PAPER

NJC
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Design of well balanced hydrophilic–lipophilic catalytic surfaces for the direct and selective monoesterification of various polyols†

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Received (in Montpellier, France) 9th December 2004, Accepted 5th April 2005
First published as an Advance Article on the web 20th May 2005

The transesterification process is a well known reaction of organic chemistry. However, the monoesterification of unprotected polyols such as glycerol or sucrose is much more complex and the design of selective catalysts is becoming a huge challenge in order to avoid many protection and deprotection steps, harmful for the cost and the environmental impact of the resulting process. In this study, we showed that the control of the hydrophilic–lipophilic balance of heterogeneous catalysts is a crucial key in order to tune both the catalyst activity and the monoester selectivity. Indeed, whereas homogeneous guanidine led to low selectivity toward monoesters, its anchorage on a hydrophilic solid support such as silica allowed us to prepare two basic hybrid organic–inorganic materials able to selectively afford monoesters in high yield and in an environmentally-friendly process, at low temperature and starting from an equimolecular mixture of unprotected polyols and various fatty methyl esters.

Introduction

Due to the exhaustion of the earth petroleum oil reserves and the excessive production of greenhouse gases, intensive efforts over the last decade were directed towards the chemical potentialities of agroresources.[1] However, molecules extracted from biomass are often polyfunctionalized and the design of selective catalysts is becoming a tremendous challenge in order to avoid many protection and deprotection steps harmful for the cost and the environmental impact of the process.[2]

Glycerol is industrially available in large scale from the hydrolysis or methanolysis of vegetable oils and its use as raw starting material is of great interest for the industrial development of triglycerides (biofuels, biolubricants, cosmetics...).[3] The glycerol transformation into fatty monoesters is one of the viable solutions since monoglycerides find significant applications as safe and biodegradable emulsifiers in industry.[3]

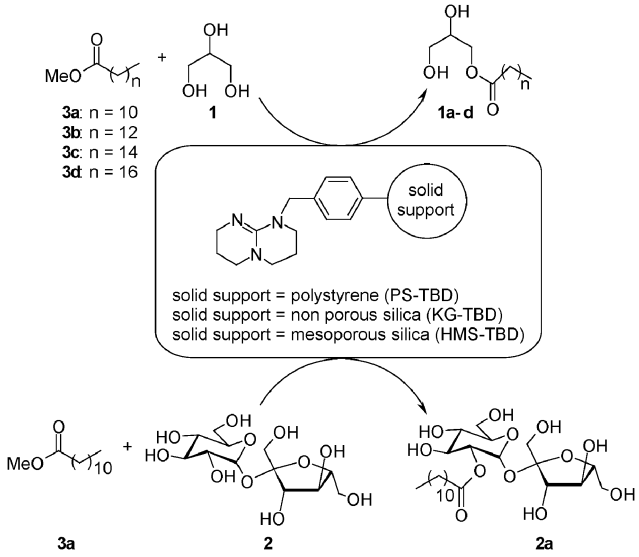
In the literature, monoglycerides are synthesized either by reaction of glycerol with fatty acids[4] or fatty methyl esters[5] and by glycerolysis of vegetable oils.[6] Hydroxide or carbonate anions and *p*-toluenesulfonic acid are the most commonly used homogeneous catalysts.[7] However, these catalysts lead to the formation of monoesters in a limited purity due to the important side production of di- and triglycerides and soap.[7] Moreover, at the end of the reaction, acidification of the reaction mixture affords salts, making the purification work-up difficult. Heterogeneous catalysts offer many advantages like easy separation from the reaction products and recycling. Acidic anion exchange resins,[4a] mesoporous materials functionalized with sulfonic groups[4b,f–h] and zeolithes[4d,e] are among the most efficient catalysts for the esterification of glycerol with fatty acids. These catalysts afforded, at 110 °C and under solvent free conditions, glycerol esters in more than 90% yield but with a poor monoglyceride selectivity of 40% which rapidly dropped to 20% at total conversion.[4] Monoglyceride selectivities higher than 90% were only obtained for conversions lower than 20% mainly because, beyond 110 °C, the fatty acid was able to autocatalyze the reaction.[4c] Indeed, at 110 °C but without catalyst, glycerol esters were produced, after 16 hours, in more than 30% yield and with a monoglyceride selectivity higher than 47% making difficult the development of a highly selective process. Up to now, only methods involving enzymes were able to quantitatively produce glycerol esters with a monoglyceride selectivity higher than 95% since enzymes were able to catalyze the reaction at room temperature avoiding the autocatalysis of the reaction by the fatty acids.[8] However, this chemical route requires a large excess of glycerol, five fold excess, and a high dilution of the fatty acids (0.1 M) to limit the production of di- and triglycerides.

In order to avoid the autocatalysis of the reaction, our group extensively studied the monoglyceride production through a transesterification process between glycerol and various fatty methyl esters.[5] Metal oxides such as MgO, La_2O_3[5b] and Mg-AlMCM-41[5c] were mainly investigated. As expected these solid catalysts led, at 80% conversion, to higher monoglyceride selectivities (55%) than those previously obtained. However, due to the greater lipophilicity of the fatty methyl esters compared to that of fatty acids, these catalytic processes require high temperature (220 °C) or the use of a solvent in order to allow a better interaction between glycerol and fatty methyl esters.

In an earlier paper, we reported that polystyrene bearing guanidine groups as strongly basic catalytic sites (PS-TBD with TBD = triazabicyclo[4.4.0.]dec-5-ene) was an efficient solid catalyst for the transesterification of various fatty methyl esters with glycerol and that without solvent and at a lower temperature (110 °C) than those usually required.[5a] Starting from a stoichiometric mixture of glycerol **1** and methyl dodecanoate **3a**, this solid catalyst afforded glycerol esters in more than 96% yield and with 48% selectivity toward monoglyceride **1a** (Scheme 1). However, when heating of the reaction mixture was maintained after total consumption of **3a** or when more hydrophobic fatty methyl esters such as **3b–d** were used, the

† Electronic supplementary information (ESI) available: experimental details. See http://www.rsc.org/suppdata/nj/b4/b418509a/

DOI: 10.1039/b418509a



Scheme 1 Catalytic esterification of glycerol and sucrose over supported guanidine.

selectivity toward **1a–d** rapidly dropped, limiting the viability of the process. This change in selectivity resulted from the hydrophobic nature of PS-TBD which interacted with monoglycerides **1a–d** more strongly than with glycerol, leading to a poor monoglyceride selectivity.[5a]

Based on these preliminary results, we report in this paper that the grafting of guanidine derivatives on a hydrophilic framework such as silica affords a very versatile catalyst able to produce monoglycerides **1a–d** or monosucroesters **2a** with higher selectivity, and that at lower temperature, than conventional catalysts, in a more environmentally-friendly process and directly starting from an equimolar mixture of polyol and various fatty methyl esters.

Results and discussion

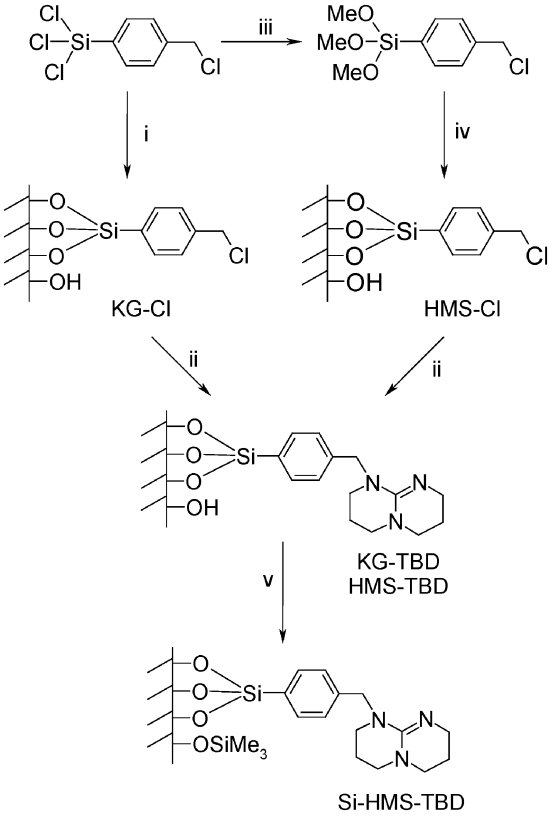
Catalyst preparation

Gelbard *et al.* extensively studied the guanidine moiety and its use as a basic catalyst in various reactions.[6b,9] Based on his results, several researchers grafted guanidine to the surface of a solid support in order to develop strongly basic heterogeneous catalysts.[10,11] However, if the catalytic activity of these materials is now widely studied, their use as selective catalysts or selective sorbents was much less investigated.

A triazabicyclo[4.4.0.]dec-5-ene (TBD) derivative was anchored to two different functionalized silicas prepared by post-synthesis grafting and by a copolymerization procedure affording KG-TBD and HMS-TBD, respectively. Usually, 3-chloropropyltrimethoxysilane and 3-glycidoxypropyltrimethoxysilane are used as linkers between the guanidine and the silica surface.[11] However, in order to strictly show the influence of the silica framework on the catalyst activity and the monoester selectivity, we deliberately chose the same linker, *i.e.* the benzyl group, as in the case of the PS-TBD catalyst. The synthetic procedures for the two basic hybrid organic–inorganic materials were inspired by the methods described in the literature (Scheme 2).

For the preparation of KG-TBD, the first step was the reaction of the trichloro[4-(chloromethyl)phenyl]silane with the non porous silica (KG-60) in refluxing toluene (Scheme 2). Elemental analysis of the collected KG-Cl revealed the presence of 0.94 mmol of chlorobenzyl groups per gram of silica.

For the HMS-TBD synthesis, the trichloro[4-(chloromethyl)phenyl]silane was first reacted with methanol in the presence of triethylamine in order to exchange the chlorosilane



Scheme 2 Synthetic procedure for KG-TBD and HMS-TBD: i) non porous silica, toluene, reflux, 24 h; ii) TBD, toluene, reflux, 12 h; iii) methanol, triethylamine, 0°C, 12 h; iv) tetraethoxysilane, dodecylamine, water, ethanol; v) HMDS, reflux, 24 h.

groups for trimethoxysilane groups (Scheme 2).[12] The replacement of the trichlorosilane by the trimethoxysilane groups was easily monitored by ^{1}H NMR spectroscopy, where the apparition of an intense peak localized at 3.60 ppm and assigned to the –Si(OCH$_3$)$_3$ group was observed. This prior transformation of the trichlorosilane groups was necessary in order to avoid an important, harmful, evolution of HCl during the next stage. In the second step, the HMS-Cl was prepared by copolymerization of tetraethoxysilane (TEOS) with the trimethoxy[4-(chloromethyl)phenyl]silane, in a molar ratio TEOS–organosilane of 15, in the presence of dodecylamine as structure directing agent (Scheme 2). Our procedure was inspired by the method described by Macquarrie *et al.* who gave rise to the so-called HMS silica.[13] The organic loading of HMS-Cl was determined by elemental analysis data which indicated the presence of 2.02 mmol of chlorobenzyl groups per gram of silica.

Then, for both HMS-Cl and KG-Cl solids, the guanidine heterogeneization procedure was similar. TBD species were anchored to the functionalized silica by nucleophilic attack on the benzylic position, affording the KG-TBD and the HMS-TBD catalysts (Scheme 2). However, as described in the literature for the PS-TBD catalyst, a guanidine quaternization occurred during the grafting process due to the *in situ* evolution of HCl and so consequently the unavoidable partial protonation of the guanidine sites.[9d,11e,14] This guanidine quaternization was clearly observed by infrared spectroscopy. Indeed, the IR spectra of KG-TBD and HMS-TBD exhibited two bands located at 1642 and 1618 cm^{-1} and respectively attributed to the $\nu_{C=N}$ stretching of the guanidine and guanidinium chloride groups (Fig. 1). In order to deprotonate all guanidinium sites, the two hybrid silica-TBD materials were treated with a solution of 0.1 M free TBD in acetonitrile. After this post treatment, the IR spectra of both KG-TBD and HMS-TBD exhibited only one single band located at 1642 cm^{-1}, indicating that no more guanidine sites were protonated (Fig. 1).

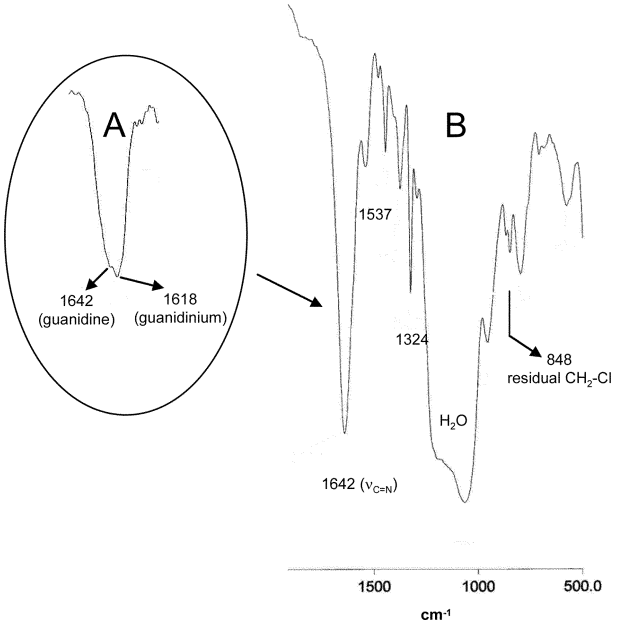


Fig. 1 FT-IR spectra of (A) crude HMS-TBD and (B) HMS-TBD after deprotonation.

The guanidine content of both catalysts was determined by thermal analysis. For both catalysts, thermal analysis revealed three different weight losses. The first weight loss, between 20 °C and 160 °C (*ca.* 5%), corresponded to the removal of water from the solids whereas the two following weight losses, which began at 250 °C and continued up to 650 °C, corresponded to the loss of the benzyl guanidine groups from the surface. In this range, the weight loss for KG-TBD was 20.8% and 38.6% for HMS-TBD which, respectively, corresponded to an organic loading of 0.9 mmol g^{-1} and 1.7 mmol g^{-1}. These results are in excellent agreement with those obtained from elemental analyses (see ESI†).

Catalyst activities

Catalysis in solvent free conditions. Both KG-TBD and HMS-TBD solids were first tested as catalysts under a nitrogen atmosphere and solvent free conditions. Typically, unprotected glycerol **1** (10 mmol) was reacted with 10 mmol of a fatty methyl ester **3a–d** in the presence of 0.12 equivalent of supported guanidine (Scheme 1). The reaction mixture was stirred at 110 °C in order to distil out the methanol produced *in situ* and shift the equilibrium towards the formation of glycerol esters.

Surprisingly, whereas PS-TBD was an efficient catalyst leading to the formation of glycerol esters **1a–d** in more than 96% yield, the two HMS-TBD and KG-TBD catalysts were totally inactive and no trace of glycerol esters was detected.

We assumed that this difference of reactivity between PS-TBD, KG-TBD and HMS-TBD was the result of strong hydrophilic interactions. Indeed, due to the greater hydrophilicity of the silica framework compared to that of polystyrene, we suggested that glycerol was strongly adsorbed all around the HMS-TBD and KG-TBD catalysts making impossible the approach of the fatty methyl esters **3a–d** to the TBD sites.

In order to validate this hypothesis, a phase transfer agent was co-added with the HMS-TBD and KG-TBD catalysts. Addition of 10 mol% of cetyltrimethylammonium bromide (CTAB) to the reaction mixture immediately started the reaction and glycerol esters were produced in more than 45% yield, with a monoglyceride selectivity of 90%. However, no significant difference in monoglyceride selectivity was observed between the PS-TBD and the two silica-TBD catalysts since the CTAB broke all the hydrophilic interactions expected to raise the monoglyceride selectivity.

Catalysis in DMSO. In order to gather more information about the key role played by the silica framework, the glycerol was diluted in a hydrophilic solvent with the aim of limiting its adsorption to the HMS-TBD catalyst and making easier the approach of the methyl dodecanoate to the grafted TBD catalytic sites. Dimethyl sulfoxide (DMSO) was chosen as the hydrophilic solvent because this latter is today one of the rare organic solvents still authorized in the food and cosmetic industries. DMSO was progressively added to the reaction mixture containing the HMS-TBD solid and, when the glycerol concentration reached 2 mol L^{-1}, the reaction immediately started. It is worth noting that below this concentration no reaction occurred, which confirmed that the HMS-TBD–glycerol interaction was strong enough to totally inhibit the catalytic process. Based on this result, the following catalytic tests were carried out, all at 110 °C, under a static nitrogen atmosphere, in the presence of 12 mol% of grafted guanidine and starting from unprotected glycerol **1** (10 mmol) and methyl dodecanoate **3a** (10 mmol) diluted in 5 mL of DMSO.

Whereas, under these conditions, the PS-TBD catalyst led to a very low formation of glycerol esters (2.1 mmol h^{-1} per equiv. TBD), the two silica-TBD solids initially catalyzed more than 7 times faster and rapidly led to the formation of glycerol esters in more than 96% yield (Table 1, Fig. 2).

As in the case of solvent free conditions, this important difference in reactivity between HMS-TBD, KG-TBD and PS-TBD catalysts was still the result of hydrophilic interactions. Indeed, due to its greater hydrophilicity, HMS-TBD interacts more strongly with glycerol than does PS-TBD, thus enhancing the production of glycerol esters. Curiously, the KG-TBD catalyst exhibited an intermediate catalytic activity since this latter catalyzed faster than PS-TBD (15 mmol h^{-1} per equiv. TBD *vs.* 2.1 mmol h^{-1} per equiv. TBD) but slower than HMS-

Table 1 Impact of the surface hydrophilicity on the monoester selectivity and the catalyst activity

					Molar yield[c][d] (%)				
Entry	Catalyst	Activity (mmol h^{-1} per equiv. TBD)[a]	Time (h)	Conversion[b] (%)	Mono-	Di-	Tri-	Acid	Selectivity[e][f] (%)
1	HMS-TBD	25	20	96	60	14 [28]	0 [0]	8	81 [68]
2	KG-TBD	15	40	96	53	20 [40]	0 [0]	3	73 [57]
3	Si-HMS-TBD	16	40	91	48	16 [32]	0.5 [1.5]	9	74 [59]
4	PS-TBD	2.1	220	96	44	19 [38]	3 [9]	5	67 [48]

[a] Glycerol (10 mmol), methyl dodecanoate **3a** (10 mmol), DMSO (5 mL), 0.12 equiv. TBD, 110 °C, under a static nitrogen atmosphere. [b] Conversion was calculated with respect to the fatty methyl ester: conversion = $100 \times (n_{mono} + 2n_{di} + 3n_{tri} + n_{acid})/(n_{mono} + 2n_{di} + 3n_{tri} + n_{acid} + n_{remaining\ ester})$. [c] Molar yield based on glycerol: % product = $100 \times n_{product}/n_{initial\ glycerol}$. [d] Molar yield based on the fatty methyl ester: % di = $100 \times 2n_{di}/n_{initial\ ester}$ and % tri = $100 \times 3n_{tri}/n_{initial\ ester}$. [e] Selectivity of glycerol transformation into mono-, di- and triglycerides: $100 \times n_{mono}/(n_{mono} + n_{di} + n_{tri})$. [f] Selectivity of fatty methyl ester transformation into mono-, di- and triglycerides: $100 \times n_{mono}/(n_{mono} + 2n_{di} + 3n_{tri})$.

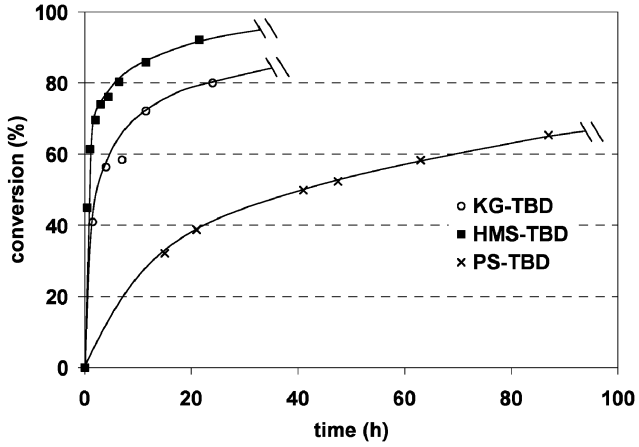


Fig. 2 Comparison of initial reaction rate between PS-TBD, KG-TBD and HMS-TBD catalysts.

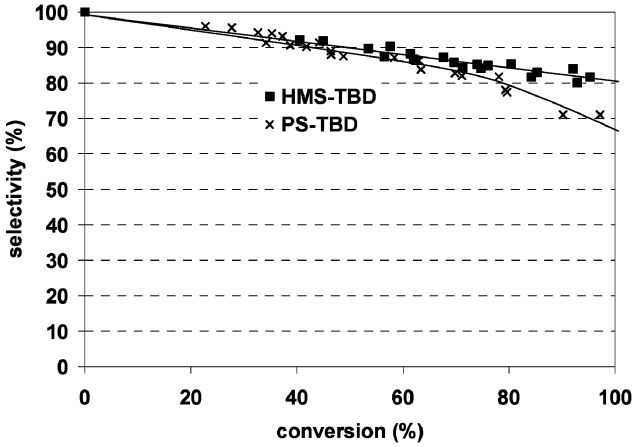


Fig. 3 Monoglyceride selectivity *vs.* methyl dodecanoate conversion for PS-TBD and HMS-TBD.

TBD (15 mmol h^{-1} per equiv. TBD *vs.* 25 mmol h^{-1} equiv. TBD) (Table 1, entries 1, 2 and 4). This difference in behaviour between KG-TBD and HMS-TBD was due to the greater hydrophilicity of HMS-TBD compared to that of KG-TBD. Indeed, Macquarrie *et al.* reported that the grafting of organic species on a non porous silica such as KG-100 led to an important decrease in the surface hydrophilicity, even with low organic loading.[13] However, hybrid organic–inorganic materials such as HMS functionalized with 1 mmol g^{-1} of organic species and prepared as above by a cocondensation procedure, exhibited a greater hydrophilicity due to the presence of numerous free silanol groups.[15] Thus, the resulting polarity of these materials closely approaches that of purely siliceous compounds.[13]

In order to clearly illustrate the great contribution of HMS-TBD to the reaction rate, the free silanol groups present at the HMS-TBD surface were protected. As described in the literature, the HMS-TBD catalyst was mixed with neat hexamethyldisilazane and stirred under reflux for 24 h affording the Si-HMS-TBD solid (Scheme 2).[16] As expected, the passivated Si-HMS-TBD catalyst led to a decrease in the initial reaction rate, which dropped from 25 to 16 mmol h^{-1} per equiv. TBD (Table 1, entry 3). This latter practically behaved like the KG-TBD catalyst, showing that the hydrophilic–lipophilic balance of the catalytic surfaces was a determinant parameter for an efficient esterification of glycerol.

In order to ensure that no leaching occurred during the catalytic process, the catalyst was removed from the reaction mixture after 20% of conversion. The filtrate was then heated and no reaction was observed, indicating that the catalytic process only took place on the grafted guanidine.

Remarkably, we noticed that the HMS-TBD catalyst did not only allow an improvement of the reaction rate in DMSO but, as expected, also played a very important role in the monoglyceride selectivity. Indeed, HMS-TBD afforded, at total conversion, a very high **3a** monoglyceride selectivity of 81% (Table 1, Fig. 3). In our knowledge, HMS-TBD is the first example of a catalyst able to reach, at total conversion and starting from a stoichiometric mixture of unprotected glycerol **1** and fatty methyl ester **3a**, a monoglyceride selectivity higher than 81% (or 68% if selectivity is based on **3a**).

As previously illustrated, KG-TBD and Si-HMS-TBD exhibited a weaker hydrophilicity compared to that of HMS-TBD and led to a lower monoglyceride selectivity (73%, Table 1). For comparison, under the same conditions, the homogeneous Me-TBD and PS-TBD solid catalysts led, at total conversion, to a monoglyceride selectivity of only 67%. This result clearly indicates that the improvement of the monoglyceride selectivity obtained with the HMS-TBD catalyst was not only the result of the poor miscibility of **3a** into the glycerol–DMSO phase, as was the case in the enzyme route, but closely depends on the chemical nature of the solid support. Indeed, an increase in the hydrophilic nature of the catalyst surface allowed a stronger interaction with glycerol than with monoglycerides, thus raising the monoglyceride selectivity and affording a more selective process. Moreover, contrary to what was reported with all the other catalysts, the monoglyceride selectivity did not dramatically drop between 80% conversion (**1a** selectivity: 83%) and total conversion (**1a** selectivity: 81%), pushing forward the very important role played by the siliceous framework in the monoglyceride selectivity.

Extension to other fatty methyl esters. Contrary to what was observed in DMSO with the PS-TBD catalyst, the HMS-TBD solid was also able to catalyze the same reaction starting from more hydrophobic fatty methyl esters such as methyl tetra- (**3b**), hexa- (**3c**) and octadecanoate esters (**3d**) (Table 2). However, a strong deactivation of the catalyst was observed with **3b–d** since glycerol esters were produced in only 75% yield and with a **1b–d** monoglyceride selectivity of 80% (Table 2, entries 2–4). Nevertheless, addition of an extra amount of HMS-TBD catalyst (0.2 mol%) allowed us to obtain similar results to those obtained starting from **3a** since glycerol esters were produced in more than 96% yield and with a **1b–d** monoglyceride selectivity of 78%.

We suggested that, at 110 °C and under a static nitrogen atmosphere, traces of water present in the reaction mixture could not be distilled out and were trapped by the grafted guanidine leading to the formation of fatty acid and consequently to catalyst poisoning. As a perfect illustration, under a static nitrogen atmosphere, fatty acids were detected in the reaction mixture in 3–8% yield, confirming the harmful role of water regarding the catalytic mechanism pathway (Table 2, entries 1–4). Due to the higher miscibility of methyl dodecanoate **3a** in the DMSO phase, the reaction proceeded faster with **3a** than with **3b–d** and so consequently the catalyst deactivation was less important leading to a higher glycerol ester production.

At the end of the reaction, the catalyst was recovered by filtration and reactivated by washing with a solution of free TBD in order to deprotonate all grafted guanidinium and to remove the fatty acid from the catalyst (see experimental section). After this treatment, the reactivated solid exhibited the same catalytic activity as the initial HMS-TBD, confirming that guanidine was poisoned but not destroyed during the catalytic process.

Reaction under nitrogen flow. In order to avoid the catalyst poisoning, the catalytic reaction was carried out at 110 °C but

Table 2 Synthesis of monoesters of polyols over HMS-TBD catalyst[a]

Entry	Polyol	Fatty ester	Glycerol–ester molar ratio	T (°C)	N_2	Time (h)	Conversion[b] (%)	Molar yield[c][d] (%) Mono-	Di-	Tri-	Acid	Selectivity[e][f] (%)
1	**1**	**3a**	1	110	Static	20	96	60	14 [28]	0	8	81 [68]
2	**1**	**3b**	1	110	Static	21	76	47	12 [24]	0	5	80 [66]
3	**1**	**3c**	1	110	Static	22	75	47	11 [22]	0.5 [1.5]	4	80 [67]
4	**1**	**3d**	1	110	Static	20	75	48	12 [24]	0	3	80 [67]
5	**1**	**3a**	1	110	Flow[i]	3	98	47	24 [48]	1 [3]	0	65 [48]
6	**1**	**3b**	1	110	Flow[i]	3	94	46	24 [48]	0	0	66 [49]
7	**1**	**3c**	1	110	Flow[i]	4	96	45	24 [48]	1 [3]	0	64 [47]
8	**1**	**3d**	1	110	Flow[i]	4	94	46	24 [48]	0	0	66 [49]
9	**1**	**3a**	1	40	Flow[i]	48	20	20	0 [0]	0	0	100 [100]
10	**1**	**3a**	1	40	Vacuum[j]	48	93	51	19 [38]	1 [3]	1	72 [55]
11	**1**	**3a**	2[g]	40	Vacuum[j]	30	96	72	12 [24]	0	0	86 [75]
12	**1**	**3a**	5[g]	40	Vacuum[j]	24	96	94	1 [2]	0	0	99 [98]
13	**1**	**3a**	5[h]	40	Vacuum[j]	40	95	94	0.5 [1]	0	0	99 [99]
14	**2**	**3a**	1	110	Static	20	96	36	16 [32]	7 [21][k]	7	61 [40]
15	**2**	**3a**	4	110	Static	5	92	69	7 [14]	1 [3]	6	90 [80]

[a] Polyol (10 mmol), fatty methyl ester (10 mmol), DMSO (5 mL), 0.12 equiv. TBD. [b] Conversion was calculated with respect to the fatty methyl esters: conversion = $100 \times (n_{mono} + 2n_{di} + 3n_{tri} + n_{acid})/(n_{mono} + 2n_{di} + 3n_{tri} + n_{acid} + n_{remaining\ ester})$. [c] Molar yield based on glycerol: % product = $100 \times n_{product}/n_{initial\ glycerol}$. [d] Molar yield based on the fatty methyl ester: % di = $100 \times 2n_{di}/n_{initial\ ester}$ and % tri = $100 \times 3n_{tri}/n_{initial\ ester}$. [e] Selectivity of glycerol transformation into mono-, di- and triglycerides: $100 \times n_{mono}/(n_{mono} + n_{di} + n_{tri})$. [f] Selectivity of fatty methyl ester transformation into mono-, di- and triglycerides: $100 \times n_{mono}/(n_{mono} + 2n_{di} + 3n_{tri})$. [g] The quantity of DMSO was adjusted in order to have a glycerol concentration of 2 M. [h] Enzymatic conditions: glycerol concentration of 0.8 M. [i] 15 mL min^{-1}. [j] 15 mmHg. [k] Sucrose triesters were not detected by HPLC and their quantity was calculated based on the remaining quantity of methyl dodecanoate.

with a nitrogen flow of 15 mL min^{-1} in order to remove water from the reaction mixture. Under these conditions, the reaction proceeded much more rapidly and glycerol esters **1a–b** were produced in more than 95% yield in less than 4 hours instead of 20 hours under a static nitrogen atmosphere (Table 2, entries 5–8). As expected, at the end of the reaction, no fatty acid was detected and the recovered catalyst has been recycled at least five times, with only a slight decrease in its catalytic activity mainly due to the high hygroscopy of DMSO and glycerol which made impossible the total removal of water from the reaction mixture. However, this increase of the reaction rate led to a significant drop in the monoglyceride selectivity from 81% to 65%, mainly because hydrophilic interactions of HMS-TBD with monoglycerides were less optimal. This decrease in the monoglyceride selectivity observed when the reaction rate increases was also reported in the case of the enzyme route. To optimise the interactions between HMS-TBD and monoglycerides, the reaction temperature was decreased to 40 °C. At this temperature, the reaction rate was too slow since methanol and water were removed with difficulty from the reaction mixture, even with a nitrogen flow of 15 mL min^{-1}, and glycerol esters were produced in only 20% yield after 48 hours of reaction (Table 2, entry 9). In order to solve this problem, the catalytic reaction was carried out under 15 mmHg. Whereas most heterogeneous catalysts were totally inactive at low temperature, strongly basic HMS-TBD catalyst was able to produce glycerol esters in more than 93% yield and with a monoglyceride selectivity higher than 72% at 40 °C (Table 2, entry 10). For comparison, mesoporous silica functionalized with sulfonic groups or zeolithes require a higher temperature (110 °C) and more than two times excess of glycerol to reach 70% selectivity (or 55% if selectivity is based on the fatty methyl esters) at total conversion.[4b]

Comparison with the enzyme chemical procedure. In order to increase the monoglyceride yield and to directly compare our catalyst to the enzymatic chemical procedure, the HMS-TBD catalyst was tested under the same experimental conditions as those required for the enzyme *i.e.* with a glycerol–fatty methyl ester molar ratio of 5 and a glycerol concentration of 0.8 M.[8b] The reaction mixture was then stirred at 40 °C under 15 mmHg. Using these conditions, glycerol esters were produced in 95% yield and with a very high monoglyceride selectivity of 99%, as was obtained by Otero *et al.*, pushing forward the great contribution of HMS-TBD compared to the other catalysts (Table 2, entry 13). However, the enzymatic route remains a very efficient approach since enzyme catalysis is almost 50 times faster than that of HMS-TBD.[8b] In order to increase the reaction rate while keeping high monoglyceride selectivity, similar reactions were performed at 2 M. As expected, when the glycerol concentration was raised from 0.8 M to 2 M, the reaction rate increased and glycerol esters were quantitatively produced in less than 24 hours instead of 48 hours (Table 2, entries 11 and 12). Moreover, no change of yield and monoglyceride selectivity was observed when the glycerol concentration increased from 0.8 M to 2 M, making of HMS-TBD a very competitive catalyst. It is worth noting that, below a five fold excess of glycerol, monoglycerides were always produced along with 5 mol% of diglycerides.

In all catalytic reactions described above, the regioselectivities of the reactions were similar to those reported in the literature since 1-monoglycerides and 2-monoglycerides were obtained in a ratio 9 : 1 whereas 1,2-diglycerides and 1,3-diglycerides were produced in a ratio 1 : 3.

Sucrose esterification. In the course of our work, it occurred to us that HMS-TBD could be a versatile catalyst for the selective esterification of other polyols and for this reason we extended our procedure to the synthesis of monosucroesters **2a**. Typically, sucrose **2** (10 mmol) was reacted with methyl dodecanoate **3a** (10 mmol) in the presence of 12 mol% of grafted TBD and the resulting mixture was stirred at 110 °C, under static nitrogen, in 5 mL of DMSO. Whereas under these conditions the PS-TBD was almost totally inactive, the HMS-TBD solid, as in the case of glycerol, afforded sucroesters in more than 90% yield and with a monosucroester selectivity higher than 60% (Table 2, entry 14). This lower monoester selectivity obtained in the case of sucrose compared to that reached starting from glycerol was due to the higher number of hydroxyl groups of the sucrose moiety. Using four times excess

of sucrose, sucroesters were produced with 92% yield and a monosucroester selectivity of 90% (Table 2, entry 15). In the case of sucrose, it was impossible to determine the regioselectivity of the reaction mainly due to important intramolecular transesterification reactions. This phenomenon was clearly evidenced in the literature by Queneau *et al.*[17] This last example clearly demonstrated that our catalytic procedure can be easily generalised to other polyols, affording a very versatile catalytic pathway.

Conclusion

In this paper, guanidine moieties were anchored to two different siliceous frameworks and the catalytic activity of the resulting solids was investigated in the selective monoesterification of unprotected glycerol. Here, we reported that the solid supports on which are grafted the guanidines do not act as simple spectators but actively participate in the catalytic process. Indeed, we found that the greater hydrophilicity of HMS-TBD silica compared to other catalysts such as KG-TBD or PS-TBD, allowed the production of glycerol esters in high yield and with a much higher monoglyceride selectivity than those usually obtained. Moreover, due to its strong basicity, HMS-TBD was able to catalyze the reaction at 40 °C whereas most of the other solid catalysts require higher temperatures. Compared to the reference enzymatic chemical route, HMS-TBD gave, under the same experimental conditions, a similar yield and monoglyceride selectivity. The enzyme chemical procedure still has the great advantage of catalyzing the reaction much more rapidly than HMS-TBD. However, compared to the enzymatic chemical pathway, HMS-TBD is able to catalyze the reaction in much less toxic solvents and starting from a much more concentrated glycerol solution than those required for the enzyme and that without affecting the reaction yield or the monoglyceride selectivity. Moreover, according to the experimental conditions used, the HMS-TBD solid can be easily recovered by filtration and reused at least five times with only a slight decrease in its catalytic activity.

HMS-TBD catalyst appears to be a very versatile catalyst for the selective monoesterification of natural polyols since this catalyst was also effective starting from other polyols such as sucrose and from various fatty methyl esters. Moreover, it is worth noting that during the catalytic process no secondary products such as polyglycerol, acrolein issued from the dehydration of glycerol, or other polyol degradation products were detected affording a very green catalytic process.

Experimental

Chemicals

Industrial glycerol (97%) and fatty methyl esters **3a–d** (99%) were kindly provided by Stearinerie Dubois and sucrose was supplied by Beghin-Say. Dimethyl sulfoxide, tetraethoxysilane and hexamethyldisilazane (HMDS) were purchased from Acros. Triazabicyclo[4.4.0.]dec-5-ene (TBD), dodecylamine, trichloro[4-(chloromethyl)phenyl]silane and PS-TBD catalyst were purchased from Sigma Aldrich. PS-TBD solid catalyst was a polystyrene network crosslinked with 2% of divinylbenzene and functionalized with 2.5 mmol g^{-1} of benzylguanidine. Silica (KG: Kieselgel 60, 0.040–0.063 mm, 480–540 m^2 g^{-1}) was purchased from Merck. All solvents and reagents were used as received without any further purification. Chemical procedures and physical properties of solid catalysts prepared in this work are reported in the ESI†.

Physical methods

IR spectra were recorded on a FT-IR Perkin Elmer (spectrum GX) spectrophotometer and samples were prepared as a 1% dispersion in KBr. The ^{1}H NMR spectrum of the trimethoxy [4-(chloromethyl)phenyl]silane derivative was recorded on a Bruker Avance 300 DPX 300. Chemical shifts are expressed in ppm relative to Me_4Si. Organic content of all hybrid organic–inorganic materials was determined by microanalysis on an NA 2100 instrument and by thermal analysis on a SBT 2960 TA Instrument.

Chromatographic analyses

The sucrose esterification reaction progress was monitored on a Shimadzu HPLC (SIL 10A) equipped with a column Touzard & Matignon Nucleosil C8 (250 mm × 4.6 mm) and using a methanol–water (78 : 22) mixture as eluent with a flow of 0.8 mL min^{-1}. The detector was a refractometer (Waters 2410). This analytical technique allowed the quantification of sucrose mono- and diesters, methyl dodecanoate and dodecanoic acid. The glycerol esterification reaction progress was monitored and quantified on a Varian 3300 GPC equipped with a BPX5 column (12 m × 0.22 mm) supplied by SGE. Prior to analysis, products were silylated according to the Sahasrabudhe method described in ref. 18. This analytical technique allowed the quantification of glycerol, fatty methyl esters **3a–d**, fatty acids, 1-monoglycerides, 2-monoglycerides, 1,2-diglycerides, 1,3-diglycerides and triglycerides. For both HPLC and GC, the molar composition of the mixture was determined by an external calibration method. In this study, the monoglyceride selectivity was calculated by both manners: based on the glycerol transformation into **1a–d** and based on the fatty methyl ester transformation into **1a–d**, in order to make easier the comparison with all results reported in the literature and industrial patents (Tables 1 and 2).

Catalytic tests

Glycerol **1** or sucrose **2** (0.01 mol) and methyl dodecanoate **1a** (2.14 g, 0.01 mol) were charged in a Schlenk tube and diluted in 5 mL of DMSO. The reaction mixture was stirred with a magnetic stirring bar (600 rpm) and heated to the desired temperature. Then 12 mol% of grafted TBD (1.3 g of KG-TBD or 0.7 g of HMS-TBD) were added and the reaction mixture was stirred either under a static nitrogen atmosphere, nitrogen flow (15 mL min^{-1}) or under vacuum (15 mmHg) in order to remove the methanol and/or water from the reaction mixture. At the end of the reaction, the catalyst was removed by filtration. The filtrate was then diluted in water and addition of ethyl acetate (2 × 15 mL) allowed to extract the glycerol esters and sucroesters. The organic phases were combined and then washed three times with water (30 mL) and dried over $MgSO_4$. After removal of the organic solvent, the residue was dried under vacuum (10^{-1} mmHg) for 15 h at 50 °C. The residue isolated starting from glycerol was a white powder, whereas starting from sucrose an oily residue was obtained. Typically, as described in the literature, mono-, di- and triglycerides can be separated by silica chromatography using ethyl acetate–heptane (20 : 100 to 100 : 0) as eluent whereas all different sucroesters can be separated using an initial mixture CH_2Cl_2–acetone–methanol–water 56 : 20 : 20 : 4 as eluent.

Catalyst recycling

At the end of the reaction, the catalyst was removed by filtration at a temperature higher than 60 °C. Under nitrogen flow or under vacuum, the recovered catalyst was used as collected without any further purification.

However, under a static nitrogen atmosphere, the HMS-TBD was reactivated by washing this latter with a TBD solution (0.1 M) in acetonitrile in order to remove fatty acid from the TBD catalytic sites. Then HMS-TBD was transferred to a cellulose extraction thimble and washed using a Soxhlet

apparatus with acetonitrile for 15 h before reusing. Elemental analysis of the recovered HMS-TBD before reactivation: %C: 36.31, %H: 4.99, %N: 2.04, and after reactivation %C: 33.84, %H: 4.57 %N: 7.09

Acknowledgements

This work was supported by the CNRS and the AGRICE action (contract no 01 01 016). Authors are grateful to ADEME and Région Poitou-Charentes for a PhD grant to IA and also to the Morocco government for the PhD grant to GK.

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