Silsesquioxane-Based Homogeneous and Heterogeneous Epoxidation Catalysts Developed by Using High-Speed Experimentation

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Abstract: A set of new titanium-silsesquioxane epoxidation catalysts was discovered by exploring the hydrolytic condensation of a series of trichlorosilanes in highly polar solvents by means of high-speed experimentation techniques. The most promising silsesquioxane leads were prepared on a conventional laboratory scale and fully 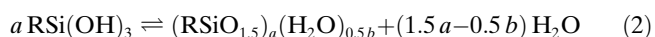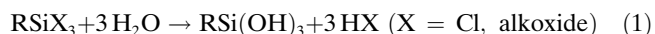characterised. The lead generated by the hydrolytic condensation of tBuSiCl$_3$ in DMSO consisted of a set of incompletely condensed silsesquioxane structures, whereas that obtained from the hydrolytic condensation of tBuSiCl$_3$ in water consisted of a single silsesquioxane structure, tBu$_2$Si$_2$O(OH)$_4$. This is the first reported example of the use of this silsesquioxane as a precursor for active Ti catalysts. The Ti complexes prepared with tBu$_2$Si$_2$O(OH)$_4$ were supported on silica to produce active heterogeneous epoxidation catalysts.

Introduction

Silsesquioxanes are inorganic–organic hybrid compounds with applications ranging from catalysis to materials science and coordination chemistry.[1–3] They have the general formula $(RSiO_{1.5})_a(H_2O)_{0.5b}$, where R is a hydrogen atom or an organic group and a and b are integers [a = 1, 2, 3...; b = 0, 1, 2, 3,...; $a+b$ = $2n$, where n is an integer; $b \leq a+2$]. Incompletely condensed silsesquioxanes ($b \neq 0$) contain silanol groups (Si−OH) that make them applicable as model compounds for silica surfaces or as ligands in coordination chemistry/homogeneous catalysis.[4,5] Silsesquioxanes are usually synthesised by the hydrolytic condensation of organosilanes [Eq. (1) and (2)].[1,6] The selectivity towards and yields of specific silsesquioxane structures are influenced by many parameters.[1] Therefore, a combinatorial chemistry and high-speed experimentation[7] approach, which allows the fast screening of broad parameter spaces, is particularly suitable to study and optimise the synthesis of these compounds. Recently, high-speed experimentation (HSE) techniques have been successfully applied to the optimisation of silsesquioxane precursors for titanium catalysts active in the epoxidation of alkenes.[8,9] This work resulted in a new and efficient way of synthesising silsesquioxane precursors and generated knowledge about the effect of the various parameters involved in the synthesis. In particular, one of the observed trends indicated favourable effects induced by high polarity solvents. This result stimulated further investigation, and herein the application of HSE techniques to the optimisation of the synthesis of silsesquioxanes in very polar solvents is presented.

$$RSiX_3 + 3\,H_2O \rightarrow RSi(OH)_3 + 3\,HX \quad (X = Cl, \text{alkoxide}) \quad (1)$$

$$a\,RSi(OH)_3 \rightleftharpoons (RSiO_{1.5})_a(H_2O)_{0.5b} + (1.5\,a - 0.5\,b)\,H_2O \quad (2)$$

The experimental approach is similar to that used in previous studies.[8,9] The synthesis of silsesquioxane precursors is optimised as a function of the epoxidation activity of the catalysts obtained after titanium complexation. Therefore, this approach is aimed at producing any incompletely condensed silsesquioxane that might result in active catalysts after titanium complexation rather than a specific silsesquioxane structure. A reaction time of 18 h was chosen for the hydrolytic condensation, since one of the goals of this work is to decrease the long time commonly required to synthesise silsesquioxane precursors.[1,10]

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Results and Discussion

The high-speed experimentation screening: Silsesquioxane precursors for titanium catalysts were synthesised by the hy-

drolytic condensation of six different trichlorosilanes (R = cyclohexyl, cyclopentyl, phenyl, methyl, ethyl, and *tert*-butyl) in three highly polar solvents (dimethyl sulfoxide (DMSO), water and formamide) by means of high-speed experimentation techniques. Previous work showed that the R group on the organosilane and the solvent in which the hydrolytic condensation is carried out are the most relevant parameters influencing the synthesis of silsesquioxanes.[8, 11] The parameter space studied was defined by the full-factorial combination of the six trichlorosilanes and the three solvents. This parameter space was screened as a function of the activity of the catalysts obtained after coordination of [Ti(OBu)$_4$] to the silsesquioxane structures in the epoxidation of 1-octene with *tert*-butyl hydroperoxide (TBHP).[12] In Figure 1, the relative activities of the titanium silsesquioxanes are shown together with those of the titanium silsesquioxanes obtained from silsesquioxanes synthesised in ace-

almost the same activity as the previous best HSE catalyst (87%) obtained from cyclopentyl silsesquioxanes synthesised in acetonitrile,[8, 9, 14] and are the first reported examples of *tert*-butyl silsesquioxanes as precursors for very active titanium catalysts. Significant catalytic activities were also obtained with cyclohexyl silsesquioxanes synthesised in DMSO (67%) and with phenyl silsesquioxanes synthesised in H$_2$O (61%).

Besides the identification of these leads, the HSE screening provided some more information about the system under study. No regular trend can be identified, that is, for each solvent the order of activity as a function of the R groups is different. This can be explained on the basis of the different natures of the solvents employed. Water acts both as solvent and reagent, and the fact that only silsesquioxanes with a very low level of condensation are soluble in water[15] means that condensed structures are rapidly precipitated from solution. Formamide has a high boiling point (220 °C), necessitating the use of high temperatures to remove the solvent from the silsesquioxane products. At these high temperatures, the silsesquioxanes tend to condense further to produce completely condensed structures, which are not suitable for binding metal centres.[1] This may explain the weak activity observed for the catalysts obtained from silsesquioxanes synthesised in formamide.

Finally, all the methyl and ethyl silsesquioxanes proved to be poor precursors for titanium-based epoxidation catalysts, in agreement with what was found in previous work.[8, 9]

Consequently, the *tert*-butyl silsesquioxanes synthesised in DMSO and water (that is, the silsesquioxane precursors that gave the most active catalysts; see Figure 1)
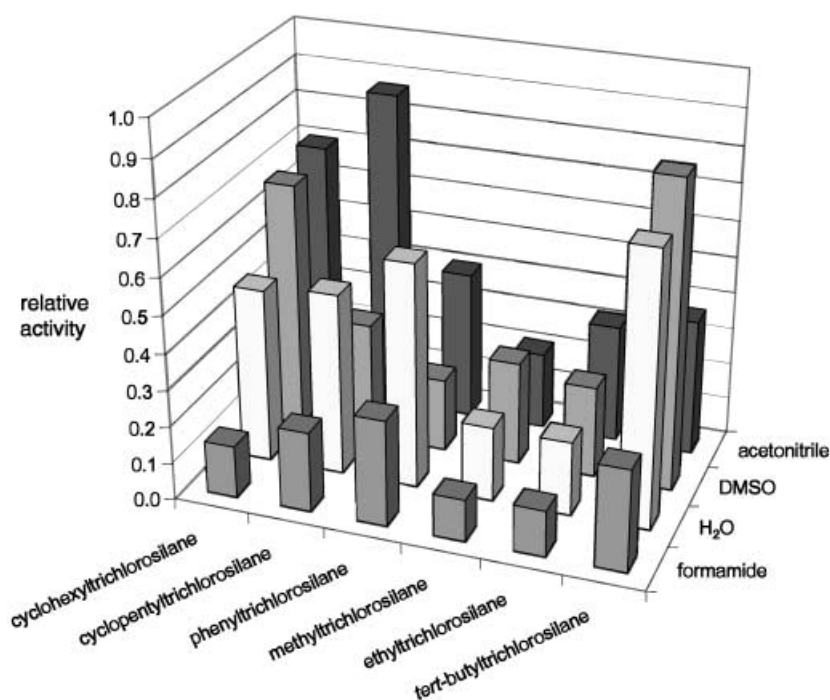

Figure 1. Screening of the epoxidation activity of the titanium silsesquioxanes as a function of the solvent and of the trichlorosilanes used in the synthesis of the silsesquioxane precursors.

tonitrile, which gave the best results among the solvents tested in previous work.[8, 9] The values are normalised to the activity of the most active titanium silsesquioxane found so far, specifically that obtained by reacting [Ti(OBu)$_4$] with cyclopentyl silsesquioxane $a7b3$ [(c-C$_5$H$_9$)$_7$Si$_7$O$_{12}$-TiOC$_4$H$_9$].[12, 13] The highest catalytic activities were found for the titanium complexes obtained from *tert*-butyl silsesquioxanes synthesised in DMSO and water, with 84% and 74%, respectively, of the activity of the reference catalyst (c-C$_5$H$_9$)$_7$Si$_7$O$_{12}$TiOC$_4$H$_9$.[1] These two catalysts exhibited

were synthesised on a conventional laboratory scale and fully characterised by appropriate analytical techniques.

***tert*-Butyl silsesquioxanes synthesised in DMSO**: The hydrolytic condensation of *tert*-butyltrichlorosilane in DMSO was performed in a 25-fold scale-up of the HSE synthesis. tBuSiCl$_3$ is a solid at room temperature, and since the HSE workstation employed can only handle liquids, the trichlorosilane was first dissolved in the minimum volume of acetonitrile. The same procedure was used for the scaled-up synthesis. After 18 h of reaction at 50 °C, the clear solution obtained was distilled under reduced pressure to give a yellow gel that still contained

[1] Under the experimental conditions employed, (c-C$_5$H$_9$)$_7$Si$_7$O$_{12}$TiOC$_4$H$_9$ gives complete and selective conversion of TBHP to the epoxide: therefore, the relative activities of the reported catalysts correspond to their conversions of TBHP to 1,2-epoxyoctane.

DMSO.[II] Adding water to the gel caused the precipitation of the silsesquioxane product, which could then be separated from the DMSO/H₂O solution. ¹³C and ²⁹Si NMR analysis showed that the sample consisted of a number of oligomeric silsesquioxane species. The ²⁹Si NMR spectrum (Figure 2) shows two sets of peaks, one in the region of silicon atoms connected to three other silicon atoms through oxygen bridges ($\delta = -61$ to -55 ppm), and the other corresponding to silicon atoms bearing one or more OH group(s) ($\delta = -51$ to -45 ppm).[1] The latter set of peaks has a much higher intensity than the former, indicating that most of the silsesquioxanes are incompletely condensed structures with a low level of condensation. Characterisation by mass spectrometry showed that the main species is an $a = 4$ structure (i.e., consisting of four $t\mathrm{BuSiO_{1.5}(H_2O)_{0.5x}}$ units), followed, in decreasing order of concentration, by $a = 5$, $a = 3$, $a = 6$, and $a = 7$ silsesquioxanes. Due to the possibility of intramolecular condensation accompanied by loss of water molecules during the ionisation process, the level of condensation of the silsesquioxanes (i.e., the b value) cannot be determined by means of MS analysis of the crude product. More information about the number of silanol groups present in the silsesquioxane structures can be obtained by their silylation with trimethylchlorosilane (CH₃)₃SiCl.[16,17] MS analysis of the products of the silylation reaction showed a main peak corresponding to a disilylated a4b4 structure; other species in significant concentrations were mono- and disilylated a3b3, mono- and disilylated a4b2, monosilylated a4b4, mono- and disilylated a5b3, and di- and trisilylated a5b5. While these MS data indicated the
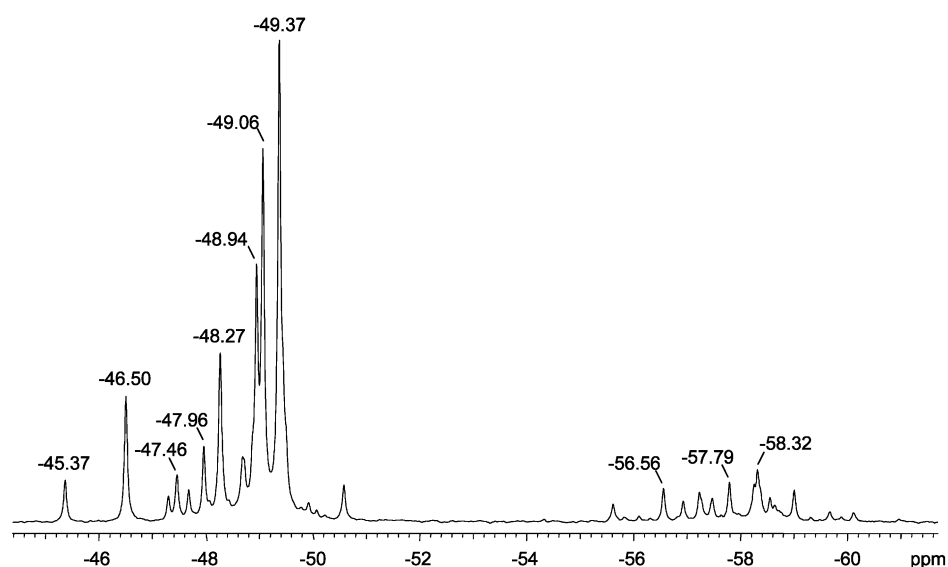

Figure 2. Liquid-phase ²⁹Si NMR spectrum of the *tert*-butyl silsesquioxanes obtained by the hydrolytic condensation of *tert*-butyltrichlorosilane in DMSO.
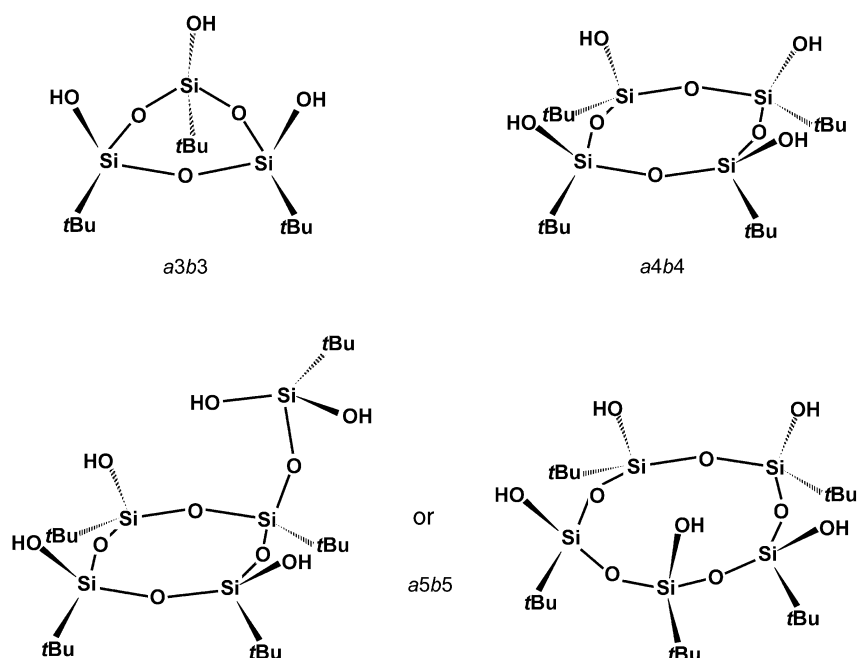

Figure 3. *tert*-Butyl silsesquioxanes a3b3, a4b4 and a5b5. For this type of structure it has been proposed that the *syn*-conformation of the hydroxyls is the favoured one (stabilisation by intramolecular hydrogen bonding).[25–27]

presence of a3b3, a4b4, and a5b5 structures, they did not allow us to establish whether structures a4b2 and a5b3 were actually present in the product mixture or were formed in the mass spectrometer. Taking together the results from the NMR and MS analyses, it is proposed that the major components of the product were silsesquioxanes a3b3 [$t\mathrm{Bu_3Si_3O_3(OH)_3}$], a4b4 [$t\mathrm{Bu_4Si_4O_4(OH)_4}$], and a5b5 [$t\mathrm{Bu_5Si_5O_5(OH)_5}$], for which the most likely structures are depicted in Figure 3.

The mixture of *tert*-butyl silsesquioxanes was treated with [Ti(OBu)₄] and the complexes obtained were tested for catalytic activity in the epoxidation of 1-octene with TBHP,

[II] Removing DMSO from the silsesquioxanes is necessary to prevent competition between the oxidation of DMSO to dimethyl sulfone and the epoxidation of 1-octene to 1,2-epoxyoctane. Complete removal of DMSO was attained in the HSE experiments by drying the samples in a vacuum centrifuge, which proved to be more effective than distillation in vacuo.

giving analogous results to those obtained with the corresponding HSE lead. An epoxidation test with aqueous H_2O_2 as the oxidant gave negligible activity accompanied by catalyst deactivation.

***tert*-Butyl silsesquioxanes synthesised in H_2O**: The hydrolytic condensation of *tert*-butyltrichlorosilane, *t*BuSiCl$_3$, in water was performed in a 25-fold scale-up of the HSE synthesis. As described above for the synthesis of *tert*-butyl silsesquioxanes in DMSO, *t*BuSiCl$_3$ was first dissolved in the minimum volume of acetonitrile and then added to H_2O. After 18 h of reaction at 50°C, the reaction mixture contained a white precipitate, which was isolated by filtration (fraction A). Upon removal of the solvent from the filtrate under reduced pressure, a further batch of white solid was obtained (fraction B). Next, the two fractions were dried in an oven at 100°C. Liquid-phase NMR characterisation showed that both fractions contained the same single silsesquioxane structure composed of equivalent *t*BuSiO$_{1.5}$-$(H_2O)_{0.5x}$ units (Figure 4). The position of the ^{29}Si NMR peak ($\delta = -49.55$ ppm) indicates that this silsesquioxane contains one or more silanol groups ($x \geq 1$).[1] The structure was assigned to silsesquioxane *t*Bu$_2$Si$_2$O(OH)$_4$ (Figure 5; structural coding *a2b4*; cf. Equations (1) and (2)) on the basis of these NMR data and a single-crystal X-ray diffraction analysis, which provided the same cell parameters of the *tert*-butyl silsesquioxane *a2b4* reported in the literature.[18] The synthetic procedure reported here allows complete and selective conversion of *t*BuSiCl$_3$ into silsesquioxane *t*Bu$_2$Si$_2$O(OH)$_4$. This method is much more straightforward and results in a higher isolated yield (90%) than the literature method (65%), in which the compound is synthesised by addition of *t*BuSiCl$_3$ in diethyl ether to a mixture of KOH, water, and methanol.[18] The selectivity of the synthesis is ascribed to the bulkiness of the *tert*-butyl group, which may hinder further reaction of *t*Bu$_2$Si$_2$O(OH)$_4$, and to the use of water as the solvent, which disfavours condensation (cf. Equation (2)).

The fact that silsesquioxane *a2b4* was obtained as the only product both as a precipitate and on removal of the solvent from the remaining reaction mixture prompted an investigation of whether a shorter reaction time would lead to the same product. Therefore, the hydrolytic condensation was performed for just 20 minutes at room temperature. The solvent was then removed by filtration to afford a white solid, which was dried in an oven at 100°C. ^{13}C and ^{29}Si NMR analysis showed that, besides silsesquioxane *a2b4*, the product contained a second species, assigned to the trisilanol *t*BuSi(OH)$_3$ (structural coding *a1b3*, cf. Equations (1) and (2))[19] on the basis of the position of the ^{29}Si NMR peak ($\delta = -40.06$ ppm).[1] The molecular ratio between the *a1b3* and *a2b4* structures was about 2:1. This experiment indicates that the formation of *tert*-butyl silsesquioxane *a2b4* takes place by the slow condensation of *tert*-butyl silsesquioxane *a1b3*. The silsesquioxane *a2b4* does not react further and it starts to precipitate as its concentration in the solution increases. Further investigation showed that 7 h of hydrolytic condensation at 50°C is necessary to obtain silsesquioxane *a2b4* as the only product.
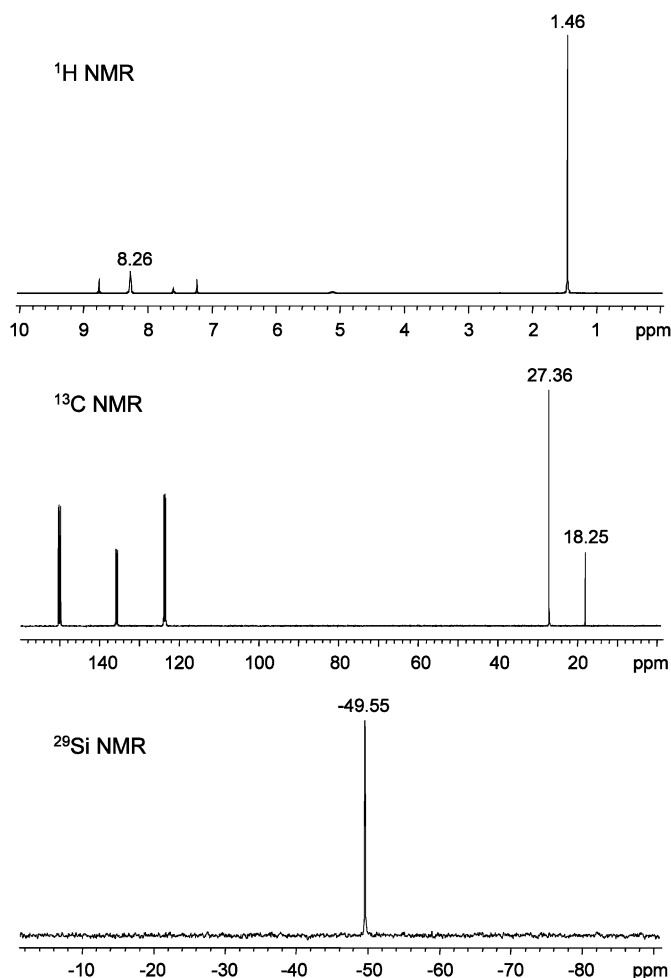

Figure 4. ^{1}H, ^{13}C and ^{29}Si NMR spectra of *tert*-butyl silsesquioxane *t*Bu$_2$-Si$_2$O(OH)$_4$, obtained by the hydrolytic condensation of *tert*-butyltrichlorosilane in H_2O. In the ^{1}H NMR spectrum (top), two peaks in a 9:2 ratio are present: the signal at $\delta = 1.46$ ppm is due to the methyl resonances of the *tert*-butyl groups, and that at $\delta = 8.26$ ppm is due to the four silanol groups. The three additional peaks in the region $\delta = 7$–9 ppm are due to pyridine (present in small amounts in the deuterated solvent). In the ^{13}C NMR spectrum (middle), two peaks in a 3:1 ratio are present: the signal at $\delta = 27.36$ ppm is due to the three equivalent methyl groups of the *tert*-butyl groups, while that at $\delta = 18.25$ ppm is due to the *ipso*-carbon atom of the *tert*-butyl group. The peaks in the region $\delta = 120$–150 ppm are due to pyridine (the solvent). The peak seen in the ^{29}Si NMR spectrum (bottom) is due to the two equivalent silicon atoms present in structure *a2b4*.
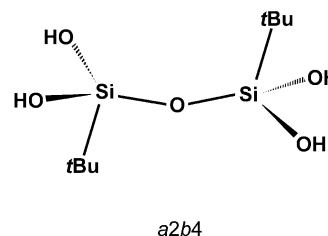
Figure 5. *tert*-Butyl silsesquioxane *a2b4*, *t*Bu$_2$Si$_2$O(OH)$_4$.

The nature of the solvent in which the *t*BuSiCl$_3$ is dissolved before being added to the water does not seem to influence the reaction: the same product was obtained if acetone was used instead of acetonitrile. On the other hand,

the amount of this co-solvent does have an effect: when the tBuSiCl$_3$ was dissolved in a fivefold smaller volume of acetone, after 18 h at 50 °C the hydrolytic condensation produced large amounts of a precipitate containing viscous polymeric silsesquioxanes together with structure $a2b4$ (as determined by NMR analysis). After removal of the precipitate by filtration, concentration of the filtrate afforded silsesquioxane $a2b4$. The lower selectivity and the increased amount of precipitate indicate that when less co-solvent is present in solution, the formation and the precipitation of silsesquioxanes take place more rapidly, probably as a consequence of the reduced solubility of the silsesquioxanes in the reaction mixture.

These observations confirm the complexity of the mechanism of formation of silsesquioxanes: small changes in the reaction conditions result in significantly different amounts and types of structures.

Besides the intrinsic value of the identification of a new, selective, and high-yielding method for the synthesis of silsesquioxane tBu$_2$Si$_2$O(OH)$_4$, this experiment proved that $tert$-butyl silsesquioxane $a2b4$ is a suitable precursor for titanium catalysts. Thus, silsesquioxane structures different from the known precursor silsesquioxane $a7b3$ [R$_7$Si$_7$O$_9$(OH)$_3$][12,13,20] can effectively coordinate titanium centres to yield almost equally active epoxidation catalysts. To investigate how the titanium centre coordinates to $tert$-butyl silsesquioxane $a2b4$ and to ascertain the optimum number of titanium centres that the structure can accommodate, catalysts with different titanium-to-silsesquioxane ratios were prepared, characterised, and tested. The HSE lead had a titanium-to-silsesquioxane ratio of about 1:3, the ratio having been tuned for more condensed silsesquioxanes (e.g. structure $a7b3$), which have a low average number of OH groups per silicon atom. Silsesquioxane $a2b4$ has four OH groups that may react with titanium alkoxide complexes. Coordination of a titanium centre to two OH groups on the same silicon would produce a geometrically strained complex and is, therefore, unlikely. In principle, each titanium could coordinate to two OH groups on two different silicons to form a polymeric chain with alternate titanium centres and silsesquioxane units (Figure 6). This chain would have a 1:1 titanium-to-silsesquioxane molar ratio. Less ordered structures with a titanium-to-silsesquioxane molar ratio >1 are also possible. Therefore, complexes were prepared by reacting [Ti(OBu)$_4$] with $tert$-butyl silsesquioxane $a2b4$ in

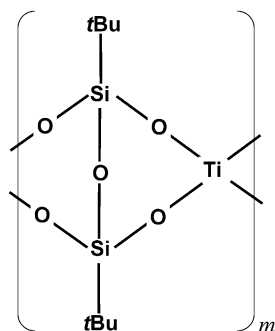Figure 6. Ideal structure of a polymeric chain obtained from the reaction of Ti(OBu)$_4$ with tBu$_2$Si$_2$O(OH)$_4$ in a 1:1 molar ratio.

1:1 (catalyst **I**) and 2:1 (catalyst **II**) molar ratios. The two catalysts were characterised and tested for epoxidation activity.

The liquid-phase ^{29}Si NMR spectrum of catalyst **I** shows a single peak at $\delta = -49.55$ ppm due to the unreacted $tert$-butyl silsesquioxane $a2b4$, while that of catalyst **II** features a very weak and broad signal at around $\delta = -56$ ppm. These data indicate that a titanium-to-silsesquioxane ratio >1 is needed to react all the silsesquioxane $a2b4$ and suggest that both catalysts consist of polymeric titanium complexes (which are difficult to detect by liquid-phase ^{29}Si NMR spectroscopy). The solid-state ^{29}Si NMR spectrum of catalyst **I** (Figure 7, top) shows the peak due to $tert$-butyl silsesquioxane $a2b4$ (already visible in the liquid-phase spectrum) and
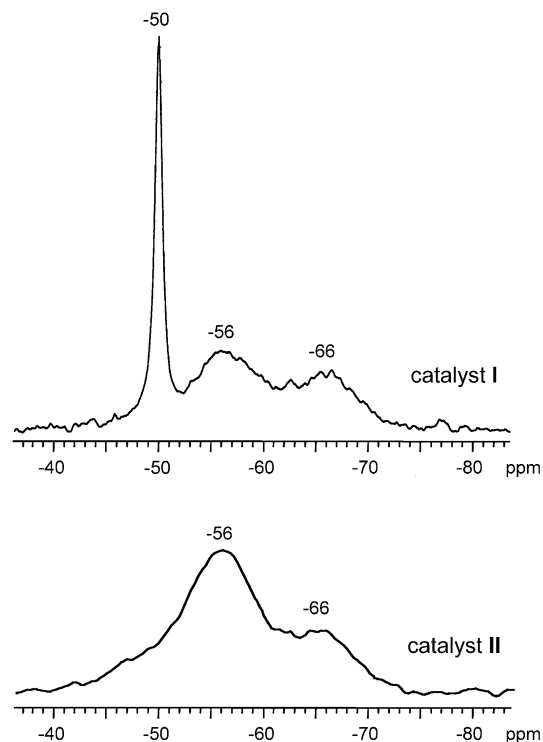

Figure 7. Solid-state ^{29}Si NMR spectra of catalyst **I** (top) and of catalyst **II** (bottom).

two broad signals centred at $\delta = -56$ ppm and $\delta = -66$ ppm (integral ratio $\approx$ 1:2:1). The complexation of titanium causes the silicon peak position to move towards higher chemical shifts,[14,21] suggesting that the signals around $\delta = -56$ ppm originate from siloxy groups to which one titanium centre is coordinated, while those at $\delta = -66$ ppm derive from siloxy groups to which two titanium centres are coordinated. The solid-state ^{29}Si NMR spectrum of catalyst **II** (Figure 7, bottom) shows two broad and partially overlapping signals. These two peaks are in the same positions as those found for catalyst **I**, but exhibit a different ratio (4:1 as compared to 2:1), consistent with catalyst **II** containing proportionally more siloxy groups to which only one titanium centre is coordinated.

The liquid-phase ^{13}C NMR spectra of both catalysts confirm that the titanium complexation took place and generated different types of complexes: a set of overlapping signals

is present in the region of the methyl resonances of the *tert*-butyl groups on the silsesquioxanes ($\delta = 27.3$ to 27.5 ppm) and another in the region of the *ipso* carbons of the *tert*-butyl groups ($\delta = 18.1$ to 18.3 ppm), see Figure 8 (top). Besides these peaks, the spectra feature four peaks of equal intensity due to *n*-butanol. The solid-state ^{13}C NMR spectra of both catalysts contain two broad signals in the expected 3:1 ratio, due to the methyl groups and the *ipso*-carbon atoms of the *tert*-butyl groups on the silsesquioxanes, respectively, consistent with what was observed in the liquid-phase ^{13}C NMR spectrum (Figure 8). Besides these signals, the spectra show four broad peaks attributable to a butoxy group coordinated to a titanium.[22,23] The extreme broadness of the peak centred at $\delta = 79$ ppm, which is due to the carbon in the position α to the oxygen atom of the butoxy group, can be attributed to the presence of different types of titanium centres and/or to fast relaxation caused by poor mobility of the α-carbon atom. Different degrees of complexation of titanium butoxide to the silsesquioxane *a2b4* may have occurred: the butoxide groups can be partially or completely substituted by coordination to the silsesquioxanes. In addition, the butoxide signals could also be due to *n*-butanol that was released during the complexation of titanium butoxide to the silsesquioxane structures and that may still have been coordinated to the titanium centres. The difference in peak position of the α-carbon signal in the solid-state and liquid-phase ^{13}C NMR spectra indicates that, in solution, the butoxy groups originally coordinated to the titanium are exchanged with pyridine (the solvent), which is known to coordinate to titanium centres.[24]

Upon gel permeation chromatography, catalyst **I** was resolved into two bands. The first, with a number average molecular weight of 273 g mol^{-1}, corresponds to the unreacted *tert*-butyl silsesquioxane *a2b4* (MW = 254.43 g mol^{-1}), as also detected by NMR spectroscopy. The polydispersity of this band is 1.24, in agreement with the presence of a single species. The second band, with a number average molecular weight of 1615 g mol^{-1}, has a polydispersity of 2.14, indicating the presence of different structures. This suggests that, on average, the titanium silsesquioxane complexes are composed of four or five *a2b4* structures and five or six titanium centres.

Catalysts **I** and **II** were tested for epoxidation activity with TBHP as the oxidant (Figure 9; Table 1), using the same titanium-to-substrate ratio for both. The two catalysts displayed higher activities (per mole of titanium) than the HSE lead (74% TBHP conversion to 1,2-epoxyoctane after 4 h of reaction): catalyst **I** gave 80% conversion after 3 h and reached a plateau at 93% conversion (TOF = 0.44 mol$_{epo}$ mol$_{Ti}^{-1}$ min^{-1}); catalyst **II** gave 90% conversion after 3 h and reached
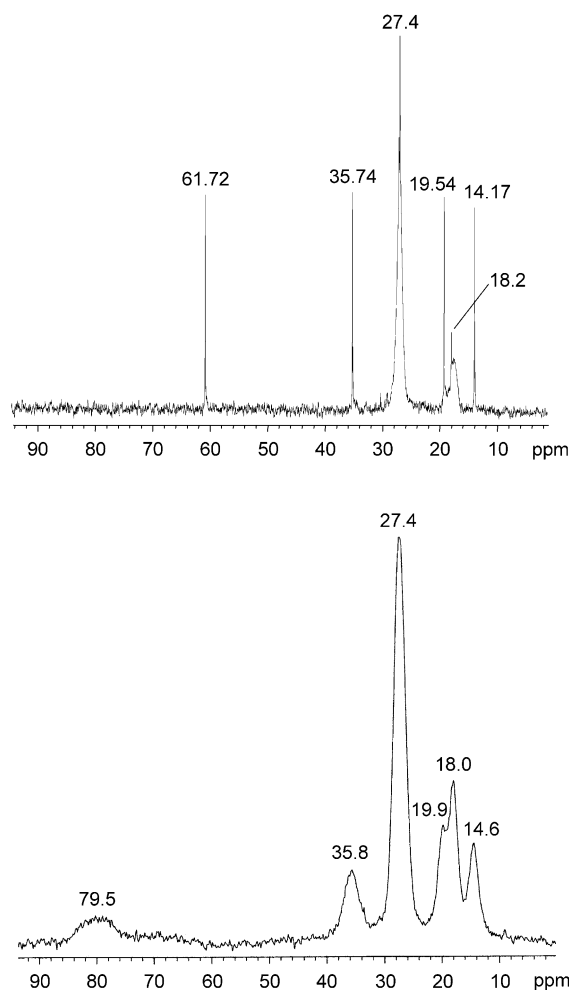

Figure 8. Liquid-phase (top) and solid-state (bottom) ^{13}CNMR spectra of catalyst **II**.

a plateau at 97% conversion (TOF = 0.54 mol$_{epo}$ mol$_{Ti}^{-1}$ min^{-1}). Both catalysts exhibited 97% selectivity in favour of 1,2-epoxyoctane. Catalyst **II** is homogeneously dissolved in the epoxidation mixture, while catalyst **I** does not dissolve completely: the insoluble fraction probably consists of un-
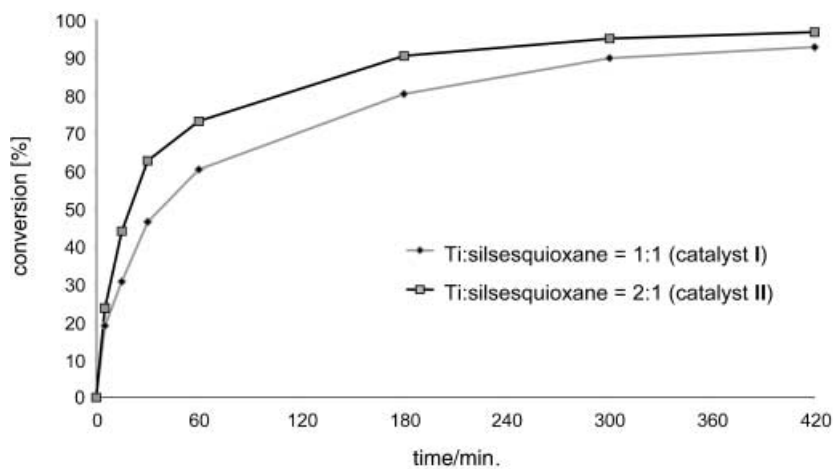

Figure 9. Activity of Ti-*a2b4* complexes with 1:1 and 2:1 titanium-to-silsesquioxane ratios in the epoxidation of 1-octene with TBHP. The concentration of titanium and the titanium-to-TBHP ratio were the same in the two catalytic tests.

Table 1. Conversions and selectivities in the epoxidation of 1-octene with TBHP. The same titanium:substrate ratio was used in all the catalytic tests.

Catalyst	Ti:silsesquioxane	Conversion (3 h) [%]	Selectivity[c] [%]
I	1:1	80	97
II	2:1	90	97
III[a]	1:1	94	92
IV[b]	1:1	94	92

[a] Supported on silica. [b] Supported on silylated silica. [c] Interestingly, the selectivity in favour of the epoxide is slightly lower in the case of the heterogeneous catalysts even though virtually no formation of diol as a side product can be detected. This is consistent with a separate oxidation pathway involving radicals of homolytically disassociated TBHP, a path promoted by the presence of a high surface area solid.

reacted silsesquioxane $a2b4$, which is not soluble in 1-octene. The difference in activity between catalyst **I** and catalyst **II** probably originated from the different nature of the titanium centres (e.g., in terms of accessibility), as determined by solid-state ^{29}Si NMR analysis.

The catalytic sites of these titanium silsesquioxanes show strong interaction with alcohols: if the epoxidation test of catalyst **I** was performed in a 1:1 mixture of 1-octene and 1-propanol, very low activity was found. This deactivation is reversible: the expected epoxidation activity was recovered when reusing the catalyst without 1-propanol as a co-solvent. The same loss of activity was observed when methanol was used as a co-solvent instead of 1-propanol. This reversible coordination of alcohols to the titanium is in agreement with the results of the ^{13}C NMR analysis of the titanium-silsesquioxane $a2b4$ complexes. The catalyst deactivation is ascribed to the interaction between the hydroxy group and the titanium centre,[13] which would reduce the accessibility of the catalytic site. The deactivation caused by coordination of alcohols to the titanium centre is not encountered when using $(c\text{-}C_5H_9)_7Si_7O_{12}TiOC_4H_9$ as the catalyst, pointing to a different nature of the catalytic centre in this case.

The main drawback of homogeneous catalysts lies in the difficulty of recovering them from the reaction mixture. In order to overcome this negative aspect, the titanium-silsesquioxane $a2b4$ complex was supported on high surface area silica and the materials obtained were tested as heterogeneous catalysts for the epoxidation of 1-octene. Titanium silsesquioxane $a2b4$ was supported by adsorption on two types of silica: one untreated and the other dehydroxylated by derivatisation with $(CH_3)_2SiCl_2$ (catalysts **III** and **IV**, respectively). The larger size of the titanium-silsesquioxane complexes compared to that of the other molecules present in the epoxidation mixture should favour their adsorption as well as prevent their leaching from the silica supports (entropic driving force). After adsorption of the complexes on the silica supports, possible leaching species were removed by prolonged Soxhlet extraction with tetrahydrofuran. The epoxidation test gave a 94% TBHP conversion and 92% selectivity in favour of 1,2-epoxyoctane after 3 h of reaction for both catalysts. The absence of leaching of the titanium silsesquioxanes from the silica support was verified by filtering the solid from the epoxidation mixture and measuring the catalytic activity of the possible soluble titanium silsesquioxanes: the soluble fractions showed negligible epoxidation activity (equal to that of a blank sample), thus proving that no leaching of active species had occurred. The hetero-

geneous catalyst supported on untreated silica (**III**) could be reused for three cycles and retained comparable epoxidation activity.

The titanium-silsesquioxane $a2b4$ complexes were supported on both untreated and silylated silica in order to investigate the nature of the adsorption. The similar activity and selectivity obtained with the two supports suggests that the adsorption of the complexes takes place by physical interaction with the silica surface rather than through chemical anchoring on the OH groups (totally or almost absent from the silica derivatised with $(CH_3)_2SiCl_2$).

Remarkably, the heterogeneous catalysts displayed epoxidation activities (per mole of titanium) similar to that of the homogeneous titanium-silsesquioxane $a2b4$ complexes (see Table 1).

Neither the homogeneous titanium-silsesquioxane $a2b4$ complexes nor the silica-supported heterogeneous catalysts showed good activity in the epoxidation of 1-octene with aqueous H_2O_2 as the oxidant.

Conclusions

The effect of highly polar solvents on the hydrolytic condensation of a series of trichlorosilanes to produce silsesquioxane precursors for titanium catalysts active in the epoxidation of alkenes was studied by high-speed experimentation techniques. The HSE screening allowed the identification of a number of leads. The most promising of these, namely *tert*-butyl silsesquioxane $a2b4$, synthesised by the hydrolytic condensation of *tert*-butyltrichlorosilane in water, was studied in detail. The catalysts obtained by complexation of titanium butoxide to the silsesquioxane $a2b4$ displayed very good activity and selectivity in the epoxidation of 1-octene with TBHP. Characterisation showed that these catalysts consist of various titanium centres and silsesquioxane units linked to each other in different arrangements. Titanium silsesquioxane $a2b4$ complexes can be supported on silica to produce an active, non-leaching, recyclable, heterogeneous epoxidation catalyst.

Experimental Section

The high-speed experimentation screening: The HSE samples were prepared by means of a Hamilton dual-arm liquid-handling robotic workstation[I] coupled with a personal computer supplied with software enabling programming of the workstation. Reagents for the hydrolytic condensation were cyclohexyl-, cyclopentyl-, phenyl-, methyl-, ethyl-, and *tert*-butyltrichlorosilanes; the latter was pre-dissolved in acetonitrile (340 μmol in 0.5 mL of CH_3CN); acetonitrile, dimethyl sulfoxide (DMSO), deionised water, and formamide were used as solvents (the organic solvents were p. a. grade). The silsesquioxane precursors were prepared by dispensing aliquots of each of the solvents (2 mL) into racks containing 6×4

[I] Kindly provided by Avantium Technologies.

arrays of glass tube reactors (3 mL working volume), and this was followed by the addition of each of the trichlorosilanes (340 μmol) and of deionised water (0.5 mL) to each reaction tube. Subsequently, the racks were placed in a steel heater block mounted on an orbital shaker and heated to 50°C for 18 h. After evaporation of the liquids in a vacuum centrifuge overnight, the silsesquioxane samples were redissolved in tetrahydrofuran (THF), titanium butoxide ([Ti(OBu)$_4$], 98% purity, 54 μmol) was added to each sample, and the solutions in the rack were stirred for 6 h at 60°C. After titanium complexation, THF was removed by vacuum centrifugation. Each sample was then tested for epoxidation activity by adding 1-octene (2.26 mL, with 2% (v/v) of decane as internal standard) and TBHP (121 μL, ≈45% (w/w) solution in cyclohexane). After having been stirred in the orbital shaker for 4 h at 80°C, the samples were analysed on an automated Unicam Pro GC under isothermal conditions. The activities were obtained by normalising the 1,2-epoxyoctane GC peak area by reference to the internal standard. The reported results are averages of multiple runs.

***tert*-Butyl silsesquioxanes synthesised in DMSO**: *tert*-Butyltrichlorosilane (*t*BuSiCl$_3$, >95% purity, 1.63 g) was dissolved in acetonitrile (12.5 mL). The solution was added to DMSO (37.5 mL), and then deionised water (12.5 mL) was added. The transparent, colourless solution was stirred for 18 h at 50°C and then distilled under reduced pressure to remove volatile species and to isolate the silsesquioxanes. The yellow gel obtained still contained DMSO, which was removed by adding H$_2$O (50 mL): the silsesquioxanes precipitated as a sticky, soft solid that adhered to the glass walls of the reaction flask, from which the water/DMSO solution was easily removed. The silsesquioxane mixture was found to be soluble in THF and pyridine.

The silylation of the silsesquioxane mixture was performed by adding trimethylchlorosilane (CH$_3$)$_3$SiCl (172 μL) to a solution of the silsesquioxanes (0.04 g) in toluene (30 mL) and triethylamine (C$_2$H$_5$)$_3$N (1 mL). The turbid solution was stirred overnight at room temperature. Thereafter, the toluene and triethylamine were removed under reduced pressure, to leave a white solid. This solid was extracted with pentane; the resulting suspension was filtered to remove the insoluble (C$_2$H$_5$)$_3$N·HCl and concentrated and dried under reduced pressure to yield a solid containing the silylated silsesquioxanes.

The titanium complexation and the catalytic tests were performed in a similar manner as described for the HSE study. The molar ratio between titanium and TBHP, as well as the concentrations of TBHP in the reaction mixtures, were the same in all the catalytic tests reported in this article.

The ^{29}Si NMR spectrum of the silsesquioxane mixture was recorded on a Varian Inova 300 spectrometer (^{1}H decoupled, 25°C). Selected data: ^{29}Si{^{1}H} NMR (liquid phase, [D$_5$]pyridine as the solvent): δ = −45.37 (relative integral ≈1), −46.50 (≈3), −47.46 (≈1), −47.96 (≈2), −48.27 (≈4.5), −48.94 (≈6.5), −49.06 (≈8.5), −49.37 (≈11), −56.56 (≈1), −57.79 (≈1), −58.32 ppm (≈1).

Mass spectrometric analysis was performed on a Micromass Quattro LC-MS with APCI+ as the ionisation technique. For the analysis, the sample (≈0.03 g) was dissolved in CH$_2$Cl$_2$/THF (4:1; 5 mL) and few drops of CH$_3$CO$_2$H were added.

Silsesquioxane product (cone voltage = 45 V): for *a* = 3, *m/z* (%): 337.50 (20) [*a3b1*+H]$^+$, 355.54 (17) [*a3b3*+H]$^+$, 409.50 (22) [*a3b5*+2H$_2$O+H]$^+$; for *a* = 4, *m/z* (%): 437.47 (100) [*a4b0*+H]$^+$, 455.52 (99) [*a4b2*+H]$^+$, 509.54 (32) [*a4b6*+H$_2$O+H]$^+$, 527.39 (28) [*a4b6*+2H$_2$O+H]$^+$; for *a* = 5, *m/z* (%): 537.45 (40) [*a5b1*−H$_2$O+H]$^+$, 555.56 (25) [*a5b1*+H]$^+$, 573.48 (52) [*a5b3*+H]$^+$, 627.43 (14) [*a5b7*+H$_2$O+H]$^+$; for *a* = 6, *m/z* (%): 655.35 (15) [*a6b0*+H]$^+$, 673.39 (33) [*a6b2*+H]$^+$, 691.25 (11) [*a6b4*+H]$^+$; for *a* = 7, *m/z* (%): 773.37 (14) [*a7b1*+H]$^+$, 791.17 (7) [*a7b3*+H]$^+$, 809.34 (9) [*a7b5*+H]$^+$; for *a* = 8, *m/z* (%): 873.34 (4) [*a8b0*+H]$^+$, 891.20 (6) [*a8b2*+H]$^+$, 909.06 (6) [*a8b4*+H]$^+$, 927.17 (5) [*a8b6*+H]$^+$; for *a* = 9, *m/z* (%): 991.30 (7) [*a9b1*+H]$^+$, 1027.15 (9) [*a9b5*+H]$^+$, 1045.32 (6) [*a9b7*+H]$^+$; for *a* = 10, *m/z* (%): 1145.23 (11) [*a10b6*+H]$^+$.

Silylated silsesquioxanes (cone voltage = 15 V): for *a* = 3, *m/z* (%): 427.66 (37) [silylated *a3b3*+H]$^+$, 499.61 (22) [disilylated *a3b3*+H]$^+$; for *a* = 4, *m/z* (%): 455.64 (16) [*a4b2*+H]$^+$, 527.53 (51) [silylated *a4b2*+H]$^+$, 545.53 (38) [silylated *a4b4*+H]$^+$, 599.53 (22) [disilylated *a4b2*+H]$^+$, 617.60 (100) [disilylated *a4b4*+H]$^+$, for *a* = 5, *m/z* (%): 645.52 (37) [sily-

lated *a5b3*+H]$^+$, 717.46 (17) [disilylated *a5b3*+H]$^+$, 735.40 (19) [disilylated *a5b5*+H]$^+$, 807.41 (11) [trisilylated *a5b5*+H]$^+$; for *a* = 6, *m/z* (%): 763.45 (7) [silylated *a6b4*+H]$^+$, 835.33 (7) [disilylated *a6b4*+H]$^+$; for *a* = 7, *m/z* (%): 953.32 (7) [disilylated *a7b5*+H]$^+$.

***tert*-Butyl silsesquioxanes synthesised in H$_2$O**: *tert*-Butyltrichlorosilane (*t*BuSiCl$_3$, >95% purity, 1.63 g) was dissolved in acetonitrile (12.5 mL). This solution was added to deionised water (50 mL). After 18 h of reaction at 50°C, upon stirring, a fine white precipitate was formed. This precipitate was collected by filtration (fraction A) and the filtrate was concentrated and dried under reduced pressure to yield a fine white powder (fraction B). To remove any water that might still have been present, the two fractions were dried for 24 h in an oven at 100°C; after drying, 0.335 g of fraction A and 1.502 g of fraction B were present. Both fractions were found to consist of *tert*-butyl silsesquioxane *a2b4*, *t*Bu$_2$Si$_2$O(OH)$_4$ [MW = 254.43 g mol$^{−1}$]. The yield of the isolated silsesquioxane *a2b4* was 90%, with >99% selectivity. The compound was found to melt in the range 192–204°C and to be soluble in pyridine, DMSO, and, to a lesser extent, in THF. To obtain suitable crystals for single-crystal X-ray diffraction analysis, the compound (0.1 g) was dissolved in THF (10 mL) at 50°C and recrystallised by carefully adding aliquots (1 mL) of acetonitrile (5 mL in total) to the THF solution.

Catalysts **I** and **II** were prepared by titanium complexation of the silsesquioxane structure under similar experimental conditions to those described for the HSE study. CAB-O-SIL fused silica EH-5 (surface area: 380 m^2 g$^{−1}$, ≈4 hydroxy groups nm$^{−2}$) was used as support for the heterogenisation of the titanium-silsesquioxane *a2b4* complexes. Dehydroxylation of the silica was performed by adding (CH$_3$)$_2$SiCl$_2$ (1 mL) to a suspension of the silica (1 g) in diethyl ether (30 mL) and stirring the suspension for 1 h at room temperature. The volatiles were removed under reduced pressure. The titanium-silsesquioxane *a2b4* complexes (catalyst **I**) were supported on the silica (both untreated and dehydroxylated) by adding a solution of the complexes in THF (150 mL) (containing 5× 10$^{−4}$ mol of titanium) to a suspension of silica (1 g) in THF (100 mL) and stirring the suspension for 3 h at 60°C. After isolation of the solid by filtration, non-adsorbed species were removed by Soxhlet extraction with THF for 7 h. Finally, the silica-supported catalysts (**III** and **IV**) were dried overnight at 120°C under reduced pressure.

The catalytic tests were performed in an analogous manner as described for the HSE study. The same ratio between titanium and TBHP and the same concentration of TBHP in the reaction mixture were employed in all the catalytic tests reported in this article.

For the single-crystal X-ray diffraction analysis of *t*Bu$_2$Si$_2$O(OH)$_4$, the crystal was mounted along an arbitrary axis on an Enraf-Nonius CAD-4 diffractometer. Lattice constants were determined from 25 reflections with 10° < θ < 17° (standard deviations are given in parentheses): *a* = 6.226(6), *b* = 6.223(6), *c* = 9.956(4) Å; α = 85.06(5), β = 80.72(5), γ = 70.51(9)°.

NMR spectra were measured on a Varian VXR-400S (^{1}H decoupled, 25°C) or on a Varian Inova 300 spectrometer (^{1}H decoupled, 25°C).

Selected liquid-phase NMR data for silsesquioxane *a2b4*: ^{1}H NMR ([D$_5$]pyridine): δ = 1.46 (*t*Bu; relative integral = 9), 8.26 ppm (Si−OH; relative integral = 2); ^{13}C{^{1}H} NMR ([D$_5$]pyridine): δ = 18.25 (*ipso* carbon of *t*Bu; relative integral = 1), 27.36 ppm (CH$_3$ groups of *t*Bu; relative integral = 3); ^{29}Si{^{1}H} NMR ([D$_5$]pyridine): δ = −49.55 ppm (*t*Bu-Si(OH)$_2$O$_{0.5}$).

Selected liquid-phase NMR data for the silsesquioxane attributed to the *a1b3* structure: ^{13}C{^{1}H} NMR ([D$_5$]pyridine): δ = 18.32 (*ipso*-carbon atom of *t*Bu; relative integral = 1), 27.51 ppm (CH$_3$ groups of *t*Bu; relative integral = 3); ^{29}Si{^{1}H} NMR ([D$_5$]pyridine): δ = −40.06 ppm (*t*Bu-Si(OH)$_3$).

Selected data for catalyst **I**: solid-state ^{29}Si{^{1}H} NMR: δ = −50 (relative integral ≈1), −56 (broad signal; relative integral ≈2), −66 ppm (broad signal; relative integral ≈1).

Selected data for catalyst **II**: liquid-phase ^{13}C{^{1}H} NMR ([D$_5$]pyridine): δ = 14.17 (δ), 19.54 (γ), 35.74 (β), 61.72 (α) (1:1:1:1; ^{δ}CH$_3$^{γ}CH$_2$^{β}CH$_2$^{α}CH$_2$OH), 18.2, 27.4 ppm (≈1:3; multiplets; *ipso*-carbon atom and CH$_3$ groups of the *t*Bu group on the silsesquioxane species, respectively); solid-state ^{13}C{^{1}H} NMR: δ = 14.6 (δ), 19.9 (γ), 35.8 (β), 79.5 (α) (≈1:1:1:1; broad peaks, α very broad; ^{δ}CH$_3$^{γ}CH$_2$^{β}CH$_2$^{α}CH$_2$OTi), 18.0, 27.4 ppm (≈1:3; broad peaks; *ipso* carbon and CH$_3$ groups of the *t*Bu

group on the silsesquioxane species, respectively); solid-state ^{29}Si{^{1}H} NMR: $\delta = -56$ (broad band; relative integral ≈ 4), -66 ppm (broad signal; relative integral ≈ 1).

Gel permeation chromatography of catalyst **I** was performed on a Waters 410 differential refractometer gel permeation chromatograph equipped with a Waters Styragel HT 6E column calibrated on polystyrene standards. THF was used as the eluent.

Acknowledgements

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