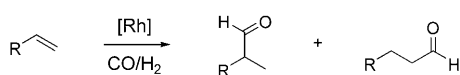


Continuous Rhodium-Catalyzed Hydroformylation of 1-Octene with Polyhedral Oligomeric Silsesquioxanes (POSS) Enlarged Triphenylphosphine**

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The efficient recovery and recycling of homogeneous catalysts is one of the major drawbacks of this area, especially when the high costs of precious metals are taken into account.^[1] Specific solutions have been developed for all larger-scale applications, however, new generic methods, preferably with low energy profiles, are highly desirable for future process intensification and development of more sustainable and “greener” processes. The various approaches that have been studied to date each have their own advantages and disadvantages, and can be divided into two main classes: biphasic catalysis,^[2–4] and immobilization on either soluble (molecular weight enlargement, MWE) or insoluble supports (heterogenization).^[5–9]

The hydroformylation of alkenes is among the largest-scale industrial applications of homogeneous catalysis (Scheme 1).^[10] An elegant example is the Ruhrchemie/Rhône Poulenc (RCH/RP) Process for the biphasic hydroformylation of propene. The water-soluble catalyst (TPPTS/Rh; TPPTS = sulfonated PPh₃, triphenylphosphino trisulfonate) is immobilized in the aqueous phase and the product, *n*-butanal, forms the organic phase, which can easily be



Scheme 1. The rhodium-catalyzed hydroformylation of *n*-alkenes.

removed by phase separation. It is important to note, however, that the applicability of this approach is limited exclusively to lower alkenes with sufficient solubility in the aqueous phase (the process is used commercially only up to butenes). A range of methods that overcome this difficulty have been investigated for the hydroformylation of higher alkenes. Table 1 gives a concise overview of results obtained

Table 1: Overview of rhodium-catalyzed alkene hydroformylation combined with catalyst recycling.

Entry	Method	Ligand	Substrate	TOF [h ⁻¹]	TON	Ref.
1	water/organic + latex ^[a]	TPPTS	1-octene	150	n.d. ^[b]	[4]
2	water/organic + CD ^[c]	TPPTS	1-decene	n.d.	2 × 770	[11]
3	water/organic + amphiphilic copolymer	covalently bound to polymer	1-octene	760	5800	[12]
4	ionic liquid	TPPTS	1-hexene	2000	10 × 1600	[13]
5	scCO ₂ ^[d]	TPPMS ^[e]	1-octene	180	n.d.	[14]
6	fluorous phase	P(4C ₆ H ₄ -C ₆ F ₁₃) ₃	1-octene	4400	n.d.	[15]
7	MWE	POSS-enlarged	1-octene	1350	120 000	this work

[a] PS-latex used as a phase-transfer agent; [b] n.d. = not determined; [c] CD = cyclodextrin; [d] supercritical CO₂; [e] TPPMS = triphenylphosphino monosulfate.

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[**] We thank W. van Herpen and T. Staring for technical assistance, A. Elemans-Mehring for help with the ICP-OES measurements, and Dr. R. Franke of the Evonik Oxeno company for helpful discussions. M.J. thanks The Netherlands Research School Combination Catalysis (NRSCC) and C.M. The Netherlands Organization for Scientific Research (NWO-CW) for financial support. Hybrid Catalysis B.V. is kindly acknowledged for POSS starting compounds.

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/ange.201001926>.

in the rhodium-catalyzed hydroformylation of alkenes followed by catalyst recycling, either by means of biphasic catalysis (entries 1–6) or by MWE (entry 7). In all cases, a modified version of triphenylphosphine was applied as the ligand.

Nanofiltration is still a relatively unexploited field for the recovery of MWE catalysts. Recently, our research group and others showed the application of nanofiltration for the recycling and reuse of homogeneous catalysts in a diffusion-driven process.^[16,17] However, traditional systems for MWE have proven to be rather inefficient in continuous processes, as low conversions were reached because of rapid catalyst deactivation, significant metal leaching, or poor retention of the whole system. Consequently, new concepts have to be developed in order to circumvent these drawbacks. Herein, we report the synthesis of molecular-weight-enlarged triphe-

nylphosphine, its application as a ligand in the rhodium-catalyzed hydroformylation of 1-octene, and its long-term behavior in a continuous flow nanofiltration reactor setup.

POSS has received relatively little attention for use in MWE.^[18–22] These compounds are commercially available at low cost, have a highly defined structure, and are kinetically and thermally stable, thus making them ideal candidates for use in MWE. Moreover, the rigid, cubical shape of the POSS cages is beneficial in nanofiltration, since rigid 3D structures are known to display better retention and less membrane fouling than more flexible macromolecules.^[23]

We initially chose to immobilize PPh₃ as it has been the ligand of choice in the industrial rhodium-catalyzed hydroformylation of alkenes. The synthesis of POSS-enlarged PPh₃ turned out to be straightforward (Figure 1). Firstly, 4-bromostyrene (**1**) was hydrosilylated with HSiCl₃ in the presence

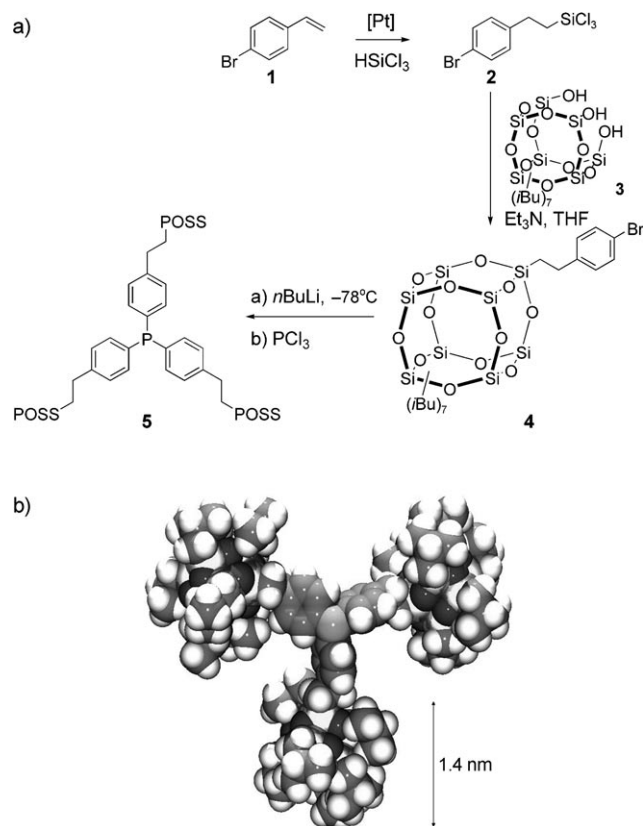


Figure 1. a) Synthesis of POSS-enlarged PPh₃. b) 3D model (MM⁺) of POSS-enlarged PPh₃ showing the steric bulk induced by the POSS moieties.

of a Pt catalyst. The product (**2**) was subsequently used in a corner-capping reaction with trisilanol *i*Bu-POSS **3** in the presence of Et₃N to produce 4-bromophenylethyl-POSS **4**. After lithiation of **4** with *n*BuLi and reaction with PCl₃, POSS-enlarged PPh₃ **5** was obtained in 80% yield (Figure 1). The ligand was fully characterized by NMR spectroscopy, elemental analysis, and MALDI-TOF mass spectrometry, and has a molecular mass of 2791 g mol⁻¹. In order to apply MWE to homogeneous catalysts, several requirements have to be

fulfilled: straightforward synthesis, high activity, high total turnover number (TTN), and high retention. Therefore, the activity of POSS-enlarged PPh₃ in the hydroformylation of 1-octene was compared with PPh₃ in an autoclave (batch) experiment. Plots of conversion versus time, based on the uptake of CO/H₂, are shown in Figure 2a. The turnover frequencies (TOF) were determined at 20% conversion, and were found to be high: 1350 h⁻¹ and 3150 h⁻¹ for POSS-enlarged PPh₃ and unmodified PPh₃, respectively. No degradation of the POSS ligand was observed by ³¹P NMR spectroscopy after the reaction was finished.

Since our catalytic system based on POSS-enlarged PPh₃/Rh fulfilled all the requirements discussed above, it was applied in a novel, continuous-flow nanofiltration reactor that was designed and developed in-house. This reactor (Figure 3) is filled continuously with substrate solution by an HPLC pump, while a capacitive level sensor controls the liquid level in the reaction vessel by operating the HPLC pump. The product-containing solution is continuously collected at the backside of the membrane module. The reactor consists of two loops: a gas-saturation/reaction loop (A), and a membrane filtration loop (B). Loop A contains the reaction vessel and the gas mixer, in which the reaction mixture is injected into the gas phase for gas saturation. Both loops meet in the crossflow chamber. The reaction mixture subsequently flows along the ceramic nanofiltration membrane in which the product-containing phase is separated from the MWE catalyst and is continuously collected. We chose a ceramic membrane because of its good solvent, pressure, and temperature resistance. The flow in the membrane loop is kept higher than in the reaction loop to guarantee turbulent flow along the membrane (Reynolds number Re ≥ 4400), thus preventing formation of a polarization layer. The reaction pressure forms the driving force for the nanofiltration in this setup. The flux through the membrane is controlled with a Rheodyne two-position six-port fluid processor (PR700-100-01) equipped with a 500 μL sample loop controlled by a flip-flop relay, and is kept constant during the course of the reaction. The whole reactor, including the membrane unit, is kept at the operation temperature of 80°C. The molecular-weight cut-off (MWCO) of this membrane is 450 Da.^[24] Further reactor and reaction specifications are given in the Supporting Information.

From our batch experiments (Figure 2a), we can conclude that under the reaction conditions applied (*T*, *P*, [1-octene], [Rh]; see the Supporting Information), the reaction is pseudo-zero-order in 1-octene up to about 90% conversion. For a zero-order reaction we can derive an equation for the conversion *X* in a CSTR, where [oct]_{in} and [oct]_{out} are the concentration of 1-octene flowing into and out of the reactor, respectively, *τ* is the space time, and *k* is the rate constant [Eq. (1)].

$$X = \frac{[\text{oct}]_{\text{in}} - [\text{oct}]_{\text{out}}}{[\text{oct}]_{\text{in}}} = \frac{\tau k}{[\text{oct}]_{\text{in}}}$$

The results of a variable-flux experiment are shown in Figure 2b, and compared with the expected values according to [Eq. (1)]. In this experiment, the conversion was deter-

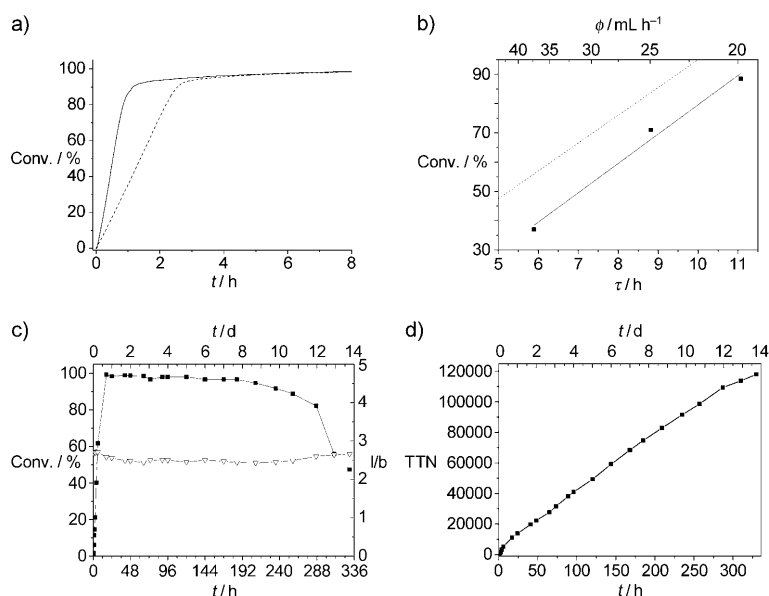


Figure 2. POSS-enlarged PPh_3/Rh catalyzed hydroformylation of 1-octene. a) Comparison of catalytic activity between PPh_3/Rh (5 equiv; —) and POSS-enlarged PPh_3/Rh (5 equiv; ----) in a batch reactor. b) Comparison between experimentally obtained conversion (■) and conversion predicted by the kinetic model ($X = k_{\text{batch}} \tau [\text{oct}]_{\text{in}}^{-1}$; ----); k_{batch} refers to the value of k calculated from the batch setup; ϕ = flux [L h^{-1}]. c) Conversion (■) and regiospecificity (▽) versus time for the continuous hydroformylation of 1-octene in the continuous flow membrane reactor. d) Accumulated turnover number obtained in the continuous-flow membrane reactor.

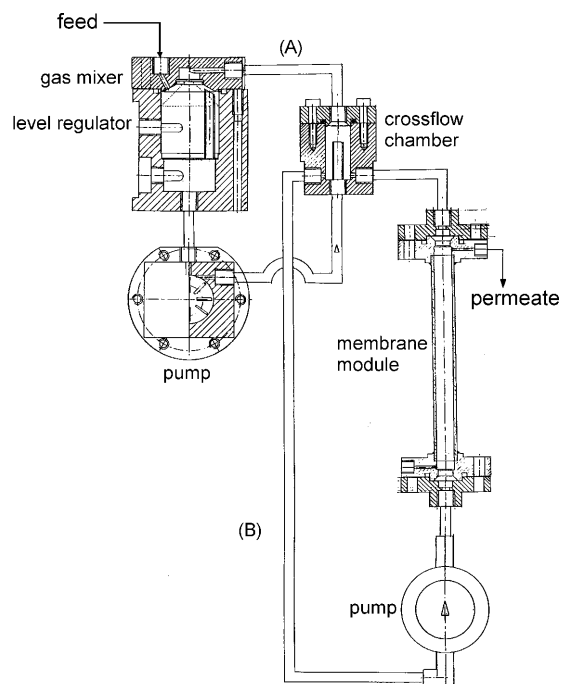


Figure 3. Schematic representation of the continuous-flow nanofiltration reactor developed in-house.

mined at a certain space time τ , after the system had reached steady-state conditions. Figure 2b shows that the conversion that is reached in the CSTR is systematically lower than the expected conversion based on [Eq. (1)]. This behavior can be

rationalized by for example, nonideal mixing, premature catalyst decomposition, slight differences in temperature between the batch and continuous setup that result in a different value for k .

Prior to use, the reactor was purged five times with syngas (CO/H_2 1:1; 20 bar). The reactor was then filled with substrate solution by HPLC pump, and again purged five times with syngas (20 bar). The reactor was heated to the reaction temperature (80°C) and pressurized to the reaction pressure of syngas (20 bar). At time $t=0$, the catalyst was added to the reaction mixture by means of a dropping funnel connected to the reactor, therefore allowing the catalyst solution to be added to the reactor under the reaction conditions. Samples were taken at regular intervals, and analyzed by GC to monitor the development of conversion and regiospecificity (linear/branched (l/b) ratio) over time (Figure 2c).

After a gradual increase, the highest conversion of 99% was obtained after 17 hours. The conversion remained greater than 90% for almost two weeks, which is unprecedented. In this period, the regiospecificity remained constant at an l/b ratio of 2.5, which is identical to the regiospecificity for unsupported PPh_3 .

The accumulated turnover number (TTN) versus time is shown in Figure 2d, which shows that the TTN steadily increases to a value of about 120 000 Rh^{-1} after 13 days. This result demonstrates the stability and robustness of our POSS-enlarged PPh_3/Rh catalyst.

The significant reduction in activity after 13 days still requires further investigation. The reduction could be caused by ligand decomposition, for example, by cleavage of the P–C bond in the ligand, as has been previously reported.^[25,26] However, the ^{31}P NMR spectrum of the reaction mixture at the end of the experiment showed signals of only the free and rhodium-coordinated ligands. Another possibility could be the formation of Rh clusters. The color of the retentate at the end of the reaction was still light yellow, whereas Rh clusters usually cause a brown coloration. Furthermore, very small amounts of impurities present in for example, the solvent or substrate could eventually accumulate in the reactor and lead to catalyst deactivation. Clearly, the observed deactivation is not caused by a substantial loss of Rh, since ICP-OES (induced coupled-plasma–optical emission spectroscopy) analysis of the total product solution revealed a total Rh leaching of only 0.045% and a total P leaching of 0.74% of the total amount of Rh and P added, respectively. This result means that 99.96% of the Rh is effectively retained by the nanofiltration membrane, thus tremendously simplifying the workup as the Rh concentration in the product is extremely low. Moreover, after removal of the retentate, the reactor does not show catalytic conversion of 1-octene (<1%), thus indicating that no active Rh species are adsorbed on the membrane or the reactor wall.

In summary, we have introduced POSS as a versatile unit for molecular weight enlargement of homogeneous catalysts, facilitating catalyst recycling, which results in continuous operation. A Rh catalyst based on the bulky, rigid, and robust POSS-modified PPh₃ ligand was applied in the hydroformylation of 1-octene in an in-house engineered continuous flow nanofiltration reactor. Unprecedented results in terms of activity, stability, and retention of the POSS-enlarged catalyst system were achieved as the hydroformylation setup was continuously operated for almost two weeks without any significant deactivation or leaching of the catalyst. These results highlight a major breakthrough in the sustainable conversion of alkenes under homogeneous catalytic conditions without the usual drawback of tedious and often expensive catalyst recovery and recycling. The full scope of the concept of MWE using POSS units is presently under investigation for a range of ligands and metal-catalyzed transformations.

Received: March 31, 2010

Published online: September 8, 2010

Keywords: catalyst recycling · homogeneous catalysis · hydroformylation · rhodium · silsesquioxanes

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