



Heterogeneously Catalyzed Hydrogenation of Squalene to Squalane under Mild Conditions

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The full chemoselective hydrogenation of highly unsaturated all-*trans* linear squalene into valuable fully saturated squalane is achieved smoothly under mild conditions over the sol-gel-entrapped Pd catalyst SiliaCat Pd⁰. The catalysis is truly hetero-

geneous, and the catalyst is stable and recyclable, which opens the route to an easier and less expensive hydrogenation of squalene.

Introduction

Identified originally at the beginning of the 20th century by Tsujimoto in deep-sea shark-liver oils, the terpenoid squalene (Figure 1; C₃₀H₅₀) is a strong antioxidant (detoxifying), immunoprotective, cholesterol-reducing, and anticarcinogenic agent used widely in traditional medicine and, today, as a nutraceutical and cosmetic ingredient.^[1] Capsules of shark-liver oil (which contain squalene in concentrations of 40–80% by weight), have been available commercially for decades.

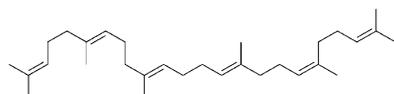


Figure 1. Chemical structure of squalene.

Squalane is the saturated hydrocarbon (2,6,10,15,19,23-hexamethyltetracosane, C₃₀H₆₂) obtained by full hydrogenation of the highly unsaturated all-*trans* linear squalene (6*E*,10*E*,14*E*,18*E*)-2,6,10,15,19,23-hexamethyltetracosane-2,6,10,14,18,22-hexaene).

With six isolated double bonds, the 24-carbon backbone squalene molecule that bears six methyl groups is very reactive and unstable towards oxidation into undesirable peroxides.

Hence, in the early 1950s Sabetay extended to squalene the common practice of stabilization through hydrogenation used in the fats industry since the early 1920s.^[2] Trade-named Cosbiol by the French cosmetic ingredients company Laserson & Sabetay, the fully saturated hydrocarbon “perhydrosqualene”, which had already been synthesized by Tsujimoto in 1916,^[3] was adopted readily by cosmetic formulators because of its remarkable properties that make it the best known emollient in the cosmetic and personal care industries.^[4]

Although squalene is highly comedogenic, the clear, colorless, odorless, tasteless, very stable, and nonirritant oil squalane^[5] has a unique ability to penetrate the human skin^[6] and imparts flexibility and smoothness to the skin (without an unpleasant greasy feel). In addition to skin hydration, squalane increases the absorption of other active substances dramatically.

For decades, the main raw material of squalane has been the liver oil of small sharks from the deep sea. Approximately 25% of the weight of a deep-sea shark (average weight of 100 kg) is made up of its liver, which contains about 50% oil, of which 80% is squalene. Squalene, with a purity of > 98%, is obtained directly from the liver oil after a single distillation step under vacuum at temperatures of 200–230 °C. Typically, the livers of approximately 3000 sharks are required to produce 1 ton of squalene.

The massive depletion of the deep-sea shark population led the European Union to reduce the fishing of deep-sea species by drastic quotas established in the late 1990s.^[7] Required to replace animal squalene with vegetable raw material, cosmetic companies switched partly to squalane obtained from olive oil, which has a squalene content of 0.4–0.6%.^[8] As a result of its low concentration, the extraction of squalene directly from olive oil is not economically convenient. Gas effluents called deodorization distillates (DDs) or oil physical refining condensates (OPRC) recovered by condensation are instead used in place of virgin oil. In detail, 100–300 g of squalene is obtained per kg of ultrarefined distillate deodorizer oil.^[9]

As a result of unsustainable and expensive sources, in the last decade squalane use has decreased to 2500 tons from 7500 tons, and recent selling prices are around \$30 per liter.^[10]

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More recently, however, a new phytosqualane product has entered the market. In detail, squalane is obtained from the 15-carbon sesquiterpene *trans*- β -farnesene derived from sugarcane sucrose fermentation over genetically modified *Saccharomyces cerevisiae* yeast strains.^[11]

Farnesene is first converted into squalene by catalytic dimerization over a Pd catalyst, and squalene is hydrogenated subsequently to squalane to produce a squalane composition that comprises squalane 92–93% and approximately 4% isosqualane.^[12] Trade-named Neossance, sugarcane phytosqualane has the potential to replace both olive oil and shark squalene as one hectare of sugarcane plantation can produce up to 2500 kg of squalane.

Whatever the origin, fully saturated squalane for cosmetic use needs to have more than 92% concentration and an iodine value lower than 1.00 (and preferably <0.10).^[13] Such high purity levels with commercial Ni-based catalysts require relatively harsh conditions and extensive purification of the hydrogenated product over silica and other adsorbent materials, which add cost to the hydrogenated product. A typical hydrogenation process performed in industry makes use of 0.05 wt% nickel-Kieselguhr catalyst under 4 bar of H₂ pressure at 200 °C.^[14] No solvent is employed and, if the squalene is from shark-liver oil, after 3–4 h the reaction is complete. Yet, if the squalene originates from olive oil, the inevitable presence of residual waxes requires harsher conditions and further purification.^[15] Squalene is first “winterized” to precipitate wax. Then, the process is performed in two steps: a first 3–4 h step under 5 bar of H₂ pressure, followed by 3 h at 30 bar H₂ to afford complete saturation, followed by further purification.

During the reaction over Ni-based catalysts, extensive bond migration and dehydrogenation of squalene takes place.^[16] Yet, as the saturation of double bonds is sought, as it is common in the food industry,^[17] low-cost Ni catalysts remain used the most widely in commercial operations, even though extensive purification is required to remove most Ni leached into the squalane product to meet maximum acceptable levels of toxic Ni compounds (Ni²⁺ and Ni⁰) in a cosmetic product (0.2 ppm; although out of 49 cosmetic products commercialized in Canada, all were positive for Ni with an average content of 9 ppm).^[18]

The other hydrogenation catalyst employed on an industrial scale is Pd/C (5 wt%, with a loading of 0.25 mmol g⁻¹ Pd). The reaction is performed at approximately 150–160 °C first under 3 bar and then 70 bar of H₂.^[12] In each case, the reaction temperature is controlled by cooling to maintain the temperature at 150–160 °C.

Clearly, there is a need for better hydrogenation catalysts to convert squalene into squalane at low pressure and temperature, especially now that vegetable squalene is poised to replace squalene of animal origin entirely. A large number of supported Pd⁰ catalysts for heterogeneous C=C hydrogenation reactions have been developed and are available commercially, which include Pd/C, Pd/CaCO₃, and Pd/Al₂O₃.^[19] However, such surface-derivatized catalysts, used normally for the synthesis of vitamins and other highly functionalized fine chemicals, degrade rapidly to further add to the cost of the product.^[20]

Recently, many efforts have been devoted to develop sinter-proof hydrogenation catalysts using preprepared colloidal metal nanoparticles with tuned size, shape, and composition that are then “embedded” into porous support shells.^[21] The validity of this approach was shown by McFarland and co-workers who compared the catalytic performance of Pd particles deposited either on the outer surface of silica (Pd/SiO₂) or encapsulated within the silica inner pores (Pd@SiO₂).^[22]

In this context, we have introduced a new series of catalysts that comprises noble-metal nanocrystals encapsulated within the sol-gel cages of mesoporous organosilica xerogels. Trade-named SiliaCat, these sol-gel catalytic materials are highly selective mediators in a number of important reactions that include the highly selective hydrogenation of functionalized nitroarenes,^[23] olefins,^[24] and vegetable oils under a H₂-filled balloon (1 atm H₂) at room temperature.^[25] Now we report that the Pd catalyst SiliaCat Pd⁰ is a highly selective mediator for the low-temperature hydrogenation of squalene, which provides industry with a suitable low-cost process to make a substance of high demand, the sourcing and production of which have to be made sustainable.

Results and Discussion

We first performed a series of experiments using a commercial squalene sample (98 wt% purity, Aldrich) aimed to identify the best solvent for the catalytic hydrogenation of squalene over the SiliaCat Pd⁰ catalyst under a H₂-filled balloon (1 atm H₂) at temperatures between 22 and 50 °C. The results shown in Table 1 allowed us to identify the best procedures and the best conditions, namely, 0.5 mol% SiliaCat Pd⁰ in ethanol 0.50 M with respect to the squalene under 1 atm H₂ at 50 °C.

The reaction was in each case truly heterogeneous because the recovered solution obtained after the catalyst was removed by filtration at 50% substrate conversion (hot filtration test) showed no further activity from Pd leached in solution.

The reaction slows down if the squalene hydrogenation over SiliaCat Pd⁰ is performed without solvent (Table 1, Entries 14 and 15). For instance, entry 14 shows that after 24 h at 30 °C, only 66% of the squalene substrate (GC–MS, MW: 410) is converted, which affords a mixture of intermediate hydrogenated products identified by GC–MS (MW: 412; 414; 416; 418). If the reaction temperature is increased to 50 °C (entry 15), after 24 h the substrate conversion increased to 98% even though the hydrogenation reaction remained nonselective and afforded a mixture of intermediate hydrogenated products identified by GC–MS (MW: 418; 420).

These results are explained by the significantly lower solubility of H₂ in squalene oil compared to the squalene/ethanol mixture, and are in full agreement with outcomes shown by entries 1–8 that show a consistent increase in the yields to squalane by increasing the EtOH volume and the reaction temperature.^[26] These conditions favor a higher solubility of H₂ in the reaction mixture and increase the accessibility of the reactants to the active catalytic sites dispersed throughout the internal pore structure of the catalyst.

Table 1. Effect of solvent on squalene hydrogenation over 0.5 mol% SiliaCat Pd ⁰ . ^[a]					
Entry	Solvent (concentration [M]) ^[b]	T [°C]	t [h]	Conversion [%] (yield [%]) ^[c]	Yield [%] ^[d]
1	EtOH (0.25)	22	6	100 (24)	–
			8	100 (71)	–
2	EtOH (0.25)	30	4	100 (53)	98.4
			6	100 (100)	–
3	EtOH (0.25)	50	4	100 (71)	99.2
			5	100 (100)	–
4	EtOH (0.33)	30	4	100 (62)	99.2
			6	100 (100)	–
5	EtOH (0.33)	50	2	100 (72)	99.5
			4	100 (100)	–
6	EtOH (0.50)	30	4	100 (30)	98.6
			6	100 (75)	–
			8	100 (100)	–
7	EtOH (0.50)	50	2	100 (70)	98.3
			4	100 (99)	–
8	EtOH (0.75)	50	24	100 (67)	–
9	EtOH (1.0)	50	24	100 (36)	–
10	MeOH (0.50)	50	8	100 (32)	–
11	MeTHF (0.50)	50	8	100 (45)	–
12	MeTHF/EtOH 1:1 v/v (0.50)	50	4	100 (75)	–
			6	100 (98)	–
13	<i>i</i> PrOH (0.50)	50	8	95 (0)	–
14 ^[e]	neat	30	24	66 (0)	–
15 ^[e]	neat	50	24	98 (0)	–

[a] Experimental conditions: 10 mmol squalene (98% purity), HPLC-grade EtOH from 40 mL (0.25 M squalene in EtOH) to 10 mL (1.00 M squalene in EtOH), and 0.5 mol% SiliaCat Pd⁰ catalyst (0.2 mmol g⁻¹ Pd loading) under a H₂-filled balloon with magnetic stirring (800 rpm). [b] Squalene molar concentration solutions in HPLC-grade solvent. [c] Conversion of the squalene/squalane yield evaluated by GC-MS analysis. [d] Isolated yield. [e] Without solvent.

Effects of the squalene purity

Squalane yields obtained if squalene samples of different purity were hydrogenated under the identified optimal conditions are presented in Figure 2. The 98 wt% pure squalene commercial sample was converted into squalane completely after 4 h (Table 1, entry 7). A less pure (92 wt%, VWR) commer-

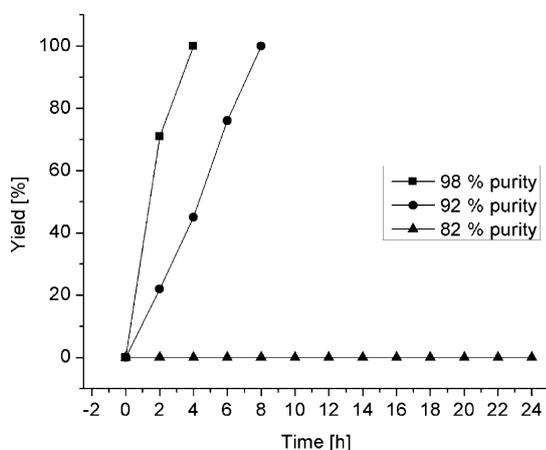


Figure 2. Effect of squalene purity on the conversion to squalane over 0.5 mol% SiliaCat Pd⁰, 1 atm H₂, 50 °C, 0.50 M squalene in ethanol.

cial squalene oil sample was also converted completely into squalane, but the reaction was slower and took twice as long (8 h).

However, if an 82 wt% pure olive squalene oil was tested under the same reaction conditions, complete hydrogenation and squalane formation was not observed. After 24 h of reaction, only four double bonds were hydrogenated, and no further reaction took place even at longer reaction times.

The influence of the amount of SiliaCat Pd⁰ catalyst on the conversion of squalene using the 92 wt% squalene commercial sample under the optimal conditions is shown in Figure 3.

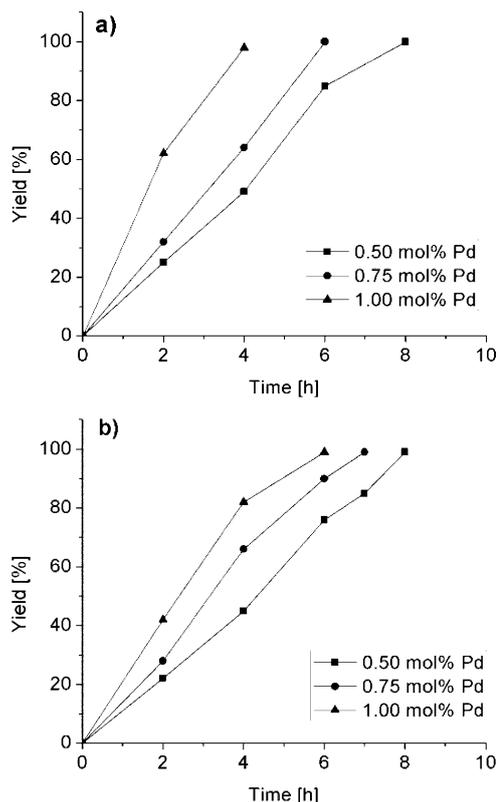


Figure 3. Influence of the amount of SiliaCat Pd⁰ on the rate of squalene hydrogenation (92 wt% purity), for: a) 0.33 and b) 0.50 M (molar concentration of squalene ethanol solution).

If 0.5 mol% catalyst was used, the complete conversion to squalane requires 8 h for both 0.50 and 0.33 M squalene solutions. However, over 1.0 mol% catalyst, almost complete conversion of squalene to squalane was obtained in 4 h for the 0.33 M mixture; and in 6 h for the 0.50 M squalene solution in EtOH. Again, the solubility of H₂ in the reaction mixture is a crucially important factor for the heterogeneous reaction under the present mild H₂ pressure conditions. We examined the influence of this parameter by scaling up the hydrogenation reaction at 50 °C from 5 to 20 mmol squalene in a 0.33 M squalene solution in EtOH.

Early kinetic data shown in Figure 4 reveal that, for a 100 mL round-bottomed flask capacity, the rate of squalene hydrogenation decreases with the increase of the volume of the reac-

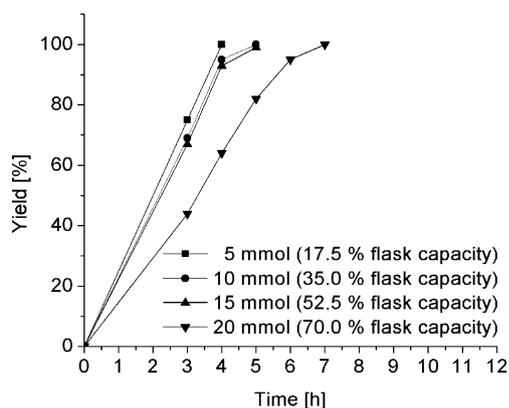


Figure 4. Performance of SiliaCat Pd⁰ in the scaled-up squalene hydrogenation reaction from 5–20 mmol starting material in a 100 mL round-bottomed flask.

tion mixture. In the hydrogenation of 5 mmol substrate in a 17.5 mL reaction mixture (17.5% flask capacity), complete conversion to squalane was obtained after 4 h with 99.6% isolated yield. If 10 mmol substrate was reacted in 30 mL reaction mixture (35% flask capacity), the complete conversion to squalane was obtained after 5 h with 99.7% isolated yield.

The same results were obtained if 15 mmol of squalene was used in 52.5 mL reaction mixture (at 52.5% flask capacity). However, if 20 mmol squalene was used in 70 mL of reaction mixture (70% flask capacity), the complete conversion to squalane required 7 h to afford 99.4% isolated yield. Again these results may be explained by the lower solubility of H₂ in the reaction mixture if the gas–liquid contact surface is decreased.

Reproducibility of the heterogeneous reaction

The reproducibility of the reaction yield upon scale-up of the reaction from 10–50 mmol squalene at 35% flask-volume capacity over 1 mol% SiliaCat Pd⁰ at 50 °C is shown in Figure 5. The complete conversion of squalene to squalane was obtained after 5 h reaction under a H₂ balloon for the 10 mmol

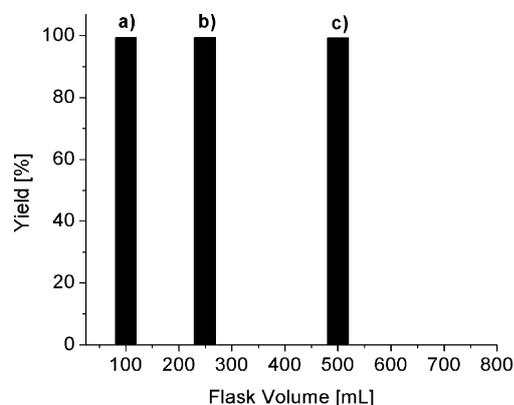


Figure 5. Reproducibility of yield upon scale-up of the squalene hydrogenation reaction after 5 h reaction over 1 mol% SiliaCat Pd⁰: a) 10, b) 25, and c) 50 mmol squalene in EtOH (0.33 M; 35% flask volume capacity).

substrate solution in a 100 mL round-bottomed flask (Figure 5a), for the 25 mmol substrate solution in a 250 mL round-bottomed flask (Figure 5b), and with 50 mmol squalene in a 500 mL round-bottomed flask (Figure 5c).

We used these conditions to examine squalene hydrogenation for the olive squalene sample of 82 wt% purity. To our delight, now complete conversion to squalane could be obtained also for this low-purity sample. In detail, the complete conversion of squalene to squalane with 99.3% isolated yield required 8 h reaction.

Leaching and catalyst stability

To investigate the leaching of both Pd and Si from the SiliaCat Pd⁰ catalyst during the reaction, we analyzed the crude solid products by inductively coupled plasma optical emission spectroscopy (ICP-OES). In general, the measured values of leached Pd and Si in the isolated crude product were <5 and <10 ppm, respectively, independent of temperature, reaction time, molar concentration, nature of solvent, and the amount of catalyst used in the reaction (Table 2).

Reusability of the solid catalyst

We examined the reusability of the catalyst in the heterogeneous squalene hydrogenation for the 92% purity sample under the optimal conditions (1 mol% SiliaCat Pd⁰, 0.33 M squalene in EtOH, 5 h, 1 atm H₂ at 50 °C). The catalyst employed in the 20 mmol (8.22 g) substrate test was collected by filtration after the first run, washed extensively (three times with EtOAc), dried at room temperature, and reused in a subsequent run.

Overall, six consecutive runs were performed by recovering and washing the catalyst each time as described above. After each run, the heterogeneous catalyst was separated from the reaction mixture and the solvent was evaporated. The leaching of Pd and Si was assessed by ICP-OES analysis of the isolated crude product in 1,1,2,2-tetrachloroethane solvent (concentration 100 mg mL⁻¹). The results indicate that less than 0.002% of the Pd in the initial catalyst was leached from the catalyst inner pores.

In all five consecutive reactions, complete conversion was obtained in 5 h (Figure 6). Then a slight decrease in activity was observed that was compensated for by an increase of the reaction time from 5 to 6 h. Clearly, the SiliaCat Pd⁰ heterogeneous catalyst was stable and robust, which is a crucially important factor for the practical application of a heterogeneously catalyzed process using this new sol–gel-entrapped catalyst in place of conventional Pd/C and Ni-Kieselguhr commercial catalysts.

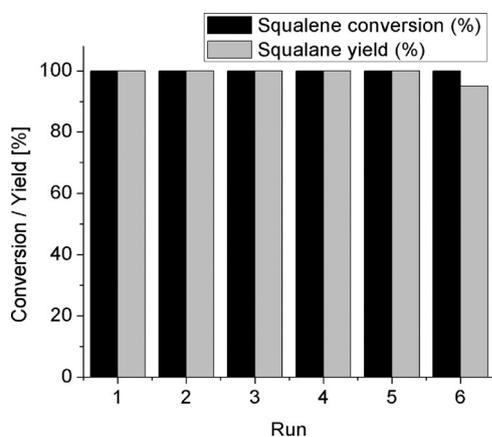
Conclusions

A recent investigative journalism analysis^[27] found that the cosmetic industry is still supplied largely with animal squalene, and around 90% of world shark-liver oil production feeds the needs of the cosmetics industry (which corresponds to 2.7 million deep-sea sharks caught every year). Estimates from the

Table 2. Pd and Si leaching from SiliaCat Pd⁰ in squalene hydrogenation under different conditions.^[a]

Entry	Solvent (concentration [M])	Catalyst amount [mol%]	T [°C]	t [h]	Conversion [%] (yield [%]) ^[b]	Yield [%] ^[c]	Leaching [mg kg ⁻¹] ^[d]	
							Pd	Si
1	EtOH (0.25)	0.50	22	8	100 (71)	–	1.22	2.59
2	EtOH (0.25)	0.50	30	6	100 (100)	98.4	n.d.	n.d.
3	EtOH (0.25)	0.50	50	6	100 (100)	99.2	0.73	2.65
4	EtOH (0.33)	0.50	50	4	100 (100)	99.5	1.69	2.54
5	EtOH (0.50)	0.50	50	4	100 (100)	99	0.39	3.51
6	EtOH (0.75)	0.50	50	24	100 (67)	–	0.75	2.45
7	EtOH (1.00)	0.50	50	24	100 (36)	–	0.82	2.03
8	MeOH (0.50)	0.50	50	8	100 (32)	–	1.80	2.20
9	MeTHF (0.50)	0.50	50	8	100 (45)	–	3.06	6.30
10	MeTHF/EtOH 1:1 v/v (0.50)	0.50	50	6	100 (98)	–	1.45	2.35
11	iPrOH (0.50)	0.50	50	8	95 (0)	–	1.95	2.40
12 ^[e]	neat	0.50	50	24	98 (0)	–	3.50	2.94
13 ^[f]	EtOH (0.50)	0.50	50	8	100 (98)	–	0.82	5.17
14 ^[f]	EtOH (0.50)	0.75	50	7	100 (100)	99.6	1.02	3.63
15 ^[f]	EtOH (0.50)	1.00	50	6	100 (100)	99.4	<0.5	4.84
16 ^[f]	EtOH (0.33)	0.50	50	8	100 (100)	99.5	1.50	1.20
17 ^[f]	EtOH (0.33)	0.75	50	6	100 (100)	99.6	2.00	3.33
18 ^[f]	EtOH (0.33)	1.00	50	5	100 (100)	99.6	1.68	1.50
19 ^[g]	EtOH (0.33)	1.00	50	8	100 (100)	99.3	1.15	7.62

[a] Experimental conditions: 10 mmol squalene (98 wt% purity) in EtOH from 0.25–1.00 M (molar concentration of squalene) and SiliaCat Pd⁰ from 0.5–1.0 mol% Pd catalyst (0.2 mmol g⁻¹ Pd loading) under a H₂-filled balloon at room temperature. [b] Conversion of squalene/squalane yield evaluated by GC–MS analysis. [c] Isolated yield. [d] Leaching in Pd and Si assessed by ICP–OES analysis of the isolated crude product in 1,1,2,2-tetrachloroethane (concentration 100 mg mL⁻¹) and reported as mg kg⁻¹ of product. (LOD_{Pd} = 0.50 mg kg⁻¹ and LOD_{Si} = 0.20 mg kg⁻¹ in the crude product). [e] Without solvent. [f] Squalene of 92% purity was used. [g] Squalene of 82% purity was used.

**Figure 6.** Reusability of the SiliaCat Pd⁰ catalyst in squalene hydrogenation.

sugarcane phytosqualene manufacturer, however, point to the following 2012 global squalane market share: 46% olive oil, 44% shark-liver oil, and 10% sugarcane-derived squalane.^[28]

As phytosqualene replaces squalene of animal origin, a new heterogeneous hydrogenation process that can be performed under low pressure and temperature is required urgently to decrease the cost of the squalane. The current manufacturing process, hydrogenation, accounts for approximately 40% of the overall production cost.^[14]

Recently, Tran and co-workers lamented that “very little work”^[29] has been reported on catalyst development for terpene hydrogenation. For example, during the hydrogenation of squalene over Ni and Pt catalysts (especially on Raney nickel) extensive bond migration and dehydrogenation was observed as early as of 1956.^[16] As we continue to advance the scope of these materials, we have shown that the organosilica SiliaCat catalyst doped with Pd⁰ nanocrystals is a highly active, selective, and reusable catalyst for the hydrogenation of squalene under remarkably mild conditions, namely, 1 atm H₂ pressure at 30 °C, or at 50 °C if shorter reaction times are needed, which uses in each case an ultralow amount of valuable catalyst (0.5–1.0 mol%).

The extent of hydrogenation depends crucially on the squalene purity. If squalene oil of olive origin with a typically low (82%) purity is used, the complete conversion requires the use of a low flask-volume capacity (35%) to increase the gas–liquid surface and enhance the H₂ dissolution in the ethanol solution.

Experimental Section

The squalene samples with different purities (98 wt% from Aldrich, 92 wt% from VWR, and 82 wt% from an olive squalene manufacturer based in Europe) were used as received. All organic solvents used were of HPLC grade and were used without purification. All hydrogenation reactions were conducted under 1 atm H₂. The organosilica SiliaCat Pd⁰ catalyst does not swell or stick to the reactor surface and could be filtered easily and handled and showed no tendency to ignite upon exposure to air.

Catalyst preparation

First described in 2011,^[30] the preparation of SiliaCat Pd⁰ involves the alcohol-free sol–gel polycondensation of alkoxy silanes such as methyltrimethoxysilane (MTMS) and TEOS. The resulting SiliaCat Pd⁰ catalyst is made of uniformly, highly dispersed Pd nanoparticles (in the range 3–6 nm) encapsulated within an organosilica matrix. The commercial catalyst used throughout the present catalytic experiments has 0.2 mmol g⁻¹ Pd loading (measured by using a CAMECA SX100 instrument equipped with an electron probe microanalyzer; EPMA).

Hydrogenation reactions

Reactions were performed on a 10 mmol substrate scale. Conversion was assessed by TLC analysis (hexane/EtOAc = 5:1, using potassium permanganate stain) and by GC–MS analysis. The squalene substrate was added along with solvent (30 mL, 0.33 M) into a 100 mL round-bottomed two-necked flask, and then SiliaCat Pd⁰ (1.0 mol%) was added. The flask was charged with a stirring bar and degassed four times, in which the vacuum was replaced twice by Ar and twice by H₂. The reaction mixture in the flask was con-

nected to a H₂-filled balloon through a condenser and stirred vigorously (800 rpm) at 50 °C until GC–MS analysis showed the maximum conversion. The catalyst was then collected by filtration and rinsed with EtOAc (3 × 20 mL), and the filtrate was concentrated to give a crude product.

Reusability test

The hydrogenation was performed at 50 °C in the presence of 1 mol% sol–gel catalyst. A 200 mL round-bottomed three-necked flask connected to a H₂-filled balloon through a condenser and charged with a magnetic stirring bar, substrate (20 mmol), EtOH (60 mL, 0.33 M squalene concentration), and SiliaCat Pd⁰ was degassed four times, in which the vacuum was replaced twice by Ar and twice by H₂. The reaction mixture was stirred vigorously at 50 °C for 5 h after which the catalyst was recovered by filtration, rinsed with EtOAc (3 × 40 mL), dried under vacuum, and stored under normal conditions before reuse. The filtrate was concentrated to give a crude product.

After each reaction run, the dried catalyst was weighed and the amount of substrate and the volume of solvent were adjusted accordingly, by taking into consideration the catalyst loss during isolation and work-up. The leaching of Pd and Si was assessed by ICP-OES analysis (PerkinElmer Optima 2100 DV) of the isolated crude product dissolved in 1,1,2,2-tetrachloroethane (concentration 100 mg mL⁻¹). Values are reported as mg of metal per kg of product. The ICP-OES limit of detection (the lowest quantity of a substance that can be distinguished from a blank value, LOD) was LOD_{Pd} = 0.05 ppm in solution or 0.50 mg kg⁻¹ in the crude product and LOD_{Si} = 0.02 ppm in solution or 0.20 mg kg⁻¹ in the crude product.

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Keywords: encapsulation · heterogeneous catalysis · hydrogenation · palladium · squalene

- [1] M. Spanova, G. Daum, *Eur. J. Lipid Sci. Technol.* **2011**, *113*, 1299–1320.
- [2] a) *Hydrogenation of Fats and Oils: Theory and Practice* (Eds.: J. King, G. R. List), AOCS Press, Urbana, **2010**; b) For an insight into the health hazards posed by hydrogenated trans fats see: W. Willett, *Sci. Am.* **2014**, *310*, 13.
- [3] M. Tsujimoto, *Ind. Eng. Chem.* **1916**, *8*, 889–896.
- [4] The story of squalene in the cosmetic industry has been recounted recently by one of the industry's pioneers: F. Laserson, *Expression Cosmétique* **2013**, 325–328.
- [5] *Final Report on the Safety Assessment of Squalene and Squalene*, *Int. J. Toxicol.* **1982**, *1*, 37–56.
- [6] Z. R. Huang, Y.-K. Lin, J.-Y. Fang, *Molecules* **2009**, *14*, 540–554.
- [7] For a detailed discussion see a recent study: H. Ramos, E. Silva, L. Gonçalves, *Reduction of the deep-sea shark's by-catches in the Portuguese long-line black scabbard fishery—Final Report to the European Commission* MARE/2011/06 (SI2.602201), **2013**: http://ec.europa.eu/fisheries/documentation/studies/deep-sea-sharks-by-catches/doc/report_en.pdf.
- [8] L. Cockcroft, *Cosmetics giants agree to stop using shark oil*, *The Telegraph*, 30 January 2008, <http://www.telegraph.co.uk/news/uknews/3323530/Cosmetics-giants-agree-to-stop-using-shark-oil.html>.
- [9] a) M. Z. Tsimidou, *Squalene and Tocopherols in Olive Oil: Importance and Methods of Analysis In Olives and Olive Oil in Health and Disease Prevention* (Eds.: V. R. Preedy, R. Ross Watson), Academic Press Life Sciences, San Diego, **2010**, pp. 561–571; b) E. Naziri, F. Mantzouridou, M. Z. Tsimidou, *Lipid Technol.* **2011**, *23*, 270–273.
- [10] *Squalene (CAS 111-01-3) Market Research Report 2014*, BAC Reports.
- [11] P. Tabur, G. Dorin, US 20120040396A1, **2012**.
- [12] K. Fisher, S. J. Schofer, D. B. Kanne, US 20110287988A1, **2011**.
- [13] V. Pandarus, R. Ciriminna, F. Béland, M. Pagliaro, *Org. Process Res. Dev.* DOI: 10.1021/op5002337.
- [14] C.-S. Wu, Y.-J. Tsay, H.-J. Liou, *Taipei. J. Fish. Soc.* **1980**, *7*, 43–55.
- [15] R. Watts, founder of CRM International, personal correspondence with M.P. (August 2014).
- [16] J. Dale, T. Årtun, *Acta Chem. Scand.* **1956**, *10*, 439–444.
- [17] *Fat Products Using Fractionation and Hydrogenation* K. K. Rajah in *Fats in Food Products*, (Eds.: D. P. J. Moran, K. K. Rajah), Springer Science & Business Media, New York, **1994**, pp. 277–317.
- [18] *Heavy Metal Hazard, The Health Risks of Hidden Heavy Metals in Face Makeup*, Environmental Defence, Toronto, May 2011: <http://environmentaldefence.ca/reports/heavy-metal-hazard-health-risks-hidden-heavy-metals-in-face-makeup>.
- [19] See for instance: *The Catalyst Technical Handbook*, Johnson Matthey, **2005**, p. 24: <http://www.jmcatlysts.com/pct/pdfs-uploaded/Pharmaceuticals%20Fine%20Chemicals/Catalyst%20Handbook%20EU.pdf>.
- [20] *Hydrogenation in the Vitamins and Fine Chemicals Industry—An Overview*, W. Bonrath, J. Medlock, J. Schütz, B. Wüstenberg, T. Netscher in *Hydrogenation* (Ed.: I. Karamé), Intech Open, **2012**.
- [21] C. J. Jia, F. Schüth, *Phys. Chem. Chem. Phys.* **2011**, *13*, 2457–2487.
- [22] A. J. Forman, J. N. Park, W. Tang, Y. S. Hu, G. D. Stucky, E. W. McFarland, *ChemCatChem* **2010**, *2*, 1318–1324.
- [23] V. Pandarus, R. Ciriminna, F. Béland, M. Pagliaro, *Adv. Synth. Catal.* **2011**, *353*, 1306–1316.
- [24] V. Pandarus, G. Gingras, F. Béland, R. Ciriminna, M. Pagliaro, *Org. Process Res. Dev.* **2012**, *16*, 1230–1234.
- [25] V. Pandarus, G. Gingras, F. Béland, R. Ciriminna, M. Pagliaro, *Org. Process Res. Dev.* **2012**, *16*, 1307–1311.
- [26] In detail: At 30 °C, complete conversion of squalene to squalane was obtained for 0.25 and 0.33 M concentrations after 6 h (entries 2 and 4 in Table 1), whereas 0.50 M squalene required 8 h reaction time (entry 6). If the temperature is increased from 30 to 50 °C, the complete conversion to squalane is obtained after 4 h for both the 0.33 and 0.50 M concentrations (entries 5 and 7). The conversion to squalane further decreases with the increase of the substrate concentration in the reaction mixture (entries 8 and 9) because of the lower solubility and diffusivity of H₂ gas in the more concentrated reaction mixture. Entries 10–13 show the results if other solvents, which include methanol, MeTHF, and isopropanol, were tested at 50 °C for 0.5 M squalene. Complete conversion to squalane was obtained only in a 1:1 MeTHF/EtOH solvent mixture after 6 h (entry 12).
- [27] *Le prix hideux de la beauté: Le secteur cosmétique responsable de l'extinction de requins profonds*, Bloom, Paris, **2012**: http://www.bloomassociation.org/download/FR_Squalene_LONG.pdf.
- [28] S. R. Mills, *Investor Presentation*, 2013 Credit Suisse Small & Mid Cap Conference Future of Energy Track, Amyris, September 18 **2013**.
- [29] L. O. Garciano II, N. H. Tran, G. S. Kamali Kannangara, A. S. Milev, M. A. Wilson, H. Volk, *React. Kinet. Mech. Catal.* **2013**, *108*, 127–138.
- [30] V. Pandarus, R. Ciriminna, F. Béland, M. Pagliaro, *Catal. Sci. Technol.* **2011**, *1*, 1616–1623.

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