedures.

Esterification in batch. In a vial equipped with a magnetic stirrer, 4.5 mg (0.5 wt%) of catalyst was weighted. Then, octanoic acid (0.4 ml, 2.5 mmol, 1 eq), 2-ethyl-1-hexanol (0.4 ml, 2.5 mmol, 1 eq) and dodecane (0.25 ml, 1 mmol, 0.4 eq) were added. The reaction mixture was stirred at 120 °C and aliquots were periodically taken to be analyzed by GC. The product structure was assessed by combining GC, GC-MS, NMR and FT-IR measurements, and confirmed by comparison with real samples.

Scope for different alcohols and acids in batch. In a 6 ml vial equipped with a magnetic stirrer, 4.5 mg of Amberlyst-16 dry was weighted. Then, the corresponding acid (2.5 mmol, 1 eq), alcohol (2.5 mmol, 1 eq) or dialcohol (1.25 mmol, 1 eq), and dodecane (0.25 ml, 1 mmol, 0.4 eq) were added. The reaction mixture was stirred at 120 °C during the required time. The product structure was assessed by GC-MS.

Fixed-bed esterification of octanoic acid. The corresponding amount of catalyst (Amberlyst-15 or PAFR) was placed in a fixed bed tubular reactor (4.4 mm diameter), a

mixture of octanoic acid and 2-ethyl-1-hexanol (1:1.1) were passed at flow rates 0.1–1 ml·min⁻¹ and heated between 110 to 140 °C. The conversion was calculated measuring the acid and ester peaks by GC.

Fixed-bed esterification of coconut oil acid. 2 g of PAFR were placed in a fixed bed tubular reactor (4.4 mm diameter), a mixture of the acids and 2-ethyl-1-hexanol (1:2) were pre-heated in order to dissolve all the acids, and the hot mixture was passed at flow rates of 0.1–0.25 ml·min⁻¹ for the reactor with the catalyst at a temperature between 110 and 120 °C. The conversion was calculated measuring the integration of the H peaks of the CH₂ signal of the alcohol and the ester by ¹H NMR.

3 Results and discussion

3.1 Synthesis of long-chain esters *in batch*.

– Esterification reactions of octanoic acid (C₈) with 2-EHA.

Table 1 shows the catalytic results obtained for the esterification reaction of octanoic acid with 2-EHA in a 1:1 molar ratio at 120 °C, in batch, using different solid acids at 0.45 wt% respect to the reaction mixture amount. Octanoic acid is not the desirable fatty acid for many ester applications. However, it is a good starting point to check the catalytic activity of solid acids in medium-length chains. Octanoic acid is the longest alkyl chain acid still liquid at room temperature, thus easy to introduce into the tubular reactor by syringe addition. Shorter monobasic and polybasic acids often have higher esterification rates, since combined steric and soluble effects favour the esterification of shorter alkyl chain acids. Since sulfonic acids are very common soluble catalysts for esterification reactions, commercial resins having these groups (Amberslyt- and Dowex-type) were firstly tested as solid catalysts. All reactions were followed by gas chromatography (GC) during time, in order to have the initial rates for all catalysts, and the resulting ester formation was checked by gas chromatography–mass spectrometry (GC–MS). For a fair comparison, the initial rate extracted from the kinetics was related to the number of active sites (protons) in the solid catalyst, to give the initial turnover frequency (TOF₀) for each catalyst.

Table 1. Scope of catalysts and TOF₀ for the esterification reaction of octanoic acid with 2-ethyl-1-hexanol (molar ratio 1:1) at 120 °C, in batch. The reaction temperature was chosen to avoid melting of catalytic resins. Final ester yields were 50–70% in most cases (equilibrium controlled). ^a PAFR: porous phenolsulfonic acid—formaldehyde resin. ^b

N.D.: Not determined. ^c All catalytic activity comes from active species in solution, disaggregated from the solid. ^d Values taken from commercial data or calculated according to the chemical formula.

Entr y	Catalyst	Amount (wt%)	v_0 (mol/L·h ⁻¹)	Acid sites (mmol H ⁺ ·g ⁻¹) ^d	TOF ₀ (h ⁻¹)
1	None	–	8.5	-	–
2	Amberlyst–15	0.45	20.9	4.7	465
3	Amberlyst–16	0.45	14.3	4.8	298
4	Amberlyst–20	0.45	15.4	5.4	285
5	Amberlyst–36	0.45	17.8	4.7	396
6	Dowex	0.45	23.3	3.3	706
7^a	PAFR	0.45	62.0	3.2	1937
8	Nafion	4.5	28.1	0.8	351
9^b	H₂SO₄@C-not_calcinated	0.45	36.4	-	N.D.
10	H ₂ SO ₄ @C-calcinated	0.45	9.0	-	N.D.
11	Sulfonated lignin	0.45	17.4	-	N.D.
12	ZrO ₂ –SO ₃ H	0.45	8.0	4.9	163
13	SiO ₂ –Al ₂ O ₃ (Davicat)	0.45	10.9	-	N.D.
14	Montmorillonite k–10	0.45	12.4	-	N.D.
15	SiO ₂ –SO ₃ H	0.45	40.8	7.2	566
16 ^c	SiO ₂ –AlCl ₃	0.45	109.7	4.5	2438

The reaction proceeds without catalyst at some extent, with an initial rate of 8.5 mol/L·h⁻¹. However, the yield of ester product is just 22% after 24 h reaction time (Figure S1 in Supplementary Material). Different commercially available Amberlyst and Dowex acid resins were tested and the results (entries 2–6) showed good initial rates (~20 mol/L·h⁻¹) and TOF₀s (300–700 h⁻¹), with final yields ~50%. This moderate yield is due the presence of water, which starts to trigger the reverse reaction at high conversions in batch (no water removal). Previous treatments of the Amberlyst solids do not improve significantly the catalytic activity (Figure S2), and the commercial and cheaper wet forms could be used directly in reaction. In view of this, a porous phenolsulfonic acid—formaldehyde resin (PAFR) was prepared through a single synthesis step (Figure S3). This acid resin has been reported as a highly active catalyst in esterification reactions in the presence of water

[26,43]. Indeed, the PAFR material gave a catalytic activity three times higher than the commercial resins ($62 \text{ mol/L}\cdot\text{h}^{-1}$, $\text{TOF}_0 = 1937 \text{ h}^{-1}$, entry 7). In contrast, a stronger organic acid polymer such as Nafion was less effective, as favored the dehydration of the alcohol (entry 8). The commercial and widely available Amberlyst resins together with PAFR were selected for further studies in flow (see ahead). The reaction conditions (temperature and ratio) were optimized using the commercially available Amberlyst-16 (Table S1). Charcoal-based solid acids were then tested for the esterification reaction in batch. Firstly, two additional materials composed of sulfur groups supported on charcoal, which are industrially used for the removal of Hg^{2+} in water, were purchased [44]. The first charcoal material ($\text{H}_2\text{SO}_4@\text{C-not_calcinated}$) required oxidation of the sulfur groups with water peroxide or oxygen, prior to the esterification reaction, in order to generate the sulfonic groups. The second material ($\text{H}_2\text{SO}_4@\text{C-calcinated}$) does not require such oxidation treatment since, in principle, already possess oxidized sulfur groups, but not necessarily sulfonic groups. The results show that, indeed, only the $\text{H}_2\text{SO}_4@\text{C-not_calcinated}$ material was catalytically active ($36 \text{ mol/L}\cdot\text{h}^{-1}$, entries 9–10), with nearly the double catalytic activity than Amberlyst materials. In view of the good result obtained for $\text{H}_2\text{SO}_4@\text{C-not_calcinated}$, which however requires an additional synthetic step to be operative, we prepared sulfonated lignin in just one step from lignin. Sulfuric acid was recovered and used for the sulfonation step (Figure S4) [45–47]. The catalytic result of the sulfonated lignin material was similar to the Amberlyst resins ($17 \text{ mol/L}\cdot\text{h}^{-1}$, entry 11, see also Figure S1), with a smooth formation of the ester along the reaction time and without requiring any further treatment (Figure S5). Inorganic solid acids were also tested. Sulfated zirconia, commercial silica–alumina (Davicat) and montmorillonite k–10 were low active for the esterification reaction, with initial rates just slightly higher than the blank experiment (entries 12–14). Commercially available silica supported sulfonic acid groups and AlCl_3 gave superior catalytic activities (40 and $110 \text{ mol/L}\cdot\text{h}^{-1}$, respectively, entries 15–16) with TOF_0 s ~ 1000 or higher. However, a hot filtration leaching test of the AlCl_3 material revealed that all the catalytic activity came from species in solution (tentatively AlCl_3 and HCl), which in principle precludes the use of this material for the industrial process. In contrast, the PAFR and sulfonated lignin solid catalysts did not show any leaching under the reaction conditions studied, since the evolution of the reaction after catalyst filtration merely corresponds to the blank (no catalyst) rate (Figure S6).

Different alcohols were then tested in batch with octanoic acid to check if the reactivity remains the same. The esterification of octanoic acid with 2-EHA and *tert*-butanol was performed at 80 °C to avoid losses of the latter, using Amberlyst-15 or sulfonated silica as catalysts. The results (Figure S7) show that the reaction is not affected by the alcohol type because the initial velocities are almost the same. This is somewhat unexpected, because most of the previous studies use small alcohols (i.e. methanol and 1-butanol), which may infer that bigger alcohols are inefficient during the esterification reaction, not the case here. Thus, these results open the door to the use of long-alkyl chain or sterically hindered alcohols during the esterification of fatty acids, which expands the potential long-alkyl chain esters to be produced. The silica supported sulfonic acid material was discarded for further studies because of its high price, nearly 100 times higher than the commercial resins.

– Esterification reactions of lauric acid (C₁₂) with 2-EHA.

The results for the solid-catalyzed esterification of octanoic acid (C₈) with 2-EHA could be extended to lauric acid (C₁₂). Figure 2 and Table 2 show that the initial rate of catalyst H₂SO₄@C-not_calcinated for lauric acid keeps approximately three times higher than Amberlyst-16, the same relationship than octanoic acid, and with better final yields, ~90–99 %. Remarkably, both solid catalysts could be easily recovered from the solution at the end of the reaction. The recycled solid catalyst gives excellent final yields of 2-ethyl hexyl laurate (EHL) even after six uses (Table 2). Furthermore, we also tested the catalyst H₂SO₄@C-not_calcinated after activating at 200 °C during 1 week (250 h), in order to remove possible organic compounds at the surface and attach the sulfonic acid on the charcoal surface, but the results were similar to the fresh catalyst.

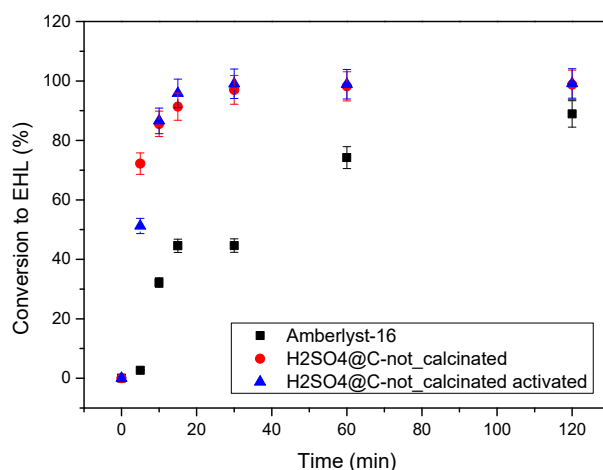


Figure 2. Kinetics for the esterification reaction of lauric acid and 2-EHA with the solid $\text{H}_2\text{SO}_4@\text{C-not_calcinated}$ and Amberlyst-16 catalysts. Error bars account for a 5% uncertainty.

Table 2. Results for the esterification reaction of lauric acid and 2-EHA [final yields of lauric ester (EHL)] after reusing the solid catalysts $\text{H}_2\text{SO}_4@\text{C-not_calcinated}$ and Amberlyst-16 up to six times.

Use	Amberlyst-16	$\text{H}_2\text{SO}_4@\text{C-not_calcinated}$, not activated	$\text{H}_2\text{SO}_4@\text{C-not_calcinated}$, activated
1	88.9%	98.7%	99.2%
2	88.6%	99.3%	94.4%
3	95.6%	99.2%	98.0%
4	—	97.2%	97.1%
5	—	95.3%	91.4%
6	—	91.0%	89.9%

Combined kinetic and elemental analysis measurements for the reused $\text{H}_2\text{SO}_4@\text{C-not_calcinated}$ catalyst showed that the initial catalytic activity decreases and that sulfonic groups are lost throughout the reuses (Figure S8 and Table S2). A good final yield is achieved anyway. In accordance with these results, a hot-filtration leaching test showed that most of the catalytic activity of charcoal-based material $\text{H}_2\text{SO}_4@\text{C-not_calcinated}$ during the esterification reaction of lauric acid with 2-EHA comes from species in solution even if the catalyst was previously activated (Figure S9). This easy loss of sulfonic groups under reaction conditions could be associated to a weak anchoring of the acid species to the charcoal surface after the oxidative activation procedure, thus the activation procedure was repeated after each use. The results (Figure S10) show that there are not improvements with this modification. Thus, the oxidation of the sulfur groups was attempted with a stronger agent such as H_2O_2 , however, the catalytic results were low again (Figure S11), probably because of the oxidation of most of the charcoal surface. With these results in hand, and in view that the $\text{H}_2\text{SO}_4@\text{C-not_calcinated}$ catalyst is decomposed with the reuses, we studied the potential higher stability of the Amberlyst catalyst [48,49]. Elemental analyses of the reused Amberlyst-16 showed that the loss of

S with the reuses is much lower, <20%, which is confirmed by the hot filtration test (after correcting with the blank experiment) and the lower loss of initial rate of the reused catalyst (Table S3 and Figure S12). Thus, with these results in hand, it seems that the resin-type polymers Amberlyst and PAFR could be more stable under in-flow reaction conditions than the charcoal-based materials and inorganic supports, despite they are intrinsically less active.

– Scope of the esterification reactions with long-chain acids and different alcohols.

As a means to extent the potential use of the Amberlyst-16 catalyst, we performed a scope of long-chain acids with different alcohols. Figure 3 shows that octanoic, lauric and oleic acids are able to form the corresponding esters with different alkyl chains alcohols in excellent yields. Long-chain acids (**3b**, **3d**) are esterified with higher conversions than medium (**3a**) and short alkyl chains (**3c**). 2-Ethylhexyl alcohol (**2a**) esterifies (**3a-3e**) with higher conversions than the linear alcohols (**3f-3k**).

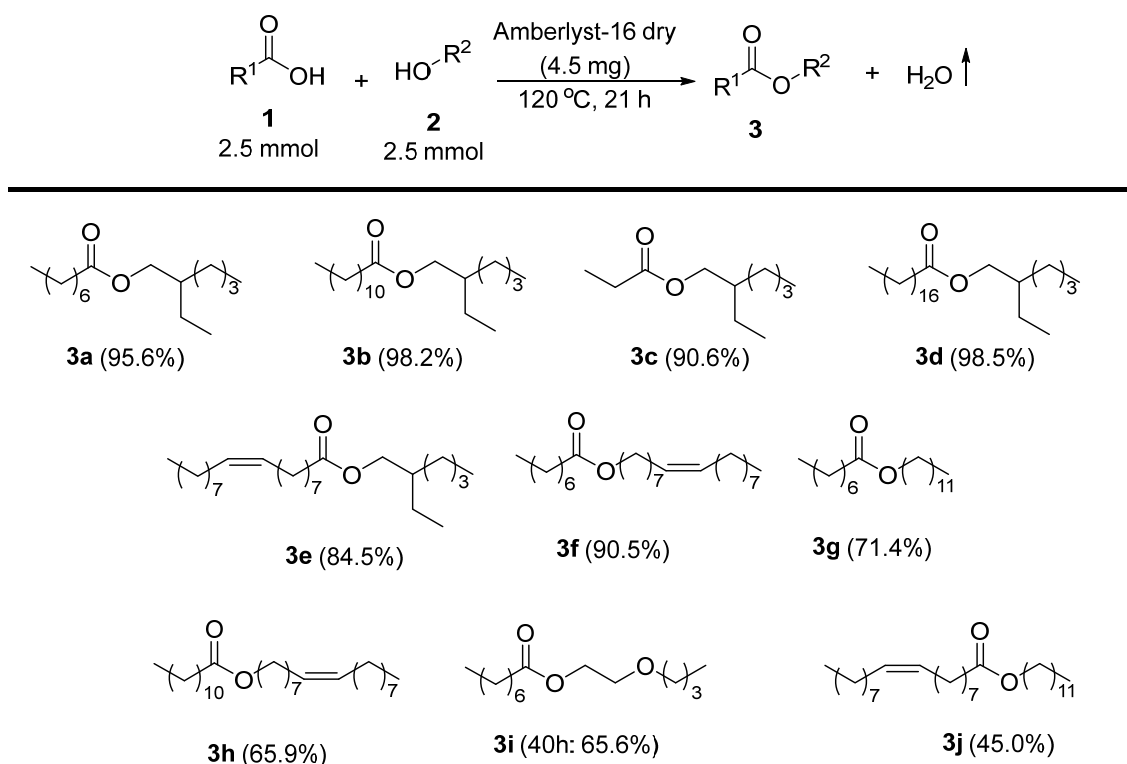


Figure 3. Scope for the esterification reaction of different long-chain acids and alcohols with Amberlyst-16. Yields were calculated by GC and the products confirmed by GC-MS.

Moreover, we were able to extend the scope to different diols using the three different acids mentioned above (Figure 4). The diesterification reactions work well, with moderated to good yields and excellent selectivity to the diesters, for linear acids (**5a**, **5b**). However, low yields are observed with oleic acid (**5c**).

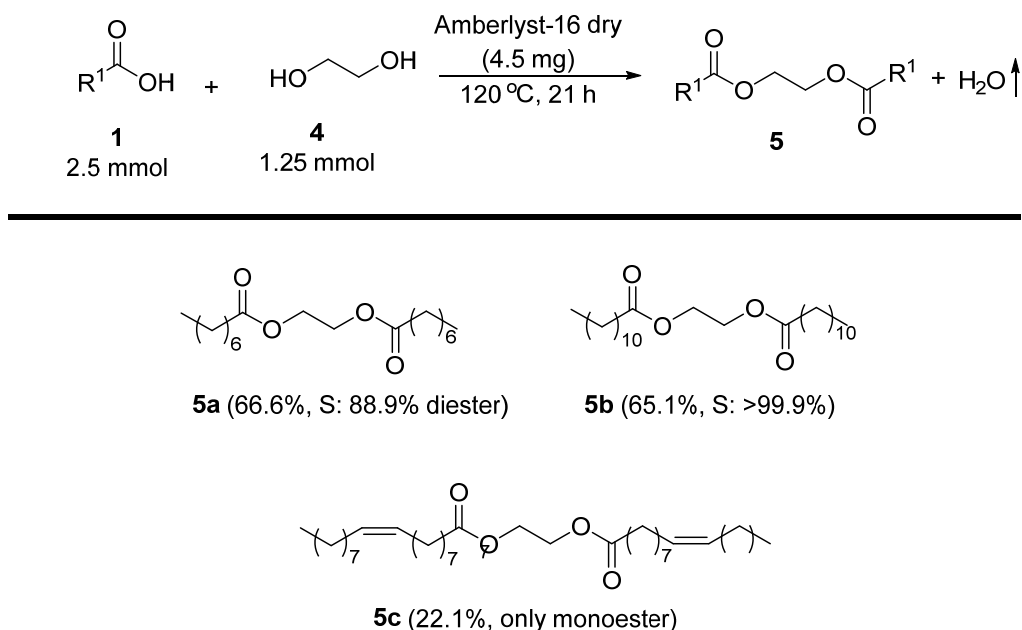


Figure 4. Scope for the esterification reaction of different long-chain acids and diols with Amberlyst-16. Yields were calculated by GC and the products confirmed by GC-MS.

3.2 Synthesis of long-chain esters *in flow* at gram scale.

– Octanoic acid (C₈)

The *in-flow* esterification of octanoic acid with 2-EHA was carried out on the basis of the previous results in batch. For that, the solid acid resins (Amberlyst-15, Amberlyst-20 or PAFR) were placed in the middle of a fixed-bed tubular reactor of 4.4 mm diameter and 250 mm length, filled with SiC and heated at the required temperature. A 1:1 mixture of octanoic acid and 2-EHA was continuously pumped through (see Figure S13 for the different set-ups).

Amberlyst-15 catalyzes the esterification of octanoic acid with 2-EHA with complete conversion and yield >95% in a flow rate of 0.15 ml·min⁻¹ at 140 °C (Table S4 for optimizing conditions and Figure S14). Higher flow rates or lower temperatures did not achieve complete conversion of octanoic acid, and 1–2 grams of the Amberlyst-15 resin were enough for the quantitative esterification reaction (see Figure S14). A systematic decrease in yield was observed with time, which could only be palliated with the addition of more 2-EHA to the reaction mixture. Amberlyst-20 achieved a 69% conversion after

optimization, however, no further conversions could be achieved due to the rapid decomposition of the resin at temperatures $>120\text{ }^{\circ}\text{C}$ (Table S5). Remarkably, and in contrast to the Amberlyst catalysts, the PAFR catalyst achieved complete conversion of octanoic acid at temperatures $<120\text{ }^{\circ}\text{C}$, in concrete $100\text{--}115\text{ }^{\circ}\text{C}$. For that, the PAFR solid was pelletized at a similar particle size than the Amberlyst resins (between 0.6 and $0.8\text{ }\mu\text{m}$) and the flow rate and reaction temperature were optimized (Figure S15). With the optimum flow rate in hand ($0.15\text{ ml}\cdot\text{min}^{-1}$), a long-time in-flow experiment was performed. Figure 5 shows that the in-flow esterification reaction could be carried out during more than one week without depletion in the yield of the octanoic ester ($90\text{--}95\%$ yield).

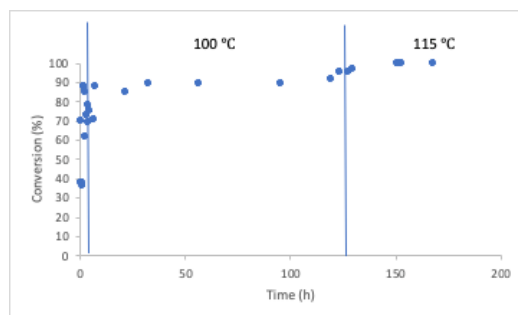


Figure 5. In-flow esterification reaction of octanoic acid with 2-EHA (1:1 molar ratio) catalyzed by the PAFR solid catalyst at a $0.15\text{ ml}\cdot\text{min}^{-1}$ flow rate during more than one week.

– Coconut oil (C_{8-18})

Octanoic acid was then replaced by coconut oil, which contains a mixture of the desired long-chain fatty acids for the esterification reaction. First, we proceed to the hydrolysis of commercially available coconut oil ester. The corresponding coconut acid mixture is apparently not commercially available, at least for academia. The hydrolysis of coconut oil ester with potassium hydroxide dissolved in ethanol at reflux conditions (Figure S16) gave a mixture of acids (from C_8 to C_{18}), which was analyzed by GC-MS and also by nuclear magnetic resonance (NMR). These analyses confirmed the similarity between the obtained fatty acid mixture and the expected for coconut oil (Figure S17). However, the low solubility of the fatty acid mixture in 2-EHA at room temperature hampered the direct pumping of the mixture to the tubular reactor, which was solved by pre-heating the mixture at $80\text{ }^{\circ}\text{C}$ and using a 1:2 molar ratio of fatty acids respect to 2-EHA. In this way, the in-flow reaction of the coconut oil with the PAFR solid catalyst could be performed.

Optimization of the flow rate showed that a flow of $0.1 \text{ ml}\cdot\text{min}^{-1}$ was sufficient to achieve full conversion of the acid mixture and complete selectivity to the desired esters (Figure S18) with PAFR as a catalyst [50]. With this flow rate, 100 grams of the desired 2-EHA ester mixture could be obtained at $115 \text{ }^\circ\text{C}$ reaction temperature using 2 grams of PAFR. Aliquots were periodically taken from the flow reaction and analyzed by GC-MS and ^1H NMR to confirm the formation of the desired ester products (Figure S19).

Amberlyst-16 (dried in the same reactor or in an oven, see experimental) was also used as a solid catalyst for the esterification reaction of the coconut oil acid mixture and 2-EHA in flow (Table S6). The results show that excellent yields of the ester mixture can be obtained with equimolecular amounts of acids and 2-EHA at a reaction temperature of $100 \text{ }^\circ\text{C}$.

– Lauric acid (C_{12})

Lauric acid was also tested since the C-12 chain provides a lower pour point, which is a highly appreciated property in the lubrication industry. Esterification of lauric acid with 2-ethyl hexanol was carried out using Amberlyst-16 as a catalyst, to give complete conversion and yield $>98\%$ at a flow rate of $0.15 \text{ ml}\cdot\text{min}^{-1}$ at $140 \text{ }^\circ\text{C}$, with an acid : alcohol ratio of 1 : 1.25. The result in batch is similar, with conversion and yield $>98\%$. Conversions were calculated using the typical titration method used in industry to measure the free fatty acid present in the reaction (acid value), shown in Equations 1 and 2. Figure 6 shows that, after a 5 h stabilization time, Amberlyst-16 catalyzes the esterification of lauric acid with 2-EHA in-flow with complete conversion ($>98\%$). Potential diffusion limitations between different fatty acids were assessed with experiments at different stirring rates. The results (Figure S20) show that Amberlyst-16 is similarly active for any fatty acid tested.

$$\text{Acid Value} \left(\frac{\text{mg KOH}}{\text{g}} \right) = \frac{(56.1 \cdot C_{\text{KOH}} \cdot V_{\text{KOH}})}{m} \quad (\text{Equation 1})$$

Where

56.1 = molecular weight of the solution for the titration ($\text{g}\cdot\text{mol}^{-1}$)

C_{KOH} = concentration of the titration KOH solution ($\text{g}\cdot\text{mol}^{-1}$)

V_{KOH} = volume of solution of KOH employed for titration (mL)

m = mass of the sample

$$\text{Conversion: } C_E = \frac{AV_0 - AV_t}{AV_0} \quad (\text{Equation 2})$$

Where

C_E = conversion to Ester

AV_0 = initial acid value ($\text{mg KOH} \cdot \text{g}^{-1}$)

AV_t = final acid value ($\text{mg KOH} \cdot \text{g}^{-1}$)

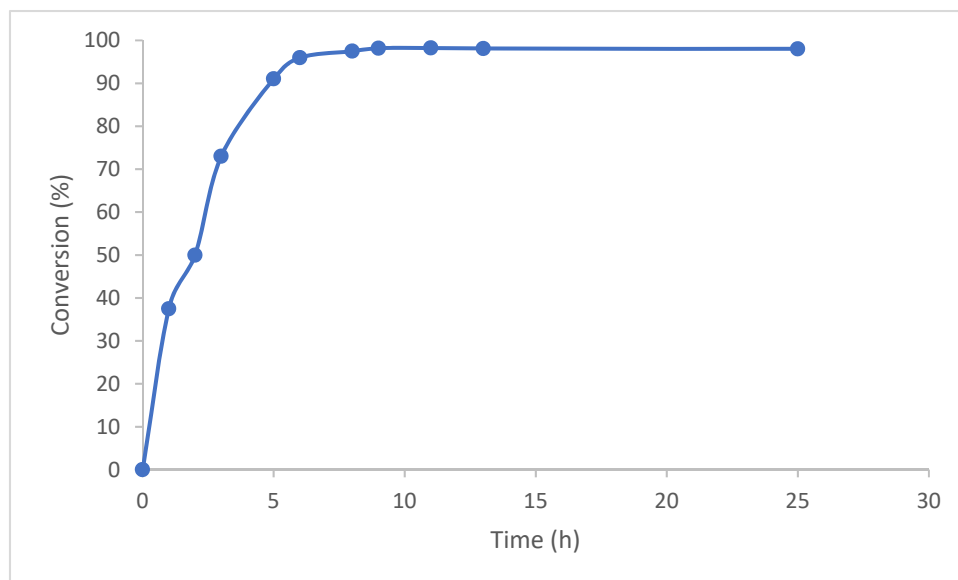


Figure 6. Results for the in-flow esterification reaction of lauric acid with 2-EHA (1 : 1.25 molar ratio) catalyzed by Amberlyst-16.

3.3 Production of long-chain esters *in flow* at multi-kilogram scale (pilot plant).

With the laboratory results in hand, we tested the in-flow esterification reaction under more realistic conditions. For that, two parallel reactors having seven tubular channels (~1 cm diameter and 3 meters long each) were run in a pilot plant, which allows to fix around 15 kg of solid catalyst. This pilot plant was designed to mix the acid and the alcohol in a first mixing tank, which is preheated to 80 °C to ensure that the reagents are perfectly mixed, then the mixture goes through a storage tank where the already homogenized and hot mixture waits to be fed from the bottom to the reactors containing the catalyst. This reaction can be done in series or in parallel. At the outlet of the reactor, once the reaction by-products, i.e. ester and water, have already been generated, the mixture is directed towards a flash reactor 1 (DF01) where the water will be eliminated, and then towards a flash reactor 2 (DF02) where the remaining alcohol will be eliminated. After carrying out this process, the product cools down and it is considered finished.

During the first tests with stearic acid, some engineering issues arose, such as cold points in the pipes, which hampered the use of stearic acid with a pour point around 60 °C. For

this reason, we chose lauric acid, with a lower pour point of 40 °C, as the fatty acid to be tested. Amberlyst-16 was used as a catalyst since kilogram amounts of PAFR could not be found by any commercial source, after extensive search. Besides, in our hands, scaling-up of the PAFR synthesis was unsatisfactory.

Table 3 shows the results after optimizing parameters such as molar ratio, temperature and feed flow. The conversion results obtained are always referred to the conversion measured at the reactor outlet, in the absence of dehydration and subsequent deodorization in the DF01 and DF02 reactor units, respectively. It was also assessed that working in parallel with the two tubular reactors is advantageous respect to working in line.

Table 3. Summary of reactions carried out at pilot plant scale.

Run	Ratio Acid : Alcohol	T (°C)	Flow (L·h ⁻¹)	Acid Value (mg KOH·g ⁻¹)	Conversion (%)
1	1:2	140	25	21.06	77.2
2	1:2	140	12	10.86	88.2
3	1:1	140	20	31.8	77.3
4	1:1	130	20	30.31	78.4
5	1:1.25	130	20	22.22	82.2
6	1:1.5	130	20	8.78	92.2
7	1:1.75	130	20	9.27	90.9

The results in Table 3 indicates the best conditions correspond to the experiment #6, with a 1:1.5 ratio acid : alcohol and a flow of 20 L·h⁻¹, at 130 °C. Under these conditions, an acid value between 6 and 10 mg KOH/g was obtained, that means a conversion around 92% at the outlet of the reactor. The reaction was easily monitored, in-situ, by FTIR. For instance, a rapid comparison between tests #1 and #2 was done, where the difference in ester yield between both reactions can be observed by the C=O band at 1680 cm⁻¹, which corresponds to the new ester. In accordance, the acid value of #2 was much lower (higher conversion) than #1. To be noticed that the amount of alcohol remaining in the sample (band 3300 cm⁻¹) is high due to the excess of alcohol present during reaction (see Figure S5 below).

In contrast with the batch reaction, we do not need to neutralize the remaining amount of acid, since we observed that, after getting rid of the water and the alcohol within the flash units DF01 and DF02, we arrived at acid value below $1 \text{ mg KOH}\cdot\text{g}^{-1}$, which is the industrial specification to go to the market. Figure 7 compares the different FTIR spectra, and the obtained ester at the end of the pilot plant reactor sample is nearly identical to the commercial ester. One additional issue found here was that, after having an acid value below $0.5 \text{ mg KOH}\cdot\text{g}^{-1}$, alcohol traces still remain in the product. The reason was a maximum temperature limitation ($158 \text{ }^\circ\text{C}$) on the steam generator when distilling the alcohol.

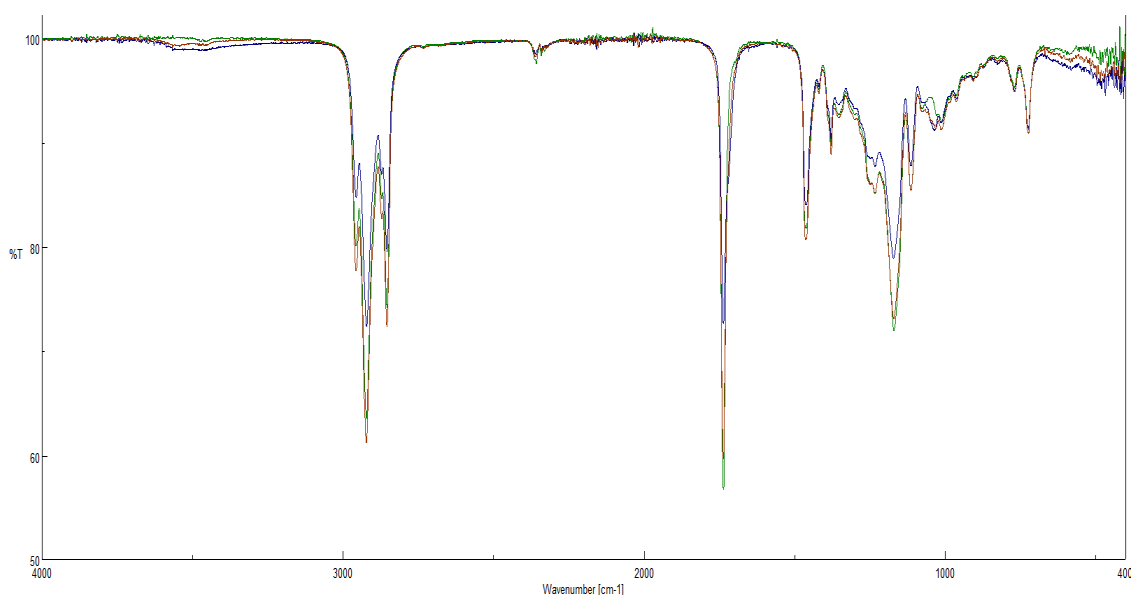


Figure 7. FTIR spectra for commercial EHL (green), sample at the outlet of the reactor (blue) and sample after distilling for 1 h (red). It can be observed that the distilled sample red is much closer to the commercial sample.

In order to determine the economic feasibility of the project an endurance catalyst test was then performed. The test consisted in performing the esterification reaction in flow as much hours as possible, with a 1 : 1.5 ratio acid : alcohol and a flow of $20 \text{ L}\cdot\text{h}^{-1}$ at $130 \text{ }^\circ\text{C}$. After 700 h (29 days), any deactivation was not detected. This result translates in a production of 11900 Kg of 2-EHL with 15 kg of catalyst. The impact of the catalyst in the raw material cost is just $0.013 \text{ €}\cdot\text{Kg}^{-1}$.

4. Conclusions.

The esterification of long-chain linear alkyl acids with 2-ethyl-1-hexanol (2-EHA) is catalyzed by simple solid acids under batch and flow conditions, obtaining the ester

products in quantitative yields. The best solid catalyst found in terms of robustness and activity is PAFR, prepared by a single synthesis step in our laboratories but not commercially available at higher scales. When pelletized to a particle size of around 700 microns, PAFR operates in-flow at 115 °C reaction temperature and between 0.1–0.2 ml·min⁻¹ rate, to give >90% yield of 2-EHA long-chain esters, running continuously for 8 days without depletion of the catalytic activity. Commercially available Amberlyst-16 can also be used as solid catalysts for the production of long-chain esters, with quantitative yields in pilot plant experiments at multi-kilogram scale. 11900 Kg of 2-EHL could be obtained with 15 kg of catalyst by working in-flow the esterification reaction for 29 days. These results open the way to manufacture long-chain esters with solid catalysts in continuous process, in order to boost the annual production of these valuable esters, with applications in many industrial fields.

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