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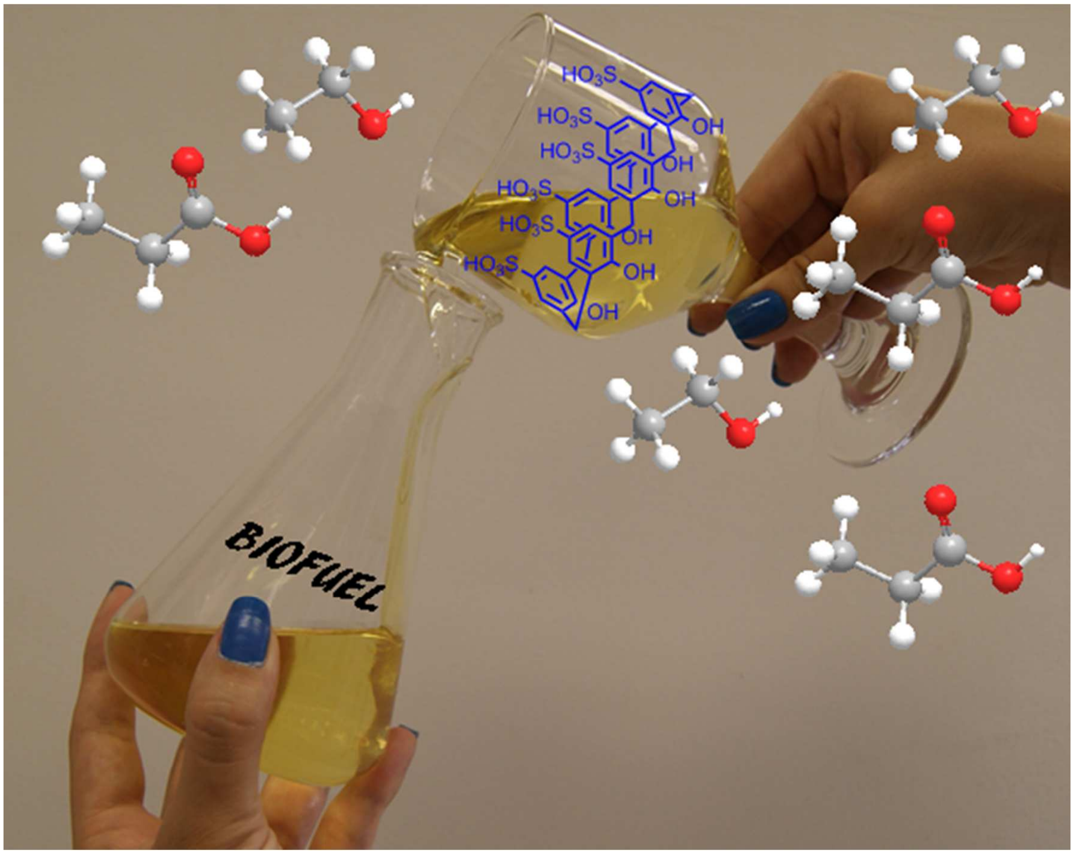

^{1}H NMR experiments showed that *p*-sulfonic acid calix[*n*]arenes were more water tolerant and active than monomeric organocatalysts in esterification reactions.

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This work reports the novel results obtained from an *in situ* kinetic study, which was conducted via ^{1}H NMR, of the palmitic acid esterification reaction with deuterated methanol in the presence of organocatalysts: *p*-sulfonic acid calix[6]arene, *p*-hydroxybenzenesulfonic acid and *p*-toluenesulfonic acid. The kinetic order of reaction relative to the catalyst concentration and the main thermodynamic properties, such as the activation energy (ΔE), entropy variation (ΔS), enthalpy variation (ΔH) and Gibbs free energy variation (ΔG), were obtained. The results indicated that the *p*-sulfonic acid calix[6]arene was the most active organocatalysts in esterification reactions, regardless of temperature or catalyst concentration employed. Additionally, by performing the reactions in the presence of increasing amounts of water, it was found that the *p*-sulfonic acid calix[*n*]arenes are more tolerant to water than the others catalysts investigated. This result, when combined with the kinetic and thermodynamic measurements, may explain their highest catalytic activity.

Introduction

Inspired by the efficiency, elegance, and selectivity of enzymatic catalysis, the design of organic molecules that are capable of efficiently promoting the formation of carbon-carbon, carbon-oxygen and carbon-nitrogen bonds has received considerable attention.[1] Compared to other types of catalysts used in organic synthesis, organocatalysts have many advantages, such as high selectivity, low toxicity, easy manipulation, and the avoidance of metal contamination in the final products. Additionally, organocatalysis commonly occurs under mild reaction conditions, allowing for the recovery and reuse of the organocatalyst, which constitutes another excellent advantage.[2]

Currently, various organocatalysts have been designed and proposed. Among them, the calix[*n*]arenes remain an interesting but under-explored alternative. Calix[*n*]arenes are macrocyclic compounds composed of phenolic units that are linked by methylene groups at the 2- and 6-positions with defined upper and lower rims and a central annulus. The simplicity of modifying these structures makes the calix[*n*]arenes versatile compounds with a broad number of applications.[3-6] In the late 1980s, the potential of calix[*n*]arenes as enzyme mimics was first highlighted in the pioneering work of Gutsche.[7] However, their use in organocatalysis has still being a great challenge to the organic chemistry.[8-10]

Esters syntheses are quite important to the chemical industry. Numerous esters and their derivatives are involved in the synthesis of polymers, perfumes, pharmaceuticals and biodiesel.[11-13] Because of the higher costs of production compared to the petroleum-based diesel, biodiesel production beginning from inedible and inexpensive raw materials has become economically attractive. These feedstocks are rich in free fatty acids (FFA), and their esterification reactions have been frequently performed using non-recyclable and highly corrosive homogeneous catalysts, which require neutralization steps at the end of their reactions and generate significant quantities of waste effluents and residues. Solid acid catalysts, which are based on Lewis acid metals, are an environmentally benign option. However, eventual catalyst leaching can cause the contamination of esters with the metal catalyst and promote undesirable reactions throughout the use of the biofuel.[14-17] The use of organocatalysts, such as sulfonic acid derivatives, can minimize these drawbacks.

In a previous report, we found that *p*-sulfonic acid calix[4]arene and *p*-sulfonic acid calix[6]arene catalysts demonstrated the most effective esterification processes for several carboxylic acids with ethanol, compared to the other catalysts investigate.[18] Further, we determined the activation energy and the thermodynamic and kinetic properties for the esterification of palmitic acid with deuterated methanol in presence of the *p*-sulfonic acid calix[4]arene.[19]

In the present work, we investigated the catalytic activity of *p*-sulfonic acid calix[6]arene (**I**) for esterification reactions in comparison with its monomer *p*-hydroxybenzenesulfonic acid (**II**) and *p*-toluenesulfonic acid (**III**) (Fig. 1). ^{1}H NMR spectroscopy *in situ* was used to obtain these novel results about the kinetic and thermodynamic properties of the organocatalysts. In addition, the water tolerance of these organocatalysts was assessed.

Combined with previous results, the data obtained in this disclosure allowed an accurate discussion about the activities of these organocatalysts in esterification reactions.

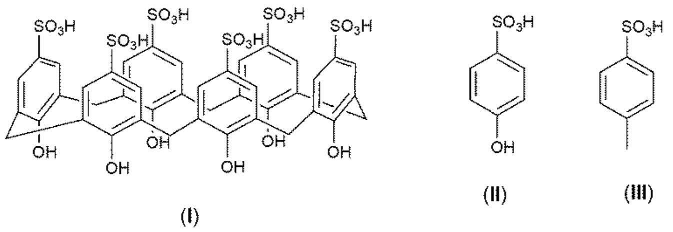

Fig. 1 Structures of the organocatalysts *p*-sulfonic acid calix[6]arene (**I**), *p*-hydroxybenzenesulfonic acid (**II**) and *p*-toluenesulfonic acid (**III**).

Experimental

Chemicals

Palmitic acid (95%) was purchased from General Purpose Reagent and used as a model substrate because it is a fatty acid in present in several raw materials for biodiesel. Deuterated methanol (99.75%), *p*-toluenesulfonic acid (99%) and *p*-hydroxybenzenesulfonic acid (99%) were purchased from Sigma-Aldrich. The *p*-sulfonic acid calix[6]arene and *p*-sulfonic acid calix[4]arene organocatalyst were prepared according to known procedures.[7,20]

Kinetic studies

All organocatalysts were used with the same hydrogenionic concentration and equal molar ratio in relation to palmitic acid (i.e., palmitic acid:H+ molar ratio = 800:1), considering the number of sulfonic acid sites of each catalyst. Because *p*-sulfonic acid calix[6]arene have six sulfonic groups, its molar concentration was six times lower than the other catalysts, which have only one sulfonic group. Generally, the organocatalysts' concentration varied within the range of 0.5 to 2.5 mol% with respect to the number of sulfonic groups. In a typical reaction, the organocatalyst was dissolved in NMR tubes containing CD_3OD (0.6 mL), and heated to the desired temperature (ca. 313-333 K). After adding the palmitic acid (0.08 mmol), the reaction was started. Kinetic data were obtained from ^1H NMR spectra acquired every 5 minutes (Mercury-300 Varian Spectrometer), and the spectra were processed using the Varian software. The operational frequency was 300.069 MHz for ^1H (64 k data points, 30º excitation pulse duration of 2.2 µs, spectral width of 6 kHz, acquisition time of 3.3 s and relaxation delay of 10 ms) in a 5-mm probe with direct detection.

Reaction monitoring

The reaction conversions were followed by analyzing the resonance signal intensity (triplet) of the methylenic groups neighbouring the carbonyl group of the palmitic acid and methyl palmitate throughout the esterification reactions.[18] Frequently, the methylenic group neighbouring to carbonyl group of the acid or ester exhibited ^1H NMR signals in the chemical shift (δ) range of 2.2-2.4 ppm. The intensity of the two signals to the right of each triplet in the ^1H NMR spectra were obtained throughout the reactions, providing feasible data for quantifying reaction conversion.

Effect of water on the activity of sulfonic organocatalysts in palmitic acid esterification reactions with methanol

To investigate the effects of water on the activity of organocatalysts, experiments were performed by dissolving palmitic acid (0.4 mmol L^{-1}) and the organocatalysts in methanol (20 mL) that contained increasing amounts of water (0 to 0.4 mmol L^{-1}). This effect was also investigated for *p*-sulfonic acid calix[4]arene and sulfuric acid. The catalyst concentration was 2.5 mol% for the *p*-hydroxybenzenesulfonic acid (**II**) and *p*-toluenesulfonic acid (**III**), 2.5 mol%/6 for *p*-sulfonic acid calix[6]arene (**I**), 2.5 mol%/6 for *p*-sulfonic acid calix[4]arene, and 2.5 mol%/4 for sulfuric acid, considering the number of acidic hydrogen of the sulfonic acid sites of each catalyst. After heating the solutions at 333 K for 30 minutes, the solvent was evaporated under vacuum, and the remaining mixtures were dissolved in $CDCl_3$ for analysis by ^1H NMR spectroscopy.

Results and discussion

Effect of the catalysts concentration on organocatalysed-palmitic acid esterification reactions with deuterated methanol

The measured kinetics were obtained *in situ* ^1H NMR spectroscopy, which is a proven and efficient technique to accurately acquire kinetic and thermodynamic data for organocatalysts.[19,21] To control the accuracy of the kinetic data, the reaction rate dependence on the substrate concentration must be pseudo-zero order. Consequently, although the reactions were conducted for a long time period (ca. 8 hours), only the kinetic measurements obtained during the first twenty minutes were used to determine the kinetic order relative to the catalyst concentration. Additionally, the use of a large excess deuterated methanol allows us to assume that only the palmitic acid concentration varied during the beginning of each run.

The effectiveness of the sulfonic acid organocatalysts (**I-III**) was investigated at the concentrations ranging from 0.5 to 2.5 mol% (Fig. 2), but because equilibrium was not reached, different conversions were observed. Regardless of the organocatalyst employed, the highest concentration (i.e., 2.5 mol%) resulted in the largest palmitic acid conversion into deuterated methyl palmitate (ca. 97%, 66% and 29%; catalysts **I-III**, respectively).

The kinetic curves displayed in Fig. 2 also reveal that the *p*-sulfonic acid calix[6]arene catalyst (**I**) was much more effective than the sulfonic catalysts **II** and **III**. For catalyst **I**, the reactions performed at the two higher catalyst concentrations reached the highest initial reaction rates, and complete conversion was obtained within 2-3 hours. Conversely, catalysts **II** and **III** led to lower conversions, but the conversion halted sooner than the reactions using **I**. Catalysts **II** and **III** also exhibited completely distinct behavior from one another. When examining the two highest concentrations tested during the initial reaction period, the initial reaction rates for the *p*-hydroxybenzenesulfonic acid catalyst (**II**) were as high as those obtained for *p*-sulfonic acid calix[6]arene (**I**), but *p*-toluenesulfonic acid (**III**) demonstrated a much lower initial rate.

After determining the initial reaction rates (Fig. 2), it was possible to determine the reaction order related to each sulfonic catalyst. The initial reaction rates were calculated in units of mmol palmitic acid consumed / ca. 1200 seconds. Because measurements were taken at the initial period of reaction, it can be assumed that the contribution of the inverse reaction is negligible. Thus, by applying a non-elementary kinetic model[21], the reaction rate is given by equation 1, where *x*, *y* and *n* are the orders in relation to the corresponding components.

$$reaction\ rate = k\,[A]^x[B]^y[cat]^n \qquad (eq.\ 1)$$

Because measurements are taken when only the catalyst concentration varies (i.e., $[A]^x[B]^y = k'$), equation 1 can be written as:

$$reaction\ rate = k'[cat]^n \qquad (eq.\ 2)$$

which can be linearized to afford equation 3:

$$ln\ rate = ln\ k' + n\ ln\ [cat] \qquad (eq.\ 3)$$

By performing several experiments using different catalyst concentration, different reaction rates were obtained, thus making possible to build a linear plot of ln (reaction rate) versus ln (catalyst concentration). Finally, the order of reaction with respect to the catalyst concentration was obtained from the slope of the curve.[21]

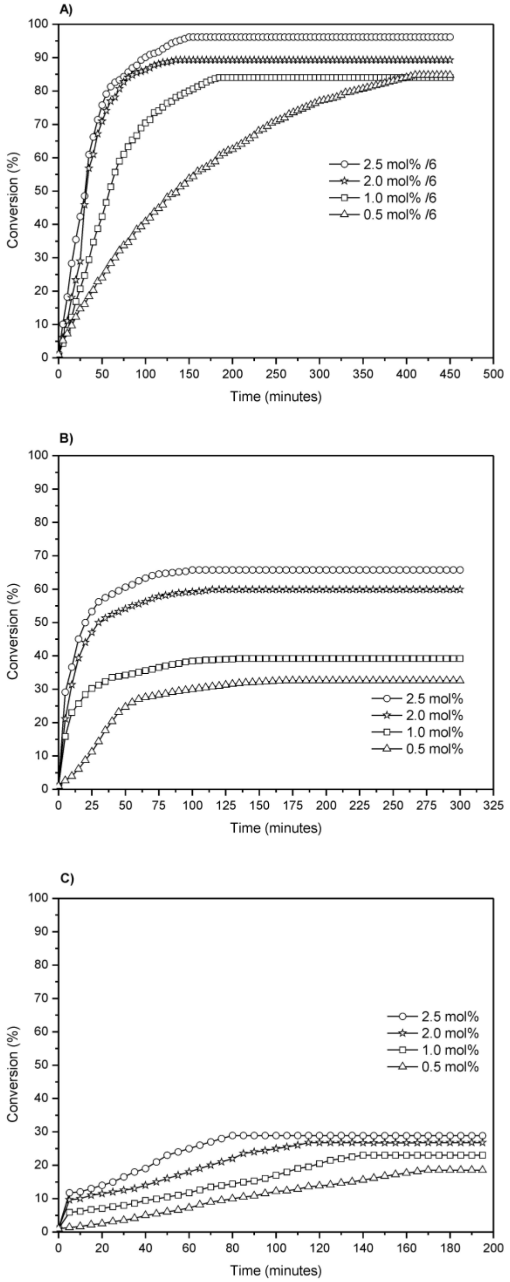

Fig. 2. Effects of increasing the organocatalyst concentration during the palmitic acid esterification using deuterated methanol at 323 K. A) *p*-sulfonic acid calix[6]arene (**I**); B) *p*-hydroxybenzenesunfonic acid (**II**) and C) *p*-toluenesulfonic acid (**III**).

The linear plots to the catalytic reactions studied in the present paper are presented in supplementary material (Fig. S1). The kinetic order of reaction relative to the organocatalyst concentrations were equal to 0.6 for *p*-sulfonic acid calix[6]arene (**I**) ($R^2 = 0.993$), 0.4 ($R^2 = 0.994$) for *p*-hydroxybenzenesulfonic acid (**II**) and 0.7 ($R^2 = 0.992$) for *p*-toluenesulfonic acid catalysts (**III**). The high R^2 values confirmed the linearity of the curves.

The esterification reactions are reversible processes in which the overall conversion should be determined by equilibrium, which is independent of the catalyst used. However, the reaction rates are certainly dependent upon which catalyst was employed. The first step in an esterification reaction is the protonation of the carbonyl group of the carboxylic acid by a H^+ ion coming from the catalyst.[22] In general, in the Brønsted acid-catalysed reactions, the acidic strength of the catalyst should be the main factor responsible for the catalyst's higher or lower activity.[23]

In aqueous solution, all of the sulfonic acid groups on the organocatalysts are completely dissociated.[24,25] Despite the scarcity of data concerning the acidic strength of calix[*n*]arenes in organic solvents, considering that the pKa values of water and methanol are very close (15.6 and 15.7, respectively),[26] it is reasonable to suppose that a similar levelling effect may also occur in methanol. Furthermore, because the pKa values of H_3O^+ and $CH_3OH_2^+$ are -1.74 and -2.5, respectively, the carbonyl group of palmitic acid should be equally protonated in both water and methanol. Consequently, if the catalyst's acidic strength is the only driving force in these reactions, all of the catalysts' activity should be equal because they were used at the same hydrogenionic concentration, regarding the number of sulfonic acid sites of each catalyst. However, this result was not observed.

Another possible explanation for the higher catalytic activity of *p*-sulfonic acid calix[*n*]arenes when compared to the monomeric organocatalysts could be the number of catalytic sites per molecule. Zhao and co-workers[27,28] demonstrated that the activity of prolinamide-type catalysts in aldol reactions can be efficiently improved by introducing additional reaction centers into the catalyst molecule. As argued by the authors, a higher number of catalytic centers per structure may increase the chances of meeting between the substrated and a reaction center, thus leading to higher reactivity.[27,28] However, the percentage of conversion obtained by using *p*-sulfonic acid calix[4]arene[18] and *p*-sulfonic acid calix[6]arene were very similar (c.a. 99 and 97 %, respectively), despite the different number of reaction sites in each catalyst. Therefore, other aspects must also be considered.

Effect of water on the activity of organocatalysts I and II

Using the highest catalyst concentration (i.e., 2.5 mol%), a comparison of the initial rates obtained during the first twenty minutes of the reactions (Fig. 2) reveals that the rate observed in the presence of catalyst **II** is very similar to the rates measured in the presence of *p*-sulfonic acid calix[6]arene **I**. Nevertheless, the activity of catalyst **II** decreases dramatically after the first hour of reaction and remains constant afterward.

We propose that the water generated within the reaction medium during the esterification reaction could be shifting the equilibrium at different extents. For the organic catalysts, a stronger interaction between the sulfonic acid group of catalyst **II** and the water molecules generated during reaction might lead to the partial deactivation of their active sites by hindering the access of palmitic acid molecules to the sulfonic sites. These interactions are less pronounced for catalyst **I** because the hydrophobicity of their cavity diminishes the extent of the solvation of their sulfonic sites. Such negative influence of water molecules generated in the reaction medium on the catalytic activity of sulfonic acid sites has been reported for etherification reactions.[29] In that work, the authors found that the higher the hydrophobicity nature of the catalyst, the lower the deactivation of the catalytic sulfonic sites.

According to the previous works,[30,31] the presence of electron-withdrawing substituent in the *para*-position relative to the phenolic unit led to a decrease in the pK_a value for the first ionization of hydroxyl groups (pK_{a1}) of *p*-substituted calix[*n*]arenes, with the resulting monoanion being strongly stabilized by a chain of intramolecular hydrogen bonds between its hydroxyl groups. As showed by Shinkai *et al.*,[32] the same effect is observed for sodium *p*-sulfonate calix[4]arene salt relative to that of the corresponding noncyclic monomer. These authors also found that the methylene hydrogens of the oxy-anions formed by the dissociation of the hydroxyl groups of *p*-sulfonate calix[4]arene give a pair of doublets in the NMR spectrum, which is due to a more rigid conic conformation resulted from the strong intramolecular hydrogen bonding.

Differently, at low pH values, the same methylene hydrogens appear as a singlet in the NMR spectrum, evidencing that a more flexible conformation is adopted by the undissociated calixarene.[32] In the ^{1}H NMR spectrum of *p*-sulfonic acid calix[6]arene (**I**), the methylene hydrogens also appear as a singlet at 3.83 ppm, thus suggesting that the calixarenes' hydroxyls are in the undissociated form. Consequently, its hydroxyl groups can be more available to form hydrogen bonds with the molecules of water released during the esterification, diminishing the extent of solvation of the calix[*n*]arenes' sulfonic sites. Thus, because the sulfonic acid groups of *p*-sulfonic acid calix[6]arene (**I**) are more available, the palmitic acid can be more efficiently protonated near the calix[*n*]arene, making this catalyst less vulnerable to the water released throughout the esterification reaction.

To validate this hypothesis, experiments were performed with the two most active catalysts (**I** and **II**) by adding known amounts of water to the solutions at the beginning of each reaction. Reactions were carried out at 333 K for 30 minutes.

Due to the high catalytic activity of sulfuric acid and *p*-sulfonic acid calix[4]arene observed in our previous work,[18] these catalysts were also included in this study. The results of these experiments are summarized in Fig. 3. Because the reactions were performed with 0.4 mmol L^{-1} of palmitic acid, the maximum amount of water added was equimolar to the palmitic acid.

These results clearly demonstrate that although activity of the three organocatalysts was affected by the increasing amount of water, this effect was much more pronounced during the *p*-hydroxybenzenesulfonic acid-catalysed esterification reactions (i.e., catalyst **II**, Fig. 3), which is consistent with the hypothesis that releasing water during esterification results in a progressive deactivation of organocatalyst **II**. For the organocatalysts *p*-sulfonic acid calix[6]arene (**I**) and *p*-sulfonic acid calix[4]arene, as well as for sulfuric acid, this effect was much less pronounced (Fig. 3), with *p*-sulfonic acid calix[4]arene showing the highest conversion for all amount of water added.

Deactivation of the monomeric catalysts by water can also explain the poor efficiency of *p*-toluenesulfonic acid (Fig. 2), despite the highest kinetic order obtained for this catalyst (Fig. S1). Kinetic order was obtained during the first twenty minutes of reaction and indicates the dependence of the reaction rate in relation to the catalyst concentration. Despite the higher value obtained for *p*-toluenesulfonic acid, its catalytic activity was the most affected by water released throughout the esterification reaction, thus making this catalyst the less effective.

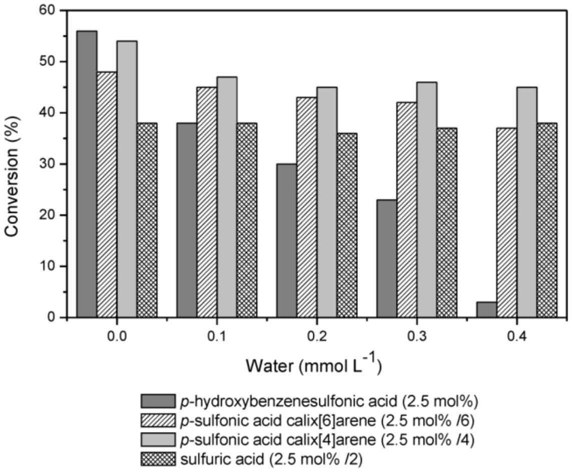

Fig. 3 Effects of increasing the amount of water initially added on the activities of organocatalysts *p*-sulfonic acid calix[6]arene (**I**) and *p*-hydroxybenzenesulfonic acid (**II**), *p*-sulfonic acid calix[4]arene and sulfuric acid.

Kinetic study of the sulfonic acid-catalysed palmitic acid esterification reactions with deuterated methanol

Through *in situ* ^{1}H NMR spectroscopy, kinetic curves were obtained for organocatalysts **I** and **II** (ca. 0.5 mol%) at different temperatures (Fig. 4). Due to its lower activity, catalyst **III** was excluded from this study.

In the *p*-hydroxybenzenesulfonic acid (**II**) catalysed-reactions, the conversion reached its maximum after 2-3 hours of reaction and afterward remained almost constant due to the deactivation of catalyst. Notably, *p*-sulfonic acid calix[6]arene (**I**) remained active after eight hours of reaction, affording higher conversions at all studied temperatures (Fig. 4). Table 1 summarizes the effects of temperature on the turnover number (TON) and turnover frequency (TOF) of the sulfonic acid organocatalysts. The TON was calculated by accounting for the time required for substrate conversion to become constant (8 hours was the period selected). However, only the first 60 minutes were considered for TOF calculations.

As can be observed, the highest values for TON and TOF were achieved with *p*-sulfonic acid calix[6]arene organocatalyst (**I**). However, at the lowest temperatures (ca. 313 and 318 K), the *p*-hydroxybenzenesulfonic acid catalyst (**II**) displayed a higher TOF value than that calculated for the *p*-sulfonic acid calix[6]arene catalyst (**I**).

The first-order dependence on the palmitic acid concentration was confirmed by plotting ln [palmitic acid] $_{t = ti}$ / ln [palmitic acid] $_{t = t0}$ versus time for each reaction performed at different temperatures. The resulting linear equations exhibited high linear correlation coefficients for all of the organocatalysed-reactions (no shown herein by simplification), a result that agrees with the data described in the literature.[19,21]

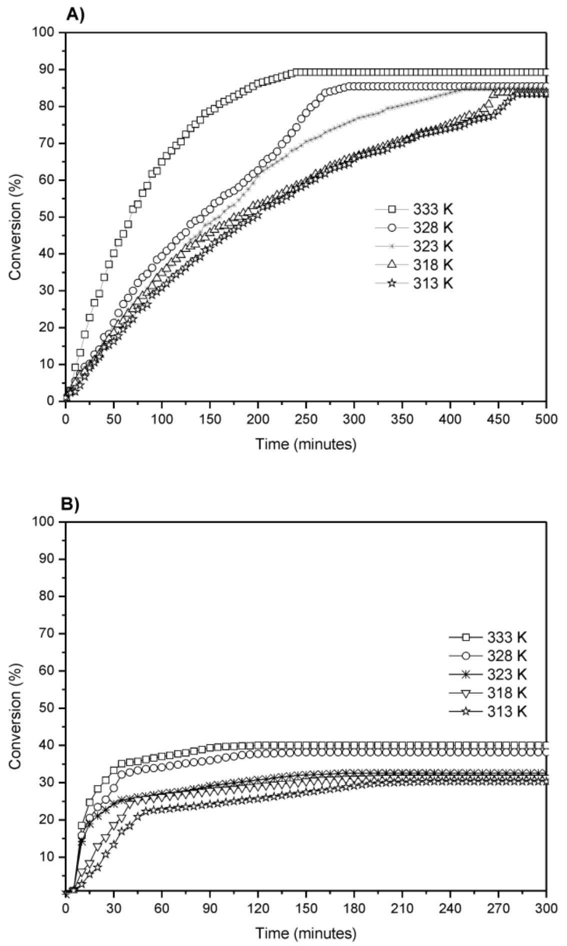

Fig. 4 Kinetic curves. A) *p*-sulfonic acid calix[6]arene (**I**) and B) *p*-hydroxybenzenesulfonic acid (**II**).

Table 1 Effect of the temperature increase on the TON and TOF measured during the esterification reactions in presence of sulfonic acid organocatalysts[a].

Temp. (K)	*p*-sulfonic acid calix[6]arene (**I**)		*p*-hydroxybenzenesulfonic acid (**II**)	
	TON[b]	TOF[c] (x 10^{-2} s^{-1})	TON[b]	TOF[c] (x 10^{-2} s^{-1})
313	672	4.0	232	5.1
318	678	4.2	248	5.8
323	686	5.8	256	6.0
328	688	6.7	304	7.3
333	720	8.7	320	8.0

[a]All catalysts were used at the same hydrogenionic concentration (molar ratio of fatty acid:H^+ equal to 800:1); palmitic acid (0.08 mmol). [b]TON (turnover number) = n mmol FA converted (480 min) /n mmol H^+ catalyst. [c]TOF (turnover frequency) = n mmol FA converted (60 min)/n mmol H^+ catalyst/3600 s.

Therefore, when considering that the dependence in relation to the CD_3OD concentration is pseudo-zero-order (because it was used in excess), the pseudo-first-order rate law can then be used to calculate the rate constant (k):

$ln\ k = ln\ A – (E/R).\ (1/T)$ (eq. 4)

The angular coefficient (-E/R) obtained from the kinetic curves provides the apparent activation energy values (ΔE). Arrhenius plots of the palmitic acid esterification reactions with deuterated methanol to at temperatures ranging of ca. 313 to 333 K for catalysts **I** and **II** are presented in supplementary material (Fig. S2).

The activation energy values of the palmitic acid esterification reactions with CD_3OD in the presence of sulfonic catalysts **I** and **II** were found to be 40.4 KJ mol^{-1}, and 64.7 KJ mol^{-1}, respectively. Values very close to these have been reported in the literature for other Brønsted acid catalysts.[26] The highest activation energy value of reactions catalysed by *p*-hydroxybenzenesulfonic acid (**II**) is in agreement with the experimental observation, that its initial reaction rates were lower than those of *p*-sulfonic acid calix[6]arene (**I**).

Thermodynamic study of the sulfonic acid catalysed-palmitic acid esterification reaction with deuterated methanol

Catalyst **III** was excluded from this section because its reactions did not reach equilibrium within studied period. In accordance with previous assumptions, the equilibrium constant (K_{eq}) of reaction studied is defined by equation 5:

K_{eq} = *[deuterated methyl palmitate]*^{2}*/ [palmitic acid]* *(eq. 5)*

The initial concentration of palmitic acid was 0.133 mol L^{-1}. From equation 5, the K_{eq} values for each reaction at different temperatures were calculated. The Van't Hoff Equation (equation 6) is valid if the enthalpy variation within the reaction is assumed to be constant with temperature.

$ln\ K_{eq} = (ΔS/R)\ – (ΔH/R)\ x\ (1/T)$ (eq. 6)

Variations in the Gibbs free energy at each temperature may be obtained using the second law of thermodynamics (ΔG = - RT ln K_{eq}). From the calculated data after linearization of equation 6, plots of ln K_{eq} versus 1/T were constructed and are displayed in supplemental file (Fig. S3).

The values of ΔS and ΔH for the acid-catalysed palmitic acid esterification were graphically determined. The slope of the curve plus RT furnishes the ΔH, and the y axis intercept provides the value for ΔS. Table 2 presents these values and the Gibbs free energy obtained for each reaction at specific reaction temperatures in the presence of the sulfonic acid-derived catalysts **I** and **II**.

Table 2 Values of ΔG, ΔH and ΔS for the palmitic acid esterification reactions in the presence of organocatalyst (**I**).

Temp. (K)	ΔG (KJ mol^{-1})	ΔH (KJ mol^{-1})	ΔS (J mol^{-1})
p-sulfonic acid calix[6]arene catalyst (**I**)			
313	-1.34	+11.18	+0.04
318	-1.54		
323	-1.74		
328	-1.94		
333	-2.14		

These results reveal that an increase in temperature affected the spontaneous characteristics of these reactions, which was denoted by a variation in the Gibbs free energy. As expected, all of enthalpy variation values were positive and lower than the activation energy values, reinforcing the endothermic nature of these reactions. The endothermic character of these reactions explained the increase in the ΔG values (in absolute value), which was triggered by increasing the temperature.

Conclusions

Kinetic and thermodynamic studies of palmitic acid esterification reactions with CD_3OD were performed using *in situ* ^1H NMR spectroscopy in the presence of organocatalysts. The activation energy, entropy variation, enthalpy variation and Gibbs free energy variation were successfully determined for systems involving *p*-sulfonic acid calix[6]arene (**I**). Although the catalysts were used in equal hydrogenionic concentrations, noticeable differences were found when comparing the obtained results. Under the conditions studied, *p*-sulfonic acid calix[6]arene (**I**) proved to be the most active catalyst, regardless of the temperature or concentration employed. The higher efficiency of the *p*-sulfonic acid calix[*n*]arenes organocatalyst, compared to *p*-hydroxybenzenesulfonic acid and *p*-toluenesulfonic acid, can be attributed the higher tolerance of the *p*-sulfonic acid calix[6]arene catalyst to the water formed during the esterification reaction.

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Notes and references

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