

# PROJECT FINAL REPORT

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**Project acronym:** HiCAT

**Project title:** Hierarchically Organized Metal Organic Catalysts for Continuous and Multi-batch Processes

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## Executive Summary

The aim of the HiCat project was to develop hierarchically organized metal-organic catalysts which can be easily recycled in multi-batch processes or can be used in continuous processes maintaining the valuable properties of homogeneous metal-organic catalysts: high selectivity, activity and stability. The catalysts should be constructed using components at the nano-scale in a bottom-up approach. Hereby, catalytically active metal complexes should be linked with nanoparticles such as polymeric microgels, or silsesquioxanes entities. Based on polymer-nanoparticles that are linked by T-responsive polymers, new types of films and membranes with graded porosity had to be prepared by varying the size of the nanoparticles. Thus, the porous structure should be graded in layers of interconnected nanoparticles spaced one above the other. This, in turn will open new opportunities for integration of catalytic steps and separation within the hierarchically structured system and, hence new opportunities for continuous reactor operation.

All major objectives of the project have been accomplished resulting in exciting commercial implications:

**POSS-modified metal catalysts for continuous membrane reactor application:** We have demonstrated the feasibility of continuous reactor operation with promising turn-over numbers and high catalyst rejection rate. Based on a large repertoire of functionalized silsesquioxane (POSS) nanoparticles metal-organic catalysts applicable for olefin metathesis and CX coupling reactions have been synthesized. We have identified processes with high turn-over number where catalyst recycle using the HiCat catalysts can offer economic benefits. Evaluation of catalytic performance showed that activity of original homogeneous catalysts can be nearly maintained also after interconnection of metal complexes with nano-particle entities. Hereby, the metal loading covers the range of conventional heterogeneous catalysts without losing the activity of homogeneous complexes. This indicates that the new nano-particulate systems take the advantages from both sides: homogeneous (high activity and selectivity due to maintenance of site isolation) and heterogeneous catalysis (separability). Straight forward syntheses pass ways which are economically feasible have been developed and patented.

**T-responsive polymer (microgel) supported metal catalysts:** We have provided proof of principle for a new class of catalysts - the T-responsive polymer (microgel) supported metal catalysts. For the first time, integration of both catalytic activity and T-responsiveness within a single catalytic system has been demonstrated. A large variety of microgel systems has been evaluated with respect to their potential in catalytic applications. Prototype catalysts have been applied in two different catalytic reactions. At the present state, intellectual property will be secured by filing patent applications.

**Membranes with graded porosity:** Methods for forming layers of nanoparticles with homogeneity of nanoparticle size distribution were developed. Based on this, we have demonstrated the possibility of preparing membranes with consecutive layers of nanoparticles with different functionalities. These membranes show similar or even better performance than the commercially available ones and are compatible with wider range of solvents. From our HiCat work we conclude that a technology using microgel particles has great potential for tailor-made membranes with finely tuned properties and separation performance.

Membrane Application at industrial scale requires flat-sheet membranes integrated into spiral-wound modules. Here production technology has to realize high reproducibility in making the spiral-wound modules without leaks using membrane materials which are stable in diverse organic solvents. Suitable membrane types were identified and fabricated into spiral-wound modules for commercial applications.

### 4.1.1 Objectives

Homogeneous catalysts which are based on soluble metal organic complexes often outclass heterogeneous catalysts with respect to selectivity and activity (turn-over number). This advantage results from the adaptation of the ligand sphere of the catalyst to the structural features of the substrates, enabling multifunctional substrates to be converted with close to 100 % selectivity. This advantage is intellectually appealing, and a huge academic literature has grown up around development of new catalysts and their application. However, the uptake of homogeneous catalytic processes by industry is unfortunately very limited at present. This is primarily because separation of the mostly expensive catalytic metal complexes from product mixtures is complex, and sometimes even impossible. It is only for large-scale industrial processes related to sufficiently high added value products that individual solutions have been developed (e. g., the oxo-process / hydroformylation, methanol carbonylation). Importantly, for the abundance of diverse medium and small scale applications there is a lack of practicable separation processes. This may partly be due to the fragmented nature of much academic research, where synthetic chemists, polymer chemists, and chemical engineers concentrate on working in their respective communities.

Innovative generic technical solutions in this field would have a major impact in many industrial sectors such as the production of fine and speciality chemicals, nutrition, pharmaceuticals and polymers. In these sectors, new applications could be made accessible. In order to break through current barriers to commercialisation of highly selective metal-organic catalysts, a team of academic and industrial experts has been established for the HiCat project. This carefully selected consortium ranges across disciplines (chemistry, physics, engineering) and organisation types (large chemical company, SMEs, university labs) and provided a multifaceted team capable of excellent research, coupled to the ability to implement step change enabling technologies resulting from the research.

The consortium intended to develop paradigm shifting hierarchically organised metal organic catalysts which can be easily recycled in multi-batch processes or, alternatively, which can be used in continuous processes without, losing the original advantages of the homogeneous soluble metal organic catalysts - high selectivity, activity and stability.

This had to be achieved by exploring innovative polymer materials which support metal organic functionalities. For the first time new polymeric materials as supports for organo metallic catalysts has been exploited, and techniques have been developed for their effective separation from reaction products. Recycling of the catalyst in multi-batch operation should be achieved utilizing the controllable solubility of the nanoparticles. I. e., the catalyst-nanoparticle entities had to be either easily separated by precipitation or, even more, the catalytic entities had to be transferred from a mobile phase to a stationary phase through which the substrate solution is eluted by controlling the solubility and the state of aggregation.

Following building blocks at the nano-scale had to be developed and linked to obtain respective hierarchically organized catalysts:

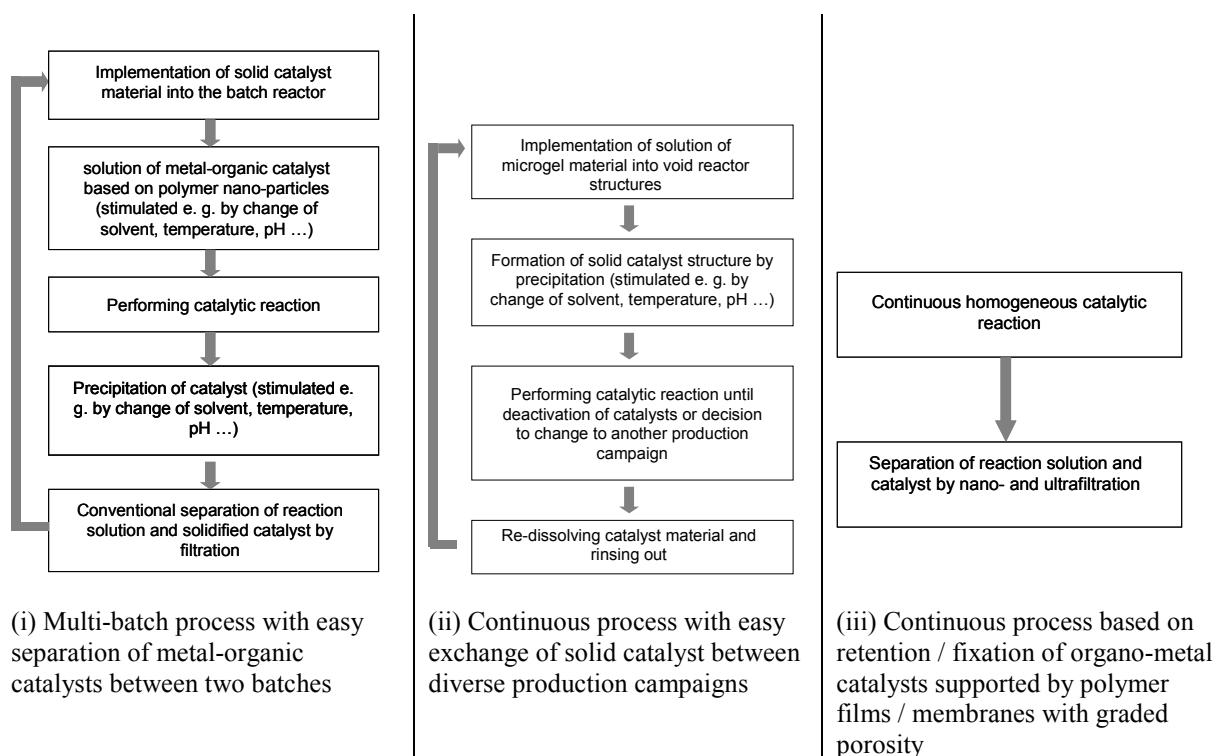
- Catalytically active metal complexes possessing functionalities to link them with polymers, and to the surfaces of polymer nanoparticles. Hereby, those ligands and catalyst complexes have been used which are available at commercial scale and offering modularity and intelligent opportunities for linkage with nanoparticles.
- Soluble polymers, and nanoparticles, based on polymer microgels or polysilsquioxane entities as supports for metal organic catalysts. These polymers and nanoparticles shall allow the separation and re-use of the catalysts. Excitingly, microgels offer the opportunity to form complex and long-range architectures and to switch between dissolved and solid state by controlling type of solvent and temperature. The optimized ligand sphere of the metal organic complexes should be

maintained by linking the ligands with the nanoparticles via hydrocarbon chains, i. e. the structural principles of tailor-made ligands shall be transferred into tailor-made functional surfaces of the nanoparticles.

Furthermore, the hierarchical organisation of HiCat catalysts it was intended to be accomplished by decoupling the residence time of the catalytic phase from the substrate solution applying innovative membrane reactor concepts which either repress the catalysts by nano-filtration membranes or where the catalytic function is integrated into the membranes itself.

Our vision was that such new type of materials, e. g., polymeric nanoparticles interconnected by T-sensitive polymers, could produce precipitative assemblies of nanoparticles, from which in turn, various macroscopic designs of catalyst could be derived such as:

- catalysts supported on soluble but precipitative polymer nanoparticles for homogeneous multi-batch process according to Scheme 1.1 (i) with easy separation of the metal-organic catalysts and reaction solution in between consecutive batches due to the switchable solubility of the catalyst by changing the reaction conditions (solvent, temperature)
- catalytically active polymer monoliths which can be dissolved and re-precipitated by application of external stimuli. This, in turn may allow the facile incorporation and fixation of the catalyst within reaction channels with sophisticated and narrow geometries as provided for example by micro-reactors. Since our new catalytic material can be displaced after re-dissolution, destruction of the microstructures can be avoided. The concept for using microgels interconnected by T-sensitive polymers in a cyclic precipitation / dissolution process is mentioned in Scheme 1.1 (ii).
- films with graded porosity obtained by successive deposition of interconnected polymer nanoparticles; this opens up possibilities for control over spatial arrangement of nanoparticle catalysts, i.e. hierarchical systems
- membranes derived from interconnected polymer nanoparticles for nano- and ultrafiltration (according to Scheme 1.1 (iii))



**Scheme 1.1:** Variants of catalytic processes based on the application of metal-organic catalysts supported on polymer-nanoparticles and their aggregates

The substantial advances that the HiCat systems shall make over the state-of-the-art of nanoparticle supported metal-organic catalysts will be the following:

- Interconnecting polymer-nanoparticles by T-responsive polymers is a completely new concept. It would allow the reversible formation of catalytically active entities in solution, integrated into polymer monolith, films or membranes with controlled void fraction and macro-pore dimensions. Hereby, catalyst systems could be adapted very flexibly to diverse types of reactor operation (batch/slurry or fixed bed).
- By controllable “in-situ” formation/dissolution of catalytically active macro-porous polymer assemblies, the application of innovative reactor geometries such as catalytic micro-structured reactors could be enabled since the catalytic material can be easily incorporated and fixed in reaction channels with sophisticated and narrow geometries, as well as displaced after re-dissolution without a destruction of the microstructures.
- The HiCat technology shall be generic and applicable in a large variety of catalytic applications. A successful project shall greatly advance the state of the art in the field as well as add new classes of materials to the technology family of catalysts – i. e. catalytically active (nano-filtrable) nanoparticles, as well as polymer nanoparticles interconnected by T-sensitive polymers. This new class of catalytic materials shall allow switching from soluble catalysts to solid structures initiated by external stimuli such as changes of temperature, solvent.
- Commercially, the project shall offer exciting new business opportunities for metal-organic catalysts due to the expansion of their applicability not only to batch and multi-batch but also to continuous processes, which are usually related to higher volume manufacturing processes.

In contrast to previous approaches for immobilization of homogeneous catalysts in mesoporous materials, in the HiCat project, the catalytically active structures shall be concentrated in the corona of the nanoparticles. Thus the accessibility of the metal complex for substrate molecules shall be similar to homogeneous catalyst complexes. Such an approach should not suffer from the diffusion limitations of many immobilization concepts based on supporting ligands in mesoporous systems. Unsurprisingly, such an innovative approach has concomitant risks such as insufficient loading capacity of polymer nanoparticles for ligand structures, insufficient exposure of catalytically active centres to the solution environment, undesired intra-molecular cross-reactions in the highly functionalized supports and undesired leaching of organo-metal structures.

Importantly, the HiCat project shall deliver solutions to outstanding problems encountered in the use of polymer-supported metal organic catalysts which had not yet been adequately solved yet as summarized below:

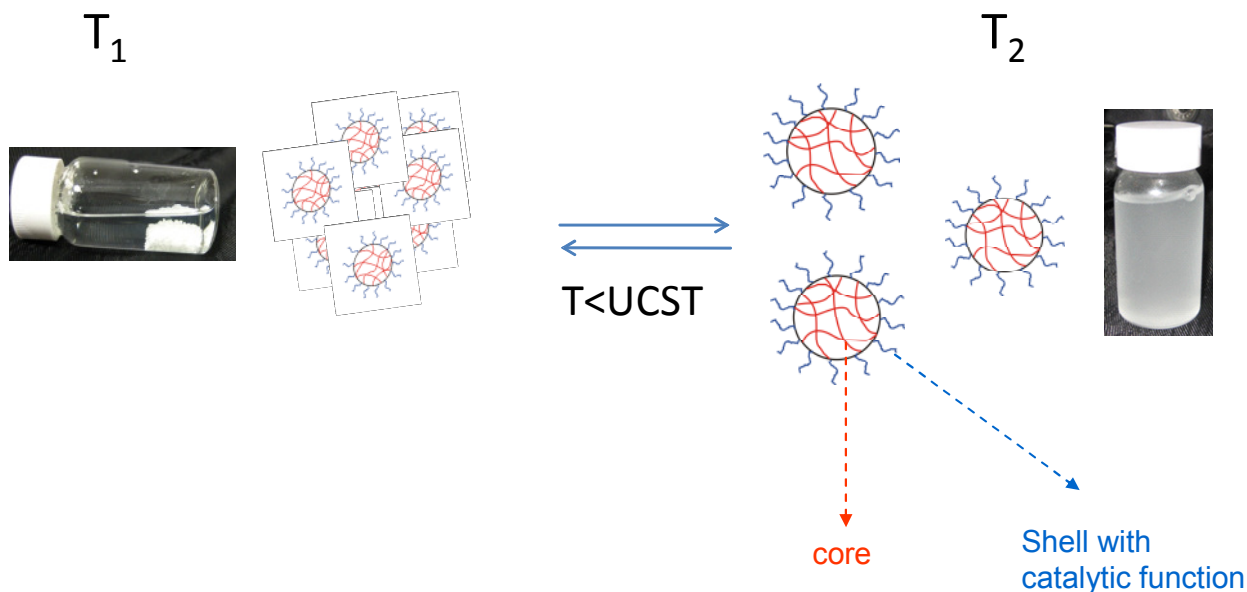
- Achieve high loading capacity of the nanoparticle supports for organo-metallic catalytic active sites (this is essential to obtain sufficient space-time yields)
- Achieve sufficient exposure of the catalytically active centres to the solution environment and avoidance of intra-molecular cross-reactions in the highly functionalized supports;
- Control of the site isolation by varying the degree of branching and/or size of the polymer particles.
- Narrow molecular weight distribution
- Ascertain availability of reactive groups which are easily functionalized by standard solution phase chemistry for linking metal-organic structures
- Prevent leaching: For industrial applications, the overall retention of the catalyst must be extremely high in order to maintain a high activity in a continuous reactor for longer reaction times. In general, a retention of > 99% per cycle (feed volume in continuous) is required to obtain a catalyst system that remains in the reactor for a prolonged period of time, even for fine chemical production processes.

## 4.1.2 Results

### 4.1.2.1 Temperature-sensitive polymer (micro-gel) catalysts for batch operation

Microgels are intramolecularly cross-linked macromolecules with a globular shape and with a diameter of 10 to a few hundred nm that are characterized by a high density of surface functional groups and form a stable dispersion in many solvents. Unlike soluble polymers, microgel solutions possess low viscosity even at high concentrations of polymer and low temperatures thus further facilitating their high loading capacity. On the other hand stimuli-responsive microgel particles exhibit reversible swelling properties in response to certain external conditions (pH, temperature, ionic strength etc). At certain conditions they exist as swollen microgels, while deswelling occurs upon changing the conditions leading to the formation of compact insoluble latex particles. The latter could be advantageous for our intended development of a unique system exhibiting a homogeneous-to-heterogeneous catalyst transformation. Microgel particles have typical diameters of a few 100 nm which implies a “surface area” in the order of 100 m<sup>2</sup>/g which seems sufficiently high for further functionalization.

Our concept on how the feature of microgels can be used for a new class of catalysts is demonstrated in Figure 1 indicating the core-shell structure of microgels. This structure allows the location of active catalytic sites within the corona, hence, carrying both functions the T-responsive and the catalytic. Thus the accessibility of the metal complex for substrate molecules should be similar to homogeneous catalyst complexes. Such an approach should not suffer from the diffusion limitations of many immobilization concepts based on supporting ligands in mesoporous systems.



**Figure 1:** Concept of catalysts based on T-responsive microgel particles (UCST stands for upper critical temperature = temperature above which the polymers are dissolved)

In the framework of the HiCat project, we have provided proof of principle for this new class of catalysts - the T-responsive polymer (microgel) supported metal catalysts. For the first time, integration of both catalytic activity and T-responsiveness within a single catalytic system has been

demonstrated. For this purpose, a large variety of microgel systems has been evaluated with respect to their potential in catalytic applications taking into account for the following questions:

- Does the material show a distinct upper critical temperature in organic solvents such as alcohols, DCM, toluene etc.
- Does the material “survive” the chemical modification during introduction of catalytic functionality?

Prototype catalysts have been applied in two different catalytic reactions. At the present state, details of developments are related to non-publishable confidential foreground and are not included into the public report due to the ongoing process of filing patent applications. Therefore, in the following paragraph we have summarized these results only in a generic manner.

Different strategies for the functionalization of the particle corona were developed.

a) Copolymerization of functionalized monomers is based on a strategy providing the already functionalized polymer after the final polymerization step. Therefore, ligand-derived monomers had to be synthesized and copolymerized;

b) Late stage functionalization deals with an approach, where the ligand is coupled to the already existing (T-responsive!) polymer. Accordingly, in a first step functionality suitable for coupling reactions needs to be introduced before the polymerization. The results of our synthesis studies show that both synthetic strategies (co-polymerization and late-stage functionalization) lead to T-responsive functionalized systems. From our evaluation we can summarize the following advantages and disadvantages for these strategies:

#### ***Co-Polymerization***

- easy synthetic pathways towards functionalized monomers
- no limitation of reaction conditions
- precise analytics can be applied to evaluate the success of synthesis (NMR, MS, GC)
- large variety of potential monomer building blocks is accessible
- exact control of ligand loading via stoichiometric ratio of monomers possible
- fine tuning of temperature responsiveness via functionalization degree

#### ***Late-stage Functionalization***

- various core-shell combinations can be applied
- coupling to an already T-responsive polymer
- no risk of (radical induced) side reactions during the polymerization

Both concepts have been applied successfully. This allows flexibility in synthesis pathway and helps to optimize production costs and composition of a commercial catalyst portfolio.

However, it must be emphasized, that the synthesis pathway and the related introduction of functional groups can have an extremely high influence on the resulting critical temperature value. Also metal coordination and type of metal itself modifies the T-responsive behaviour. This implies that the effect of these parameters has still to be explored more systematically (e.g. by high-throughput experimentation) to provide the basis for deducing structure-performance-relationships which, in turn, are required for the future rational design of T-responsive catalysts.



### ***Catalytic test of selected systems - proof of principle***

To proof the catalytic activity of metal-complexes linked with T-responsive polymers and microgel particles, respectively, classical Heck cross coupling has been chosen as model reaction as well as hydrogenation of cinnamic acid.

#### **Mizoroki-Heck coupling**

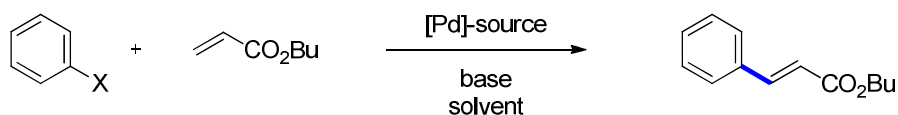


Figure 2

#### **Hydrogenation of cinnamic acid / esters**

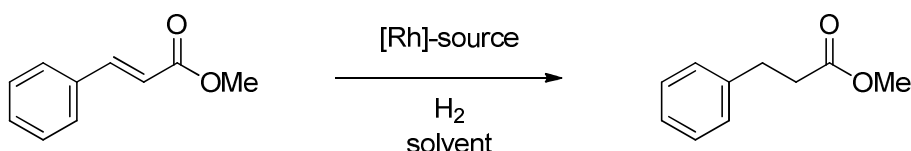


Figure 3

Based on these two catalytic reactions we could demonstrate for the first time the integration of catalytic functionality and thermo-responsiveness within a single catalytic system. This proof of principle opens a new class of catalysts which combine the advantages of homogeneous and heterogeneous catalysts and simultaneously allowing the usage of simple conventional batch reactor types.

Our results have shown that the T-responsive polymer particles reveal a high tolerance with respect to catalytic functionality allowing high degree of functionality and hence metal loading covering already a range of conventional heterogeneous precious metal powder catalysts.

#### **4.1.2.2 Show case development for nano-filtratable catalysts for continuous process operation**

The development of nano-filtratable catalysts for continuous process operation is closely related to the development of feasible membranes and membrane reactor modules, respectively. In the HiCat project these developments went hand in hand combining the unique expertise for development and production of functionalized silsesquioxane nanoparticles (POSS), for catalyst technology and for membranes technology. The respective interplay of competences is illustrated in Figure 4 for catalyst systems POSS-CataCXium and POSS-CatMETium which are close to commercialization.

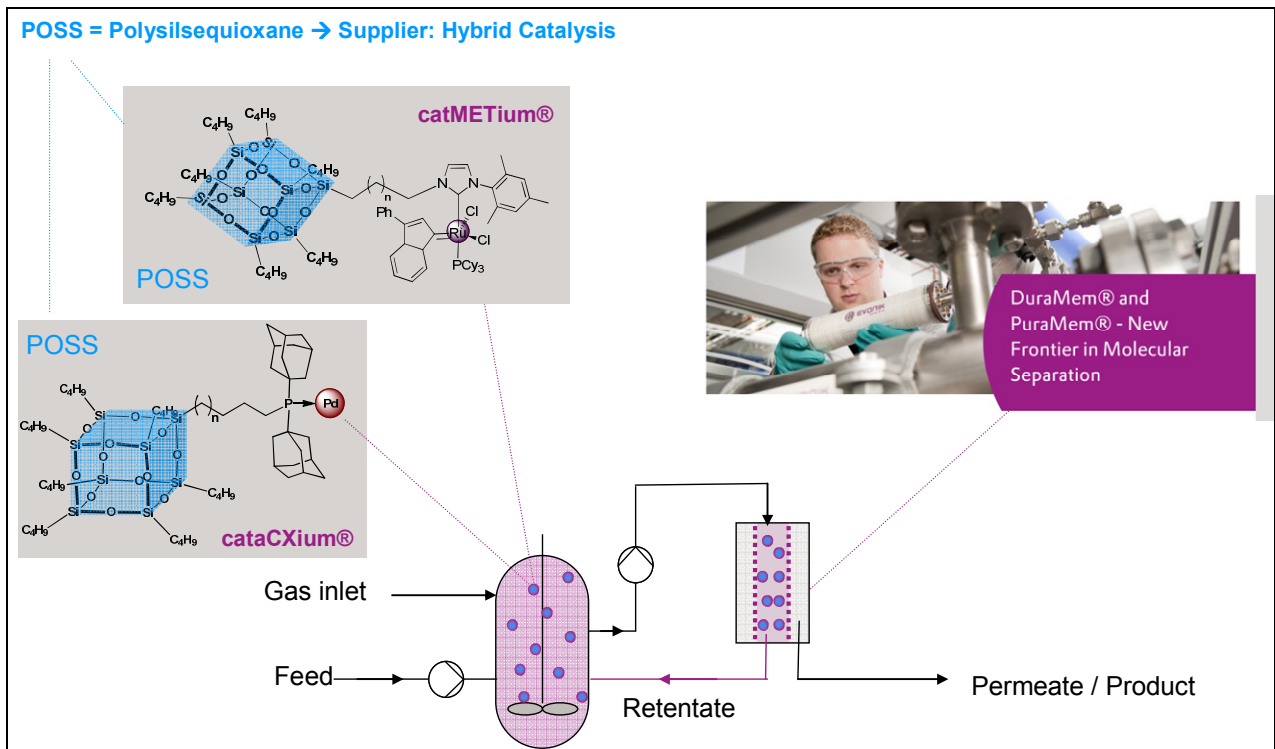


Figure 4: Illustration of catalytic reactor operation using nano- filtrable catalysts

### Synthesis of catalysts

Catalyst development for nano-filtrable systems comprises of two parts a) functionalization of nanoparticles, b) linking ligands or metal complexes with functionalized nanoparticles (here polysilsesquioxanes).

Concerning part a) functionalized silsesquioxane derivatives (POSS) with numerous functional groups including isocyanate, alkyl halide and alcohol functions have been developed and supplied (particle size  $\sim 2$  nm). The functionalities which will be modified within the HiCat project are illustrated in Figure 5.

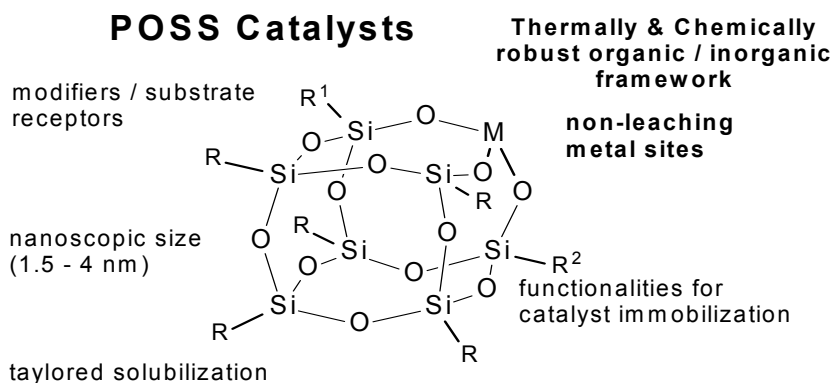
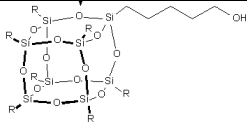
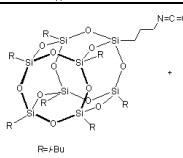
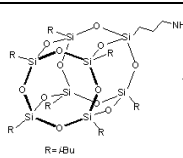
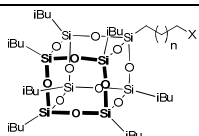
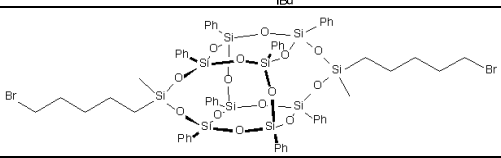
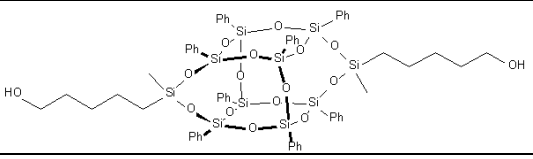
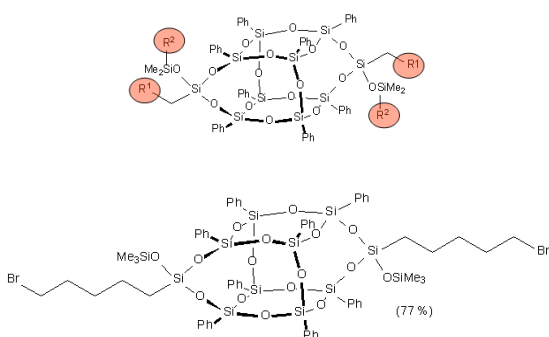


Figure 5: POSS structure and functionalities

In addition, independent routes were developed to monofunctionalized and difunctionalized POSS compounds as well as a modular route to defined tetrafunctional compounds. In majority, compounds made represent novel compositions of matter that are suitable for modification of selected ligands, catalyst complexes and T-responsive polymers. Over 40 samples were supplied to network partners. An overview about the functionalized POSS systems available is given below.

Table 1

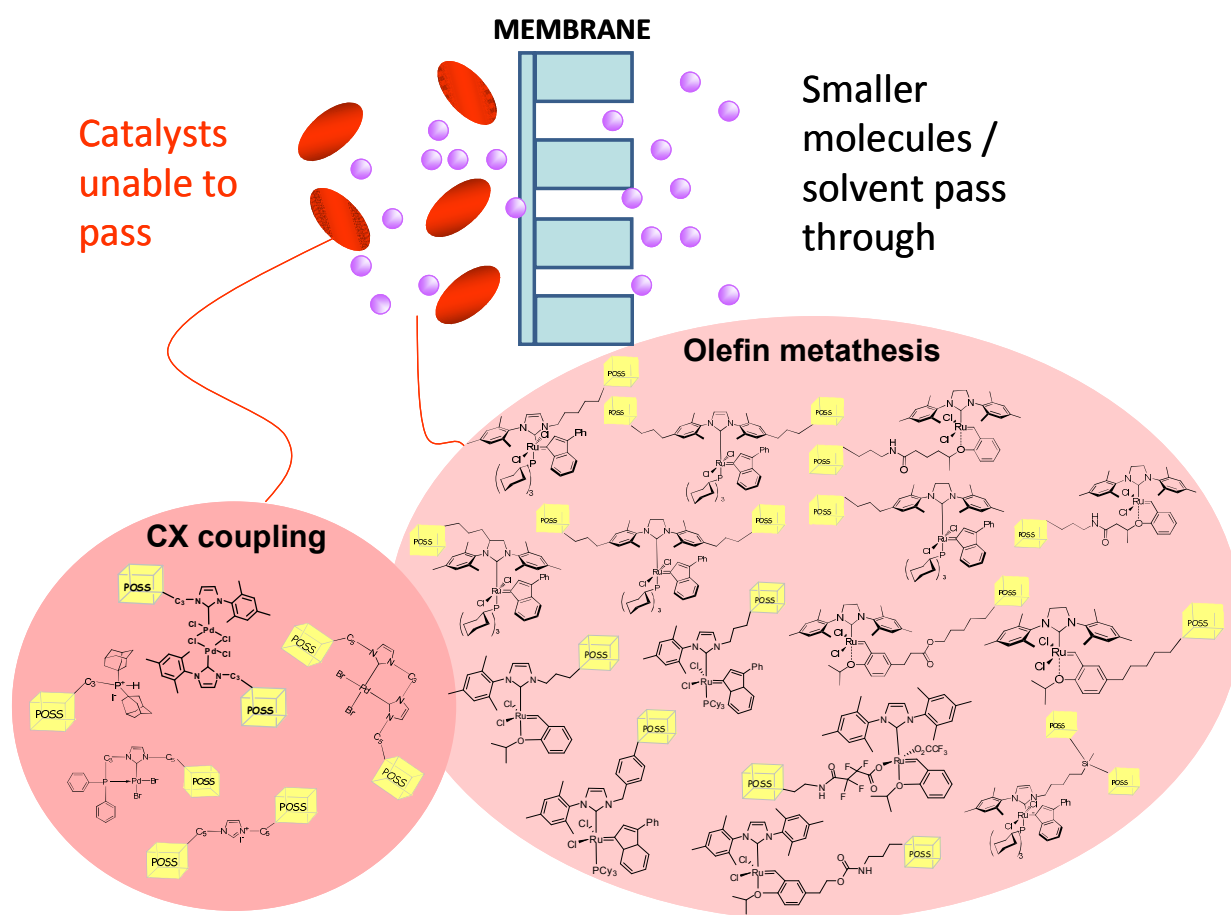
POSS monoalcohols, cost effective routes were found to afford POSS C <sub>2</sub> , C <sub>3</sub> , C <sub>5</sub> , and C <sub>6</sub> alcohols	
POSS monoalkylisocyanates	
POSS monoalkylamines	
POSS monoalkylhalides (X = Cl, Br, I)	
bi-functionalized POSS alkyl halides	
Using protective groups, the scope of this method was widened to include POSS dialcohols	
Tetrasodium silsesquioxane tetrasilanolate marks complete control in the synthesis of multi functionalized POSS compounds. Using consecutive functionalizations involving a cascade of both, trichlorosilane and dichlorosilane reagents, tetrafunctionalized derivatives can be obtained. Thus bis(bifunctional) POSS compounds can be made with two different sets of functional groups, bonding of the combination of selected ligands or catalyst complex together with T-responsive polymer should now be feasible.	

With the portfolio of different POSS entities developed within the HiCat project a variety of coupling reactions for binding ligands are now possible:

- Hydrosilylation, either employing POSS silanes or POSS alkenyls
- Direct amidation using POSS amine and methyl ester
- Transesterfication using POSS alcohol

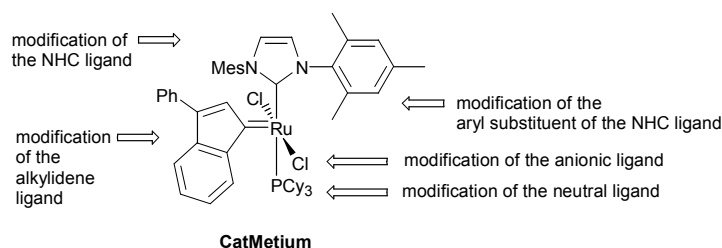
- Click chemistry using POSS azide and an acetylene functionalized substrate
- Quarternization using POSS alkyl halide and amine functionalized substrate
- Imine formation using POSS amine and aldehyde or ketone

Based on this repertoire functionalized silsesquioxane (POSS) nanoparticles metal-organic catalysts applicable for olefin metathesis and CX coupling reactions have been synthesized. This includes a large variety of POSS-Ru-N-heterocyclic-carbene complexes and POSS-ligands (phosphines and N-heterocyclic carbenes (NHC)). The final portfolio of catalysts developed in the HiCat project is shown in Figure 6.



**Figure 6:** Scheme representing nano-particulate catalysts synthesized in the HiCat project which are catalytically active and separable by membranes

Different concepts of linking have been realized based on the Ru-NHC-POSS complexes. The prepared catalysts refer strictly to the original conception from the project proposal (Annex 1) which is illustrated again in Figure 7:

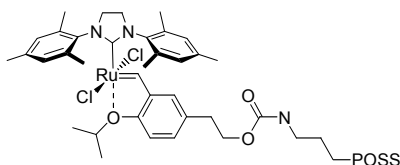


**Figure 7**

Following findings of synthesis work can be summarized:

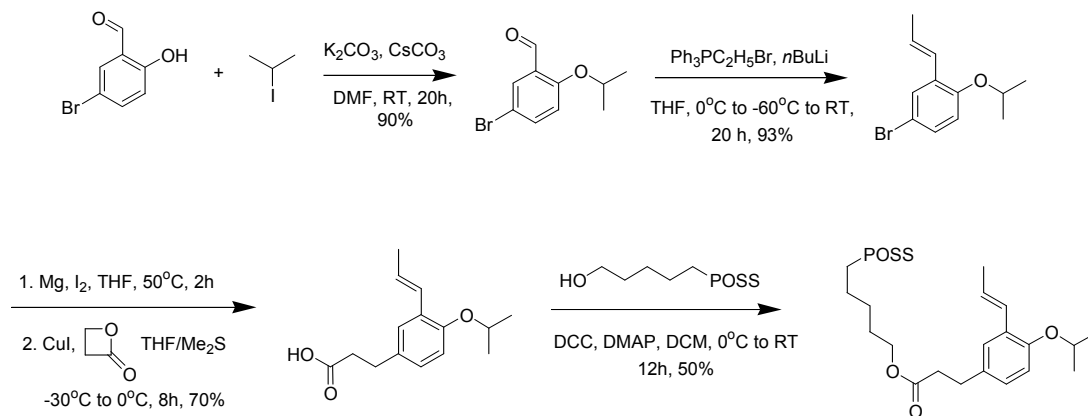
Synthesis of Ru-NHC-POSS with linkage via N-atom of the NHC ligand was optimized with respect to yields. Hereby, it was found that the yield of the ruthenium complexes depends on length of the chain between POSS and imidazolium ring. POSS moiety probably stabilizes geometry of the Ru complex. That will explain why best yield where obtained with shortest chain and why synthesis of catalyst with eleven-carbon chain was not successful.

Since catalysts with urethane linking bond were unstable in toluene alkylidene ligand were modified as well based on the hypothesis that the instability of the catalyst during metathesis reaction is caused by the urethane linking bond itself.

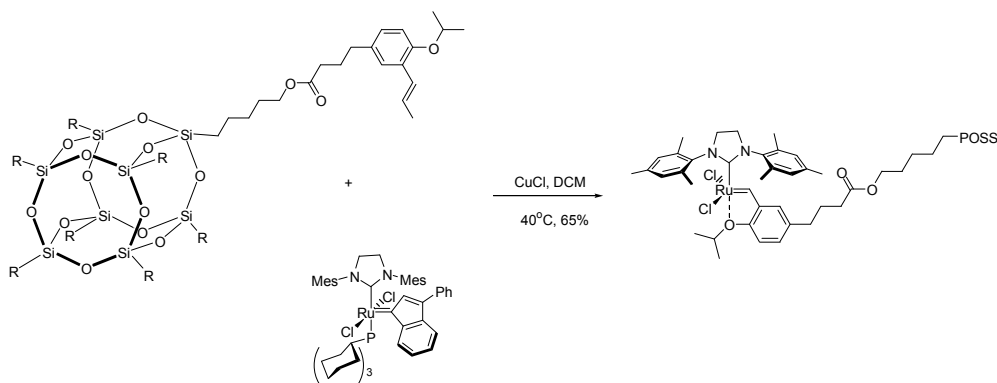


**Figure 8** Hoveyda type catalyst with urethane linking bond

For this purpose ligands and catalyst with ester linking bond have been prepared.

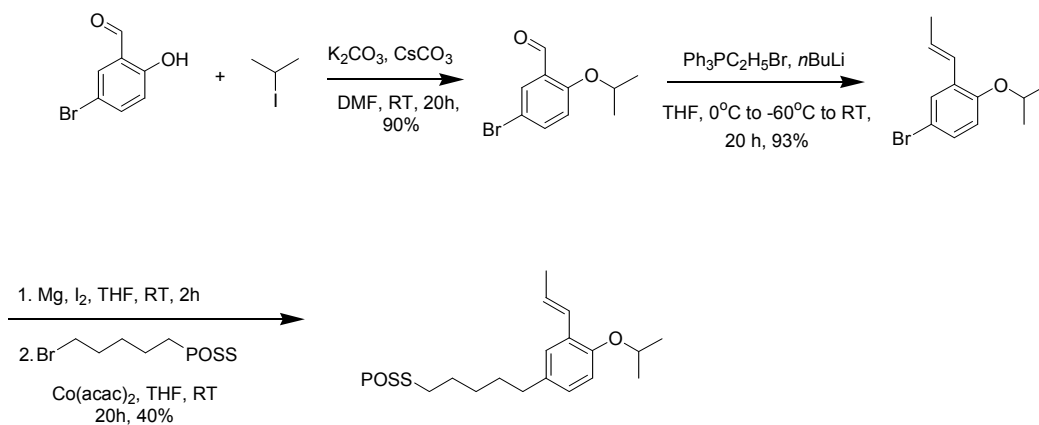


**Figure 9** Alkylidene ligand with ester linking bond.



**Figure 10** Hoveyda type catalyst with ester linking bond

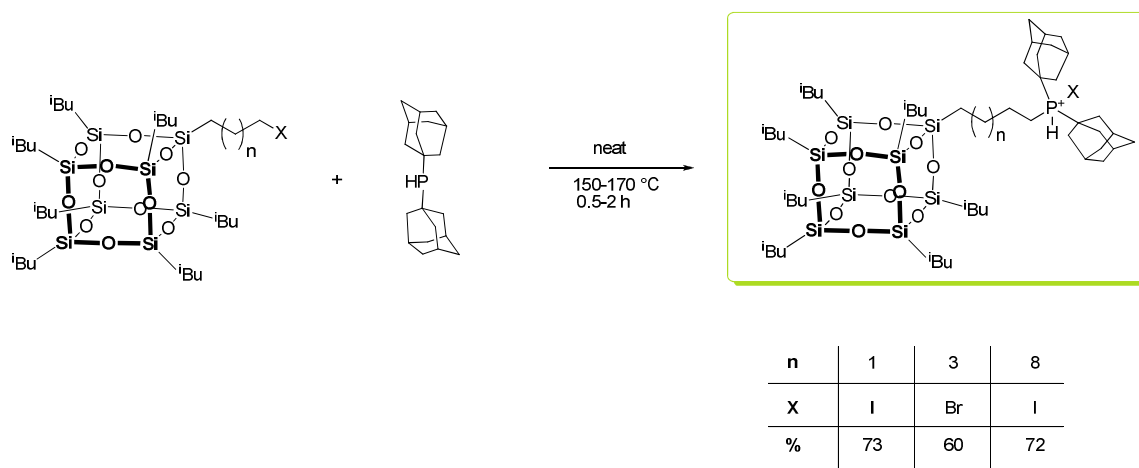
Second catalyst which was synthesised to validate the hypothesis was Hoveyda type catalyst without any linking bond. The best condition for this critical reaction step is presented below.



**Figure 11** Alkylidene ligand without any heteroatom linker.

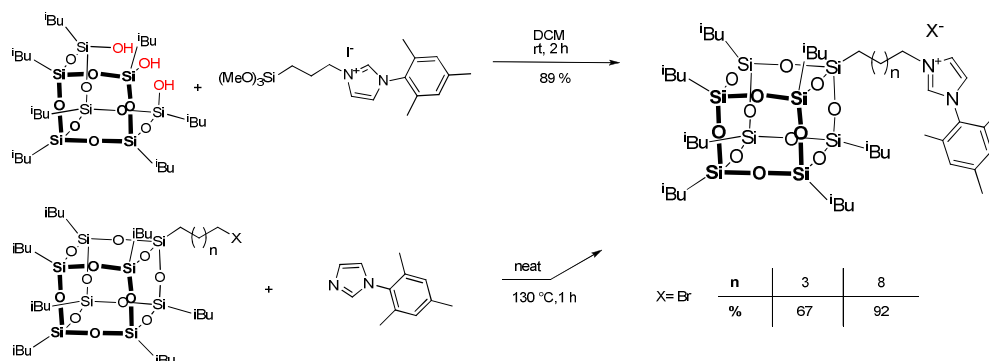
Modification catalysts intended for CX coupling was extended from pure phosphine-Pd complexes to both NHC-Pd complexes and NHC-Phosphine mixed complexes since these systems were recognized as powerful systems based on latest literature publications.

The POSS-supported cataCXiumA<sup>®</sup> compounds were synthesized as depicted in Figure 12. Under these optimized reaction conditions no solvent is used leading to the desired compounds in satisfactory yields. With regard to larger production scales, this procedure is advantageous with respect to cost-efficiency and ecological aspects.



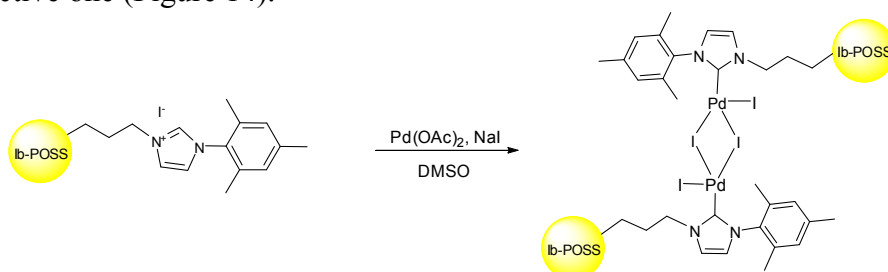
**Figure 12** Synthesis of POSS-supported cataCXiumA<sup>®</sup> compounds

POSS-supported imidazolium salts as precursors for Pd-binding N-heterocyclic carbenes were obtained following two synthetic strategies (Figure 13). The C3-derivative was obtained by a POSS-ring closing reaction of the preformed trimethoxy silane and open-POSS. C5- and C10 variants were synthesized under solvent-free reaction conditions as demonstrated for the syntheses of POSS-supported cataCXiumA<sup>®</sup> compounds.



**Figure 13** Imidazolium salts from different POSS-sources

From various POSS-supported, N-heterocyclic carbene connected Pd-catalysts that were generated from the corresponding imidazolium salts and different Pd sources, the  $\mu$ -bridged dimeric species was the most active one (Figure 14).



**Figure 14**  $\mu$ -bridged dimeric POSS-supported Pd-catalysts.

Two patent applications concerning catalyst design and synthesis have been filed:

1. Patent claiming compound structures (phosphine ligands / metal complexes and NHC-ligands / metal complexes) PCT/EP2011/052885 (1.3.2010)
2. Patent claiming method of preparation (linking polysilsesquioxane entities and ligands via neat melting) EP 11170407.8 (17.06.2011)

### ***Catalytic reactor operation – proof of principle***

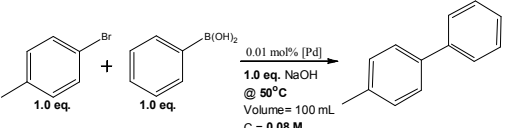
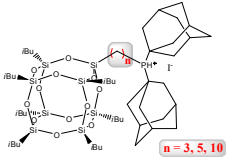
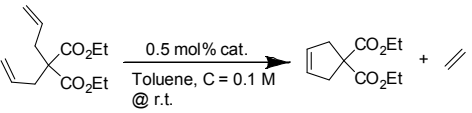
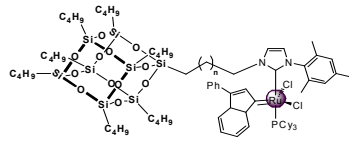
Catalytic activity was demonstrated for the nanoparticulate catalysts for ring-closing olefin metathesis of diallyl malonate (which is of interest for synthesis of pharmaceutical comprising macrocyclic molecules), for cross metathesis of methyloleate (this technology relevant for monomer, surfactant, lubricant, cosmetics production) and for CX coupling reaction (which is important for fine chemical applications).

In order to identify promising catalytic systems (nano-particulate catalysts, membranes and reaction conditions) for later continuous reactor operation, diverse Ru-NHC-POSS complexes and Pd-POSS-phosphine complexes have been pre-checked with respect to catalytic activity under batch conditions and with respect to nano-filtrability applying various membranes and solvents. Results of these pre-tests are summarized in Table 2. Table 3 summarizes results of experiments related to continuous process operation.

Both types of catalytic tests show promising performance of Ru-NHC-POSS and Pd-POSS-phosphine catalysts for metathesis reaction and for CX coupling. Preconditions of continuous catalytic reactor operations are fulfilled:



Table 2 a)

<i>Catalytic reaction</i>	<i>Catalyst applied</i>	<i>Catalytic performance (Batch mode)</i>	<i>Membrane selection → Filtration test</i>
<p><b>Suzuki-Miyaura Coupling</b></p> 		<p>TON benchmark: homogeneous catalyst) = 33,600</p> <p>TOF (Benchmark: homogeneous catalyst) = 13,600</p> <p>TON (POSS-modified catalyst) = 38,400</p> <p>TOF (POSS-modified catalyst) = 35,200 h<sup>-1</sup></p>	<p>Membrane type = DuraMem™ 300</p> <p>Flux = ≥ 30 L.m<sup>-2</sup>.h<sup>-1</sup> solvent flux.</p> <p>Catalyst rejection = &gt; 99 %</p>
<p><b>Ring-closing Metathesis A)</b></p> 		<p>TON - benchmark: homogeneous catalyst) = 1450</p> <p>TOF - benchmark: homogeneous catalyst) = 100 h<sup>-1</sup></p> <p>TON (POSS-modified catalyst) = 180</p> <p>TOF (POSS-modified catalyst) = 30 -60 h<sup>-1</sup></p>	<p>Membrane type = DuraMem™ 300</p> <p>Solvent flux = ≥ 15 L.m<sup>-2</sup>.h<sup>-1</sup></p> <p>Catalyst rejection = &gt; 99%</p>

**Table 2 b)**

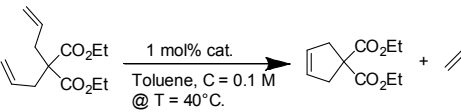
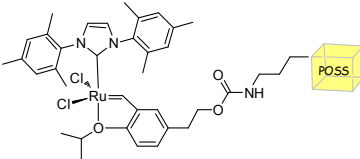
<i>Catalytic reaction</i>	<i>Catalyst applied</i>	<i>Catalytic performance (Batch mode)</i>	<i>Membrane selection → Filtration test</i>
<p><b>Ring-closing Metathesis B)</b></p>  <p>1 mol% cat. Toluene, C = 0.1 M @ T = 40°C.</p>		<p>TON (POSS-modified catalyst) = 960</p> <p>TOF (POSS-modified catalyst) = 480 h<sup>-1</sup></p>	<p>Membrane type = PI-APTS membrane</p> <p>Flux = 15 L.m<sup>-2</sup>.h<sup>-1</sup></p> <p>Catalyst rejection = &gt; 99%,</p>

Table 2c)

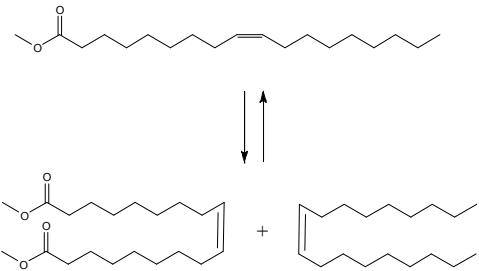
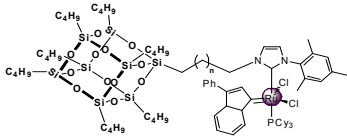
<i>Catalytic reaction</i>	<i>Catalyst applied</i>	<i>Catalytic performance (Batch mode)</i>	<i>Membrane selection → Filtration test</i>
<p><b>Cross Metathesis (HomoMetathesis)</b> 70°C, neat</p> 		<p>TON benchmark: homogeneous catalyst) = 254,300</p> <p>TOF (Benchmark: homogeneous catalyst) = &gt; 64,000 h<sup>-1</sup></p> <p>TON (POSS-modified catalyst) = 27,000</p> <p>TOF (POSS-modified catalyst) = 7,200 h<sup>-1</sup></p>	<p>Membrane type = PuraMem S380</p> <p>Flux = 30 L.m<sup>-2</sup>.h<sup>-1</sup></p> <p>Catalyst rejection = &gt; 99%</p>

Table 3 a)

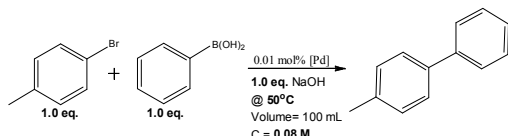
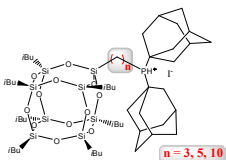
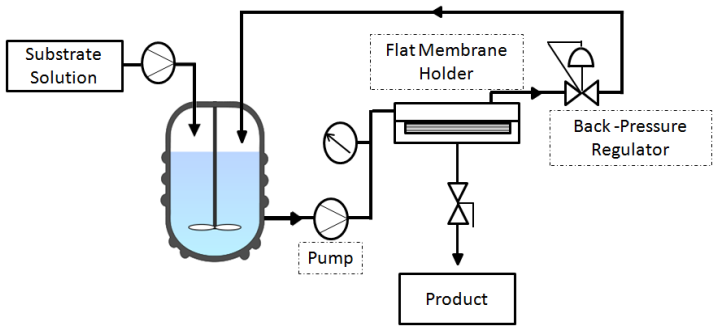
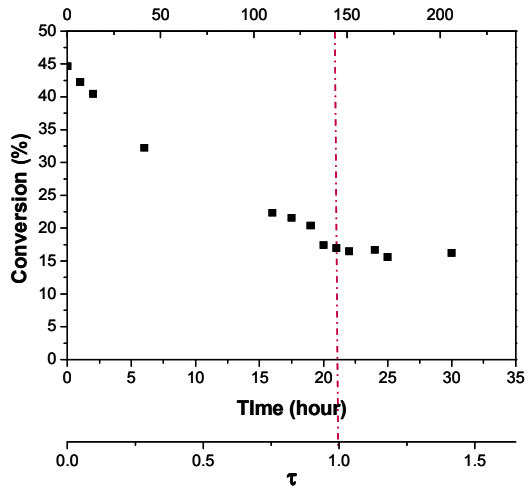
Catalytic reaction	Catalyst / Membrane / reaction conditions	Result of continuous reactor operation
<p><b>Suzuki-Miyaura Coupling</b></p> 	<p>Catalyst =</p>  <p>Membrane = DuraMem™</p> <p>Mean-residence time = 21.2 h</p> <p>Total Reaction time = 96 hrs</p> <p>Feed velocity / substrate loading = 0.1 mL min<sup>-1</sup></p> <p>Exchanged reactor volume = 1.8</p>	<p>CSTR mode; reactor volume <math>V_R = 140</math> mL</p>   <p>Accumulated turn-over number 31,000; Constant activity after 21 hours of reaction</p>

Table 3 b)

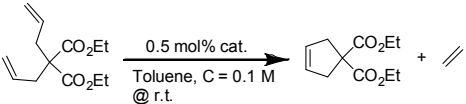
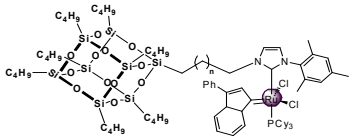
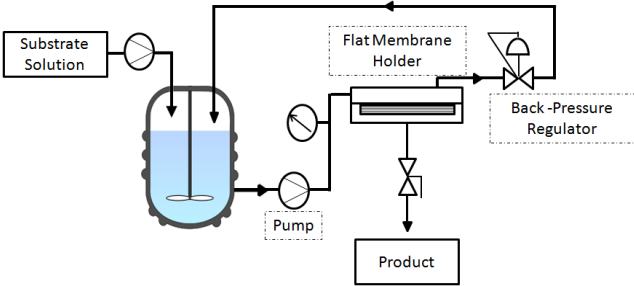
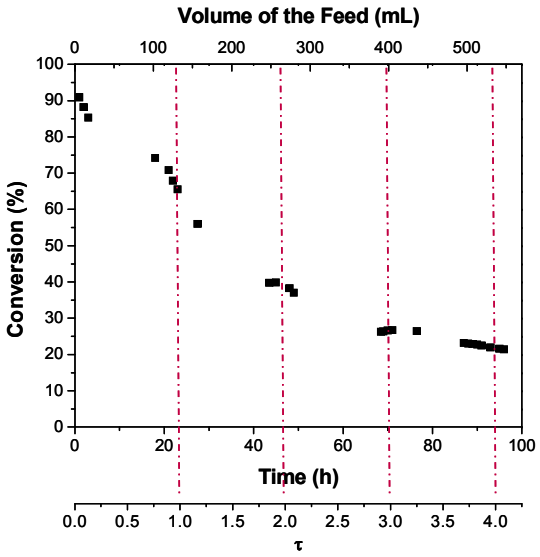
Catalytic reaction	Catalyst / Membrane / reaction conditions	Result of continuous reactor operation
<p><b>Ring-closing Metathesis</b></p>  <p>Reaction scheme showing the ring-closing metathesis of diethyl acrylate to diethyl cyclopentane-1,3-diene-1,3-dicarboxylate and ethylene, catalyzed by 0.5 mol% catalyst in toluene (0.1 M) at room temperature.</p>	<p>Catalyst =</p>  <p>Membrane = DuraMem™</p> <p>Mean-residence time = 24.6 h</p> <p>Total Reaction time = 96 hrs</p> <p>T = 25°C</p> <p>Feed velocity = 0.083 ml min<sup>-1</sup></p> <p>Exchanged reactor volume = 4</p>	<p>CSTR mode; Reactor volume: 140 mL</p>   <p>Accumulated turn-over number 483; Constant activity after 90 h of reaction</p>

Table 3 c)

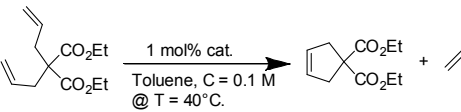
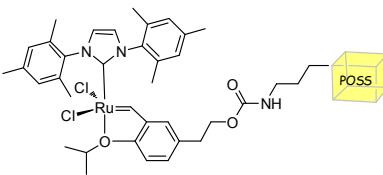
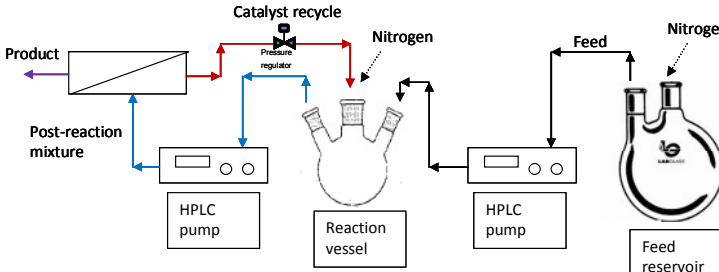
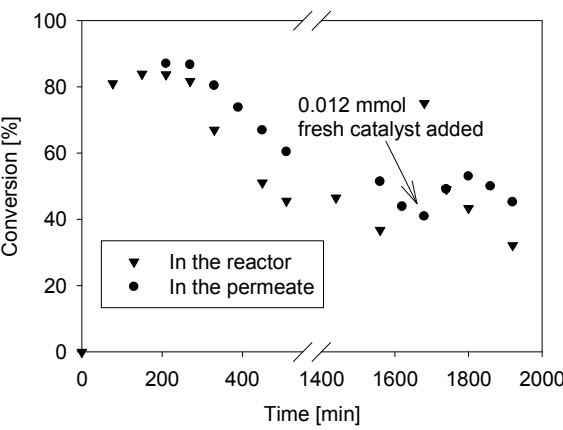

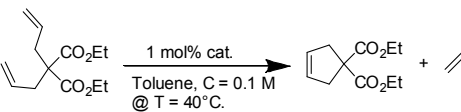
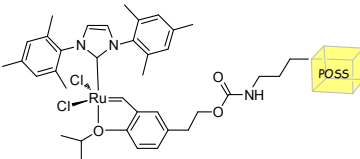
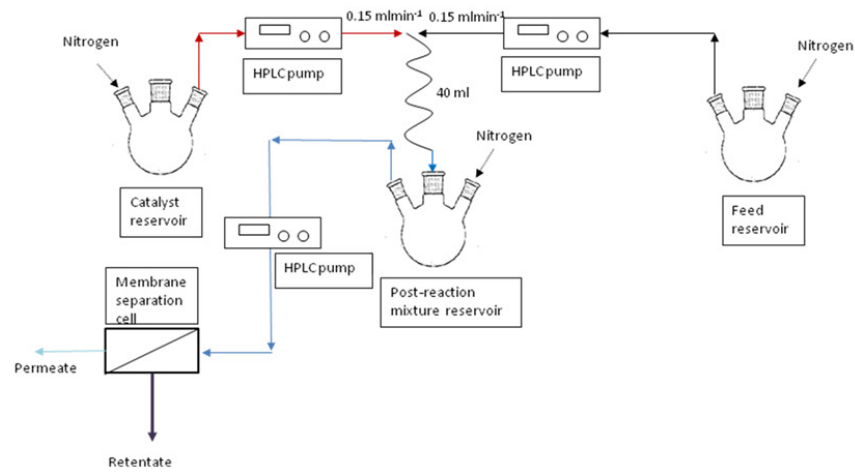
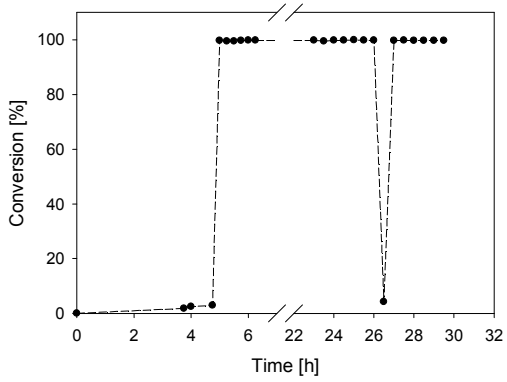

Catalytic reaction	Catalyst / Membrane / reaction conditions	Result of continuous reactor operation
<p><b>Ring-closing Metathesis</b></p>  <p>0.1 M diethyl diallylmalonate solution (solvent toluene) and 1 mol %</p>	<p>Catalyst =</p>  <p>Membrane = PuraMem280 residence time = 600 minutes</p> <p>Total Reaction time = 32 h Feed velocity/substrate loading = 0.02 mmol min<sup>-1</sup> Exchanged reactor volume = 1.5 T = 40°C</p> <p>Initially the reaction was performed in a separate flask for 2.5 hours to reach completion before being loaded in continuous mode (CSTR).</p> <p>Feed velocity = 0.2 ml min<sup>-1</sup></p>	<p><b>CSTR mode; reactor volume = 120 ml</b></p>    <p>TON = &gt;&gt; 144; Permeate ~ 1.58 mgL<sup>-1</sup> Ru ~ 1.8% losses</p>

Table 3 d)

Catalytic reaction	Catalyst / Membrane / reaction conditions	Result of continuous reactor operation
<p><b>Ring-closing Metathesis</b></p>  <p>What happened at t = 27 hrs?</p>	 <p>Membrane = PuraMem280  residence time = ~133 min  T = 40°C  Total Reaction time = 29.5 h  Feed velocity / substrate loading = 0.03 mmol min<sup>-1</sup>  Feed velocity = 0.3 ml min<sup>-1</sup>  Exchanged reactor volume = 5 (feed supply stopped overnight)</p>	<p>Plug-flow mode; reactor volume = 40 ml</p>    <p>TON~100; Permeate ~0.34 mgL<sup>-1</sup> Ru ~0.2% losses  (At 27 h due to a temporary failure of the pump supplying catalyst there was very low conversion for short period of time.)</p>

### **- Nano-filtrability of catalysts:**

Several home-made but also commercial membrane types could be successfully applied (PI-APTS, PuraMem™ S380, DuraMem™, PuraMem280, Starmem 228) in a wide temperature range (25°C to 100°C) with different solvents (toluene, THF, DCM, EtAc, MeCN). For these membranes, we can give a general statement that all stable Pd and Ru complexes bearing POSS entities show rejection > 99% over. I. e. modification of catalysts with POSS units is a feasible and general method to provide catalyst, which can be separated by nano-filtration. Also from visual evaluation it was obvious that permeate appeared as clear solution whereas the presence of catalyst in the retentate was obvious due to the coloured solution. Thus, results are very promising in terms of future use of these membranes at elevated temperatures and under catalytic reaction conditions.

### **- Sufficient total Turnover Number (TON)**

High (sufficient) turnover number is one of the most crucial criteria for economic continuous process operation. This value indicates the robustness of the catalysts in the particular reactions. Concerning this aspect, our 3 application cases – CX coupling, ring-closing metathesis and cross metathesis – are related to different challenges.

Suzuki-Miyaura coupling over Pd phosphine catalysts is a fast reaction (high catalytic activity). Turn-over number is high and in the ballpark of commercial feasibility (> 20 000). For our test example turnover number of 35.200 (Table 2a) which was also confirmed under continuous process operation with a value of 31.000 (Table 2a). The comparison of free CataCXium-A Pd complex with POSS modified CataCXium A indicates only marginal TON decrease due to POSS modification. In table 6a the substrate conversion is shown as a function of space time for Suzuki-Miyaura Coupling (CX coupling). From this a non-complete initial conversion and a drop of conversion over time becomes obvious. However we have to emphasize that the non-complete conversion is rather a consequence of choice of reaction conditions and not of insufficient catalytic activity. Higher catalyst loading and longer residence time are expected to lead to complete conversion under continuous flow conditions as demonstrated for batch conditions. The drop in catalytic activity, which corresponds to the limitation of turn-over-number (see above) is probably a result of successive decomposition of the Pd-Phosphine complex leading to the formation of Pd black.

In contrast to CX coupling, ring closing metathesis results in lower TON values for both the commercially available Ru-NHC complex (CatMETium RF1) (TON = 1450) depending on substrate and solvent purity). Taking into account that solvent and substrate purity is also a crucial factor influencing TON values we conclude that modification of Ru complexes with POSS entities does not have large impact on TON values and the differences observed are mainly due to usage of different solvent lots. However, compared to CX coupling the values are rather low and seem to be critical for commercial application.

Ring-closing metathesis was also investigated using another type of Ru-complex catalyst (Hoveyda-type, see table 2b, 3c, 3d). In contrast to The catMETium system, for this structure the POSS linkage was implemented via the alkylidene unit instead via the NHC unit. With this approach, it should be analyzed whether the linking position has an impact on the rejection rate but also on catalyst robustness and activity. As mentioned above rejection rate was also higher than 99% for this type of catalyst. The deactivation behavior of the Hoveyda / POSS system seems quite similar to the CatMETium RF1 / POSS structure (comparison Table 3b and 3c) Thus, for CSTR operation a drop of conversion from originally > 80 % to a value of around 50% after 30 hrs was observed in both cases. For both types of catalysts accumulated TON of (488 and 144) have been achieved within the time of continuous reactor operation, which was limited due to manual control of the equipment; therefore, much higher total TON are expected if the experiments would be continued over longer space time. The drop in conversion over time could be due to catalyst decomposition



and/or inhibition triggered by ethylene accumulation in the system. The addition of fresh catalyst had only very little effect on the conversion which might result from ethylene accumulation in the reaction solution over time.

For the Hoveyda system also plug-flow operation mode was studied and compared to CSTR operation mode. The reactor was run continuously for 32 hours and showed a stable conversion of ~100% within this time range (Table 3d). Obviously, the extent of back-mixing is a crucial factor for stable reactor operation. Thus the deactivation under CSTR condition might be addressed again to higher steady-state ethylene concentration in solution accelerating the deactivation process as already discussed above.

Apparently the plug-flow configuration seemed the most promising and further investigation should be performed in order to evaluate its true potential.

Cross (homo-) metathesis of methyloleate (Table 2c), in turn, is a reaction where very high turn-over numbers can be achieved with CatMETium RF1 (254,300). However, in this case, a significant decrease in the catalyst robustness was observed with the POSS modified Ru complexes (27,000). Nevertheless, the value is still high. Possibly, impurities resulting from the catalytic material itself are the reason for lower TON. This has to be clarified in the frame of future process optimization.

#### **- Catalytic Activity**

It could be demonstrated for all application cases, CX coupling, ring-closing metathesis, and cross metathesis that the linkage of metal complexes with POSS entities does not influence the activity of the catalysts significantly (see Table 2). From this, it can be concluded that the complex structures are not influenced by the POSS unit as long as the spacer unit is long enough. Here, an optimal length of spacer unit was predicted by theoretical calculation. This finding was confirmed by the experimental results for CX coupling and ring-closing metathesis.

Clearly POSS synthons serve the need for molecular weight enlargement of sophisticated homogeneous catalysts and ligands. This implies that the POSS synthons should be chemically robust and significantly more affordable than compounds as dendrimers, hyperbranched polymers and inorganic clusters that could serve the same purpose. To a large extent, this has been well demonstrated. According to this evaluation, the HiCat consortium came to the conclusion that the “proof of concept and principle” has been successful.

#### **4.1.2.3 Support of catalyst design by theoretical calculation**

Some important properties for the prediction of catalytic activity, such as the theoretically defined buried volume, are related to the conformational characteristics of these complex ligands that can be studied using molecular dynamics simulations. In this work we focus on complexes formed by a catalytic metal centre (Ru) with both phosphine and POSS linked NHC groups. The central region of these complexes contains atoms and groups that have bonds, bond angles and torsional angles whose parameters are not generally included in existing force fields. In view of this we have performed ab initio quantum mechanical calculations to obtain energies for this central section, resulting in additional parameter sets that can be used to supplement existing force fields. From subsequent molecular dynamics simulations we have obtained results that illustrate the conformational characteristics most closely connected with the catalytic activity which has been experimentally determined. In summary, our methodological implementation of different computational techniques has been able to provide some important quantitative data on the conformational characteristics related with the catalytic activity of a family of complexes formed by a metal and ligands with a relatively complex chemical. Naturally, this methodology can be applied to studies of other similar systems.

### 4.1.2.3 Economical assessment

The following economic drivers for recycling of homogeneous catalysts have to be analyzed for economic assessment:

- Reduce amount of expensive catalysts / ligands due to recycle and / or continuous process operation?
- Reduce process costs due to easier product purification (removal of catalyst from products)?

In this context, the economic assessment shall give answers to the following questions:

- What is the impact of ligand modification on ligand production costs?
- Do the advantages of continuous processes legitimate additional costs for ligand modification and investments for separation units?

In order to answer the question raised above, critical numbers have been defined which can be used as guideline for optimization of synthesis of ligands (optimization of catalyst production costs) and optimization of catalytic processes (turnover number and space time yield):

**TON<sub>crit1</sub>:** Turnover number which has to be achieved to meet the cost expectations of customers can be derived for given catalyst production cost (calculated for the synthesis of catalysts in the project).

**TON<sub>crit2</sub>:** no requirement for recycle if catalyst is very active and cheap and turnover number is higher than  $TON_{crit2}$

**TON<sub>crit3</sub>:** no sense of continuous process or catalyst recycles if turnover number is lower than  $TON_{crit3}$ . Then additional costs due to ligand modification and investment for recycle facilities cannot be compensated.

**TON<sub>crit4</sub>:** indicates above which turnover number the required annual capacity is fulfilled at a given amount of catalyst, total duration of the production campaign and catalyst activity (TOF).

Thus, the regions  $TON_{crit1}; TON_{crit3} < TON < TON_{crit2}; TON_{crit4}$  for which a catalyst recycle is economically feasible can be estimated.

For the calculation of these figures, the economy by scale of catalyst production plays an important role, i. e. the higher the batch size for catalyst production the lower the production costs due to the dilution of fixed cost contribution. Accordingly, batch size of catalyst production must be considered as parameter of economic assessment as well. Moreover, different market scenarios (pharma, specialty and commodity) related to different production scales, different accepted costs of catalyst per kg product, different prices of products etc. have to be taken into account for evaluation of economic feasibility. Hereby, it turned out that ring closing metathesis for pharma applications is does not benefit from catalyst recycling due to low turn-over-number and due to the small size of application whereas CX coupling and cross metathesis of fatty acid esters with significant higher turn-over-number could indeed avail oneself from recycling.

The methodology was applied to the POSS-CataCXium A<sup>®</sup> system and T-responsive microgel catalysts with phosphine and NHC functionality obtained via different synthesis pathways.

For estimation of production costs, variable costs were calculated from prices of chemicals involved in the synthesis. Fixed costs were estimated based on our experiences concerning rent of production facility depending on reactor size. Moreover, number of required batches to produce a required amount of catalyst, duration of synthesis, and costs for safety analysis was considered. Results show that additional production costs for both POSS modified systems as well T-responsive catalyst are lower than 50% of the costs for producing the respective homogeneous catalysts (metal complexes).

This means that additional costs can be paid back already by one recycle of catalysts

#### **4.1.2.4 Benchmarking temperature-sensitive micro-gel catalysts for batch operation and nano-filtratable catalysts for continuous process operation**

Finally, the different concepts for building up recyclable metal organic catalysts are benchmarked against state-of-the-art homogeneous catalysts. Hereby, it should be evaluated whether no-goes are obvious which would over-compensate the advantage of separability of those catalyst systems developed in the HiCat project. Respective benchmark criteria and evaluation statements are summarized in Table 4. As a conclusion, we did not find no-goes from our present perspective.

For both catalytic systems (polymer/microgel-based and POSS-based) straight forward syntheses pass ways which are economically feasible have been developed and patented. Both systems are related to less than 50% additional production costs compared to the homogeneous complexes. These additional costs are paid back as soon as the catalyst is reused one time.

Evaluation of catalytic performance showed that activity of original homogeneous catalysts can be nearly maintained also after interconnection of metal complexes with nano-particle entities. Hereby, the metal loading covers the range of conventional heterogeneous catalysts without losing the activity of homogeneous complexes.

This indicates that with the new nano-particulate systems we are able to take the advantages from both sides: homogeneous (high activity and selectivity due to maintenance of site isolation) and heterogeneous catalysis (separability).

Of course the sense and economics of catalyst recycle finally depends on the Turn-over number of the particular metal complex which appears as the most critical parameter of commercial application. Here, we have found large differences in the different applications.

I.e. economic feasibility of processes including catalyst recycle will be a case-by-case decision. However, we have clearly identified processes with high turn-over number (i.e. Suzuki-Miyaura coupling, cross metathesis of fatty acid esters) where catalyst recycle using the HiCat catalysts can offer economic benefits.

Even for ring closing metathesis, where until now still low turn-over-numbers are achieved, continuous separation of catalyst from the product solution can offer added value due to complete and easy catalyst separation from the down-stream part of complicated multi-step synthesis pathway (i.e. API synthesis).

**Table 4:**

	<b>T-responsive Polymers / Microgels</b>	<b>micro polyhedral oligosilsesquioxane cages (POSS)</b>
<b>Catalytic activity</b>	Switchable catalytic activity; high activity above UCST (TOF higher than for conventional precious metal powder catalysts) +	No significant decrease in activity compared to homogeneous complexes 0
<b>Catalyst stability</b>	Experimental data not sufficient for final evaluation; further studies required	No significant decrease in stability compared to homogeneous complexes 0
<b>Solubility / solvent variety</b>	Tunable solubility +	Soluble in variety of solvents (poor stability in basic media) +
<b>Commercial availability; Catalyst Production costs</b>	Capacity not yet in commercial range - Additional (molar) production costs of 15% compared to isolated metal complex (due to low-cost polymer raw material) → additional costs can be paid back already by one recycle of catalyst +	Capacity = 15 TON / yr + Additional (molar) production costs of 35% compared to isolated metal complex → additional costs can be paid back already by one recycle of catalyst +
<b>Metal loading capacity (referring to catalytic functionality)</b>	5 wt-% (comparable to heterogeneous catalyst) +	5 wt.%(comparable to heterogeneous catalysts) +
<b>Site isolation, exposure to solution environment</b>	Single sites, no interaction between sites up to metal loading of 4 wt-% +	Single sites, no interaction between sites due to highly defined structure and site distribution

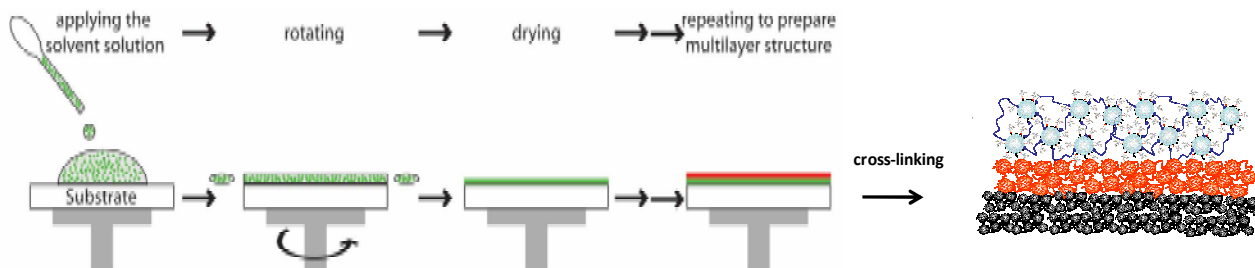
#### 4.1.2.5 New types of films and membranes with graded porosity based on hierarchical structured systems

Methods for forming layers of nanoparticles with homogeneity of nanoparticle size distribution, and controlling permeability were developed. The spin-coating technique used (Fig. 15) allows consecutive coating with different nanoparticles dispersed in solution, thus forming a multilayer structure. Although suitable mainly for laboratory applications this technique could be easily replaced by a spray coating which is suitable for large scale applications. Series of membranes from NIPAm nanoparticles (120 and 300 nm size) were produced using the spin-coating technique followed by UV radical polymerization cross-linking with photo initiator. Smooth uniform layer formation was observed (Fig. 16). The effect of different membrane formation parameters on membrane separation performance was investigated for different solvents and temperature. Correlations were observed between the nanoparticles layer thickness and the MWCO and flux of the membrane, e.g. the thinner the layer the more open structure and higher MWCO is achieved as indicated in Table 5. The solvent flux, in turn, seems to be governed mainly by the thickness of the nanoparticles layer for the layers of the same thickness but varying nano-particle size (Figure 17). The concentration of the nanoparticles in the solution seems to be additional parameter to controlling the separation performance (MWCO) of the membrane.

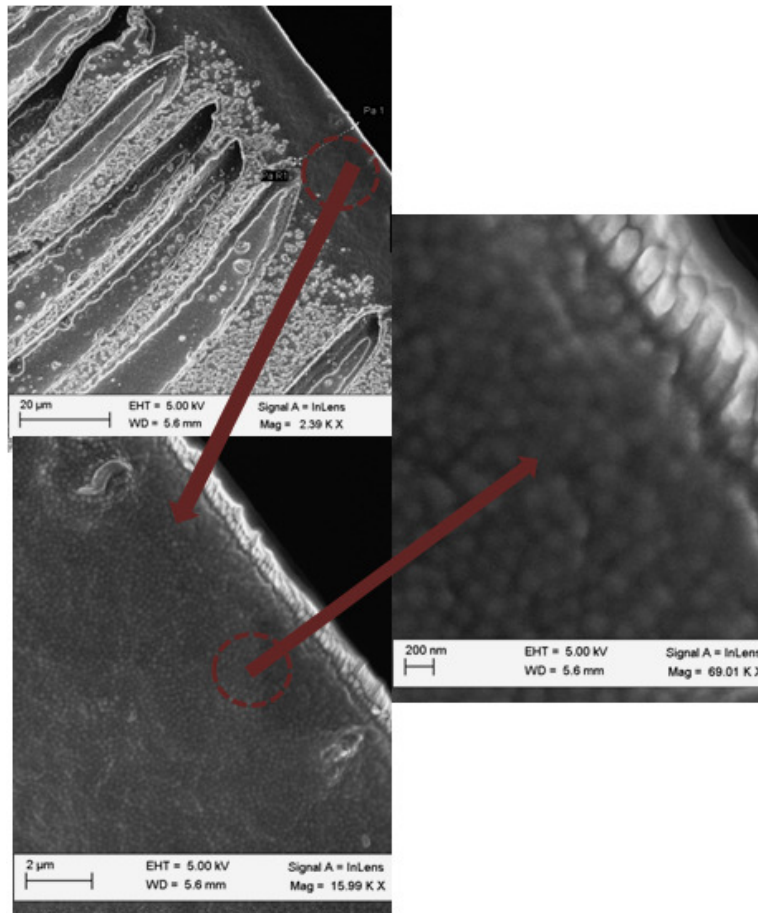
Based on these experiences and findings, membranes with graded porosity were prepared, consisting of consecutive layers of 300 and 120 nm nanoparticles, resulting in very tight membranes with MWCO 200-220  $\text{gmol}^{-1}$ . This shows the possibility of preparing membranes with consecutive layers of nanoparticles with different functionalities or/and immobilised catalysts. Using a proper combination of the above mentioned factors membranes of a wide range of MWCOs can be produced.

As shown in Table 5 membranes with MWCO range between 220-1000 Da have been successfully produced using the same nanoparticles and membrane production method.

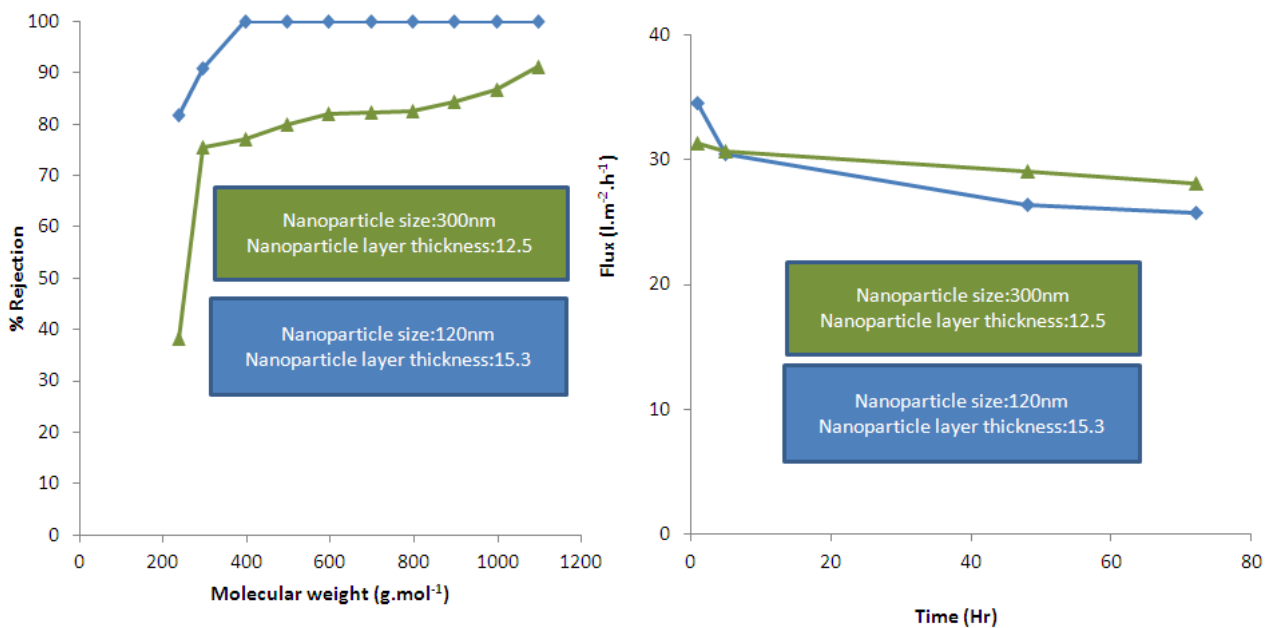
These membranes show similar or even better performance than the commercially available ones and are compatible with wider range of solvents (i. e., commercial Starmem122 is not compatible with acetone, while the commercial Duramem300 has poor performance in toluene). From our HiCat work we conclude that a technology using microgel particles has great potential for tailor-made membranes with finely tuned properties and separation performance. Development of new types of membranes with graded porosity based on layers of nanoparticles is a viable new alternative for membranes production.



**Figure 15:** Schematic representation of the proposed spin-coating technique for forming nanoparticles layers



**Figure 16:** SEM image of the membrane produced from 300 nm nanoparticles (edge view)



**Figure 17:** Effect of the nanoparticle size on the membrane performance – rejection and flux data in toluene at 30 bar pressure and 30<sup>0</sup>C.



Table 5 Performance of membranes prepared form microgel nanoparticles - summary

Nanoparticle size	no of coats	Toluene		Acetone	
		Flux Lm <sup>-2</sup> h <sup>-1</sup> 30 bar	MWCO gmol <sup>-1</sup>	Flux Lm <sup>-2</sup> h <sup>-1</sup> 30 bar	MWCO gmol <sup>-1</sup>
control	0	55	>> 1095	80	>>1095
120	1	45	~550	72	~440
	2	35	~450	68	~360
	3	23	~340	40	~260
300	1	35	> 1095	48	> 1095
	2	28	> 1095	44	> 1095
	3	15	~500	30	~500
120-300	2-2	15-20	~220	35-40	~220
S122	0	17	300	-----	-----
Duramem300	0	-----	-----	30-35	300

For production of flat-sheet membranes integrated into spiral-wound modules for applications at industrial scale, it is important to realize high reproducibility in making the spiral-wound modules without leaks using membrane materials which are stable in organic solvents. The work focused on development of membranes which cover both requirements comprised following studies: A) Preliminary tests on support material: Leak test and B) Performance of membranes fabricated on the selected support material using the bench-scale casting machine. Different support materials have been considered. The leak tests of membrane materials with varying air permeability, material thickness, and mass of material per unit area showed that more than 64% of material passed the dye test. Based on these results suitable membrane types were identified to be fabricated into spiral-wound modules used for commercial applications.

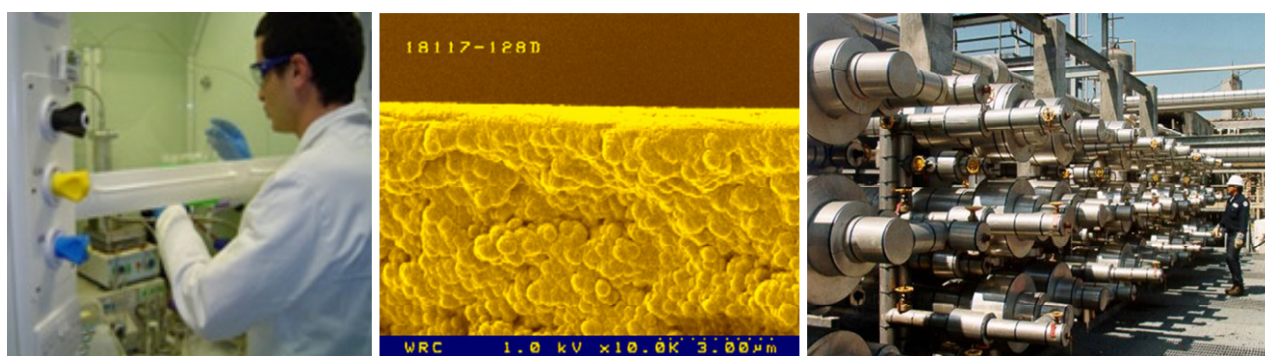


Figure 18: From membrane preparation and characterisation to spiral-wound modules used for commercial applications.

## 4.2 Impact

### 4.2.1 Market relevance / Socio-economic impact

The current situation in catalytic technology for life-science and fine-chemical applications is characterized by usage of catalysts which are traditionally based on supported precious metals and activated base metals (Raney-type catalysts) with limited selectivity. These catalyst technologies are mature, i. e. these types of catalysts can no longer be considered as specialities and have become commodity products. Due to decreases in gross margins which can be achieved with these catalysts the relocation of their production from Europe to Asia is an impending scenario. Without substitution of mature catalyst technologies by innovative ones such a process will reduce the competitiveness of European industry along the complete value added chain, even for emerging technology fields as mentioned above.

With the HiCat project work the door has been opened to an innovative catalyst technology platform which, in contrast to the established technology, will offer close to 100 % selectivity combined with an easy non-destructive recovery of the catalysts material at the customer site.

It was clearly demonstrated that the activity (turn-over-frequency per metal atom) of the HiCat catalysts can exceed that of conventional precious powder catalysts significantly. This, increase in specific activity in turn, can be used either for decrease of precious metal loading of catalysts or will increase the productivity of catalytic processes. Consequently, the technology developed in the HiCat project can remarkably increase the added value for applicants of catalytic processes. Hereby, the HiCat project does not only deliver innovative catalysts but also reactor concepts for running the respective catalytic processes (e.g.. continuous catalytic nano-filtration processes including feasible membranes).

These technology packages might have a major impact in many industrial sectors such as the production of fine and speciality chemicals, nutrition, pharmaceuticals and polymers. In these sectors, new applications could be made accessible.

Processes with high turn-over number (i.e. Suzuki-Miyaura coupling, cross metathesis of fatty acid esters) have been identified where catalyst recycle using the HiCat catalysts can offer significant economic benefits. E. g., continuous olefin metathesis of fatty acid esters is an emerging (even large-scale) technology for conversion of oleo-chemical feedstock to monomers, surfactants, lubricants etc.. At the moment, catalyst costs belong to the major cost drivers of this attractive process. Here, we expect that the opportunity of catalyst recycle will indeed push the market penetration significantly.

Even for ring closing metathesis, where until now still only low turn-over-numbers are achieved, continuous separation of catalyst from the product solution can offer added value due to complete and easy catalyst separation from the down-stream part of complicated multi-step synthesis pathway for API production.

Thus, developments from our HiCat project will help to break down current barriers to application of metal-organic catalysts in many industrial fields such as production of fine and speciality chemicals, nutrition, pharmaceuticals and polymers (functional foods, functional polymers, polymer coatings, electronic polymers, new active pharmaceutical ingredients). Products of the mentioned industrial branches, in turn, are used in all areas of daily life.



### **4.2.2 Ecological Impacts**

The catalytic systems developed in the project are of current particular interest for fine-chemical, pharmaceutical and polymer processes. Especially, fine chemicals and pharmaceutical products are usually produced in several reaction steps using toxic compounds and the waste-to-desired product ratio is traditionally very high. The usage of separable and recyclable metal organic catalysts is a step change concerning process efficiency and environmental impact since these catalysts are predestined for sustainable chemical process with nearly zero-waste emission especially in the production of fine-chemicals and pharmaceutical intermediates.

Hereby, the HiCat project has contributed to meet the societal challenges by reducing the use of raw material resources and by protecting our environment from toxic or other detrimental products.

As mentioned above, we have demonstrated that the activity (turn-over-frequency per metal atom) of the HiCat catalysts can exceed that of conventional precious powder catalysts significantly. This, increase in specific activity in turn, saves resources such as rare precious metals but also reactants and due to high selectivity and productivity. Moreover, catalyst separation via membranes (as applied in our nano-filtration technology) is highly efficient separation process from the energetically point of view and superior compared to conventional thermal separation processes such as distillation.

### **4.2.3 Impacts on SMEs**

Due to the embedding of two SMEs which deal with the commercialization of catalyst components (POSS development and production) and membrane technology together with the well established infrastructure of EVONIK and its catalyst production, the HiCat project promotes access to European chemical industry in testing the innovative catalytic systems. Especially, Hybrid Catalysis which has provided POSS as a central building block of catalysts for continuous process operation will broaden its product portfolio and strengthen its competitiveness in the market for polysilsesquioxanes. To promote the market approach with POSS-based catalysts the industrial partners (EVONIK Catalysts and Hybrid Catalysis) closed a license agreement regulating the exploitation of POSS functionalized synthons in network catalysts manufacture. Further business development should be supported by coordinated marketing and common development of well founded understanding of technology, system and market aspects.

### **4.2.4 Scientific / technological impact**

We have demonstrated the feasibility of continuous reactor operation with promising turn-over numbers and high catalyst rejection rate. Based on a large repertoire of functionalized silsesquioxane (POSS) nanoparticles metal-organic catalysts have been synthesized applicable for olefin metathesis and CX coupling reactions. Hereby, processes with high turn-over number where catalyst recycle using the HiCat catalysts offer economic benefits have been identified. Evaluation of catalytic performance showed that activity of original homogeneous catalysts can be nearly maintained also after interconnection of metal complexes with nano-particle entities. Metal loading of POSS modified catalysts covers the range of conventional heterogeneous catalysts. This indicates that with the new nano-particulate systems advantages from both sides are explored: homogeneous (high activity and selectivity due to maintenance of site isolation) and heterogeneous catalysis (separability). Straight forward syntheses pass ways which are indeed economically feasible have been developed.

Now, all process components (catalyst building blocks and membranes) can be produced in commercial scale. Two patent applications for catalyst compounds and production have been filed which secure the IP for this technology to the project stakeholders.

Therefore, we consider the technology of POSS-modified metal catalysts for membrane reactor application as rather close to commercial application. Concerning catalytic process operation, we have demonstrated the feasibility of continuous reactor operation with promising turn-over numbers and high catalyst rejection rate.

Additional technological impact results from our proof of principle for a new class of catalysts - the T-responsive polymer (microgel) supported metal catalysts. For the first time, integration of both catalytic activity and T-responsiveness within a single catalytic system has been demonstrated. A large variety of microgel systems has been evaluated with respect to their potential in catalytic applications. Prototype catalysts have been applied in two different catalytic reactions. Our results have shown that the T-responsive polymer particles reveal a high tolerance with respect to catalytic functionality allowing high degree of functionality and hence metal loading covering already a range of conventional heterogeneous precious metal powder catalysts. However, since this technology is completely new a wide field of optimization has still to be explored until commercialization. Our fundamental findings on integrating T-responsive and catalytic functionalities has not only impact for catalytic technology but can be used also for other classes of functionalized materials (for electronics, photovoltaic, coating / functional layers etc.).

Patent applications related to T-responsive catalysts are just in the filing process. After patent filing respective publications have already been scheduled among the partners of the HiCat consortium.

An overview about the status of developments and required actions for further technology implementation concerning T-responsive and nano-filtratable catalysts within the HiCat project is given in the Figure 19.

The development of nano-filtratable catalysts for continuous process operation is closely related to the development of feasible membranes and membrane reactor modules, respectively. In the HiCat project these developments went hand in hand combining the unique expertise for development of functionalized silsesquioxane nanoparticles (POSS), catalysts and membranes.

Application at industrial scale requires flat-sheet membranes integrated into spiral-wound modules. Here production technology has to realize high reproducibility in making the spiral-wound modules without leaks using membrane materials which are stable in diverse organic solvents. Suitable membrane types were identified and fabricated into spiral-wound modules for commercial applications.

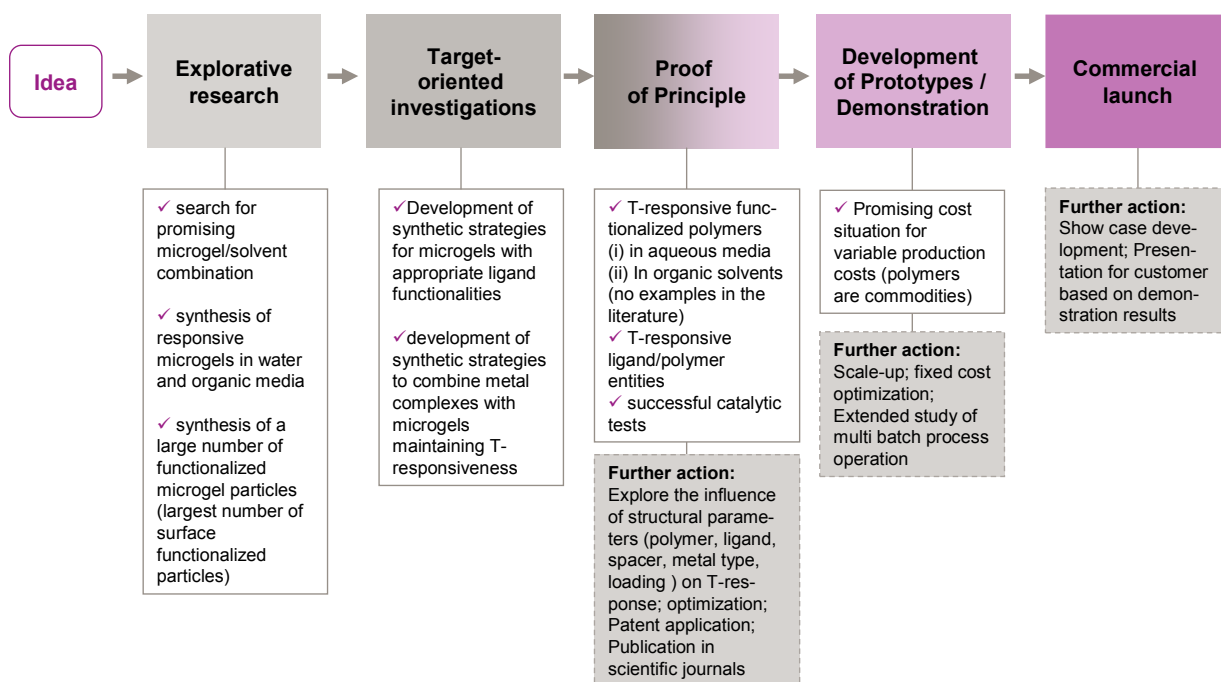
Finally methods for forming layers of nanoparticles with homogeneity of nanoparticle size distribution have been developed. Possibility of preparing membranes with consecutive layers of nanoparticles with different functionalities has been demonstrated. These membranes show similar or even better performance than the commercially available ones and are compatible with wider range of solvents. From our HiCat work we conclude that a technology using microgel particles has great potential for tailor-made membranes with finely tuned properties and separation performance not only for catalytic application but also for diverse purification processes in pharmaceutical and fine chemistry.

#### **4.2.5 Impact of Collaboration**

The HiCat project can be considered as very instructive and successful example for improving the knowledge supply chain through an industry-led programme of fundamental research which brings together Universities, SMEs and a major chemical company. By combining the work at 8 partner sites a critical mass with real multidisciplinary has been achieved. Especially, combination of broad range of different expertises from material and technology to system integration and business concepts for catalyst technology and catalyst components must be considered as a key success

factor of the HiCat project. Hereby, it has been established that partners from different fields like polymer/material science, synthetic chemistry and reaction engineering have worked together in a highly focused manner for a common product and process development. Direct exchange of researchers between academia and industry appeared to be essential for intensive and efficient exchange of experiences and knowledge. New interdisciplinary contacts and collaborations have been initiated by HiCat which will be continued beyond the project time. HiCat has involved more than 30 researchers, together with their supervisors and managers. We have realized a comprehensive programme of exchanges in particular of young researchers (PhDs and Postdocs) which ascertained the flow of technical information but a flow of experience and ideas between academic and industrial partners.

### Temperature-sensitive polymer (micro-gel) catalysts for batch operation



### Nano-filtratable catalysts and nano-filtration membranes for continuous process operation

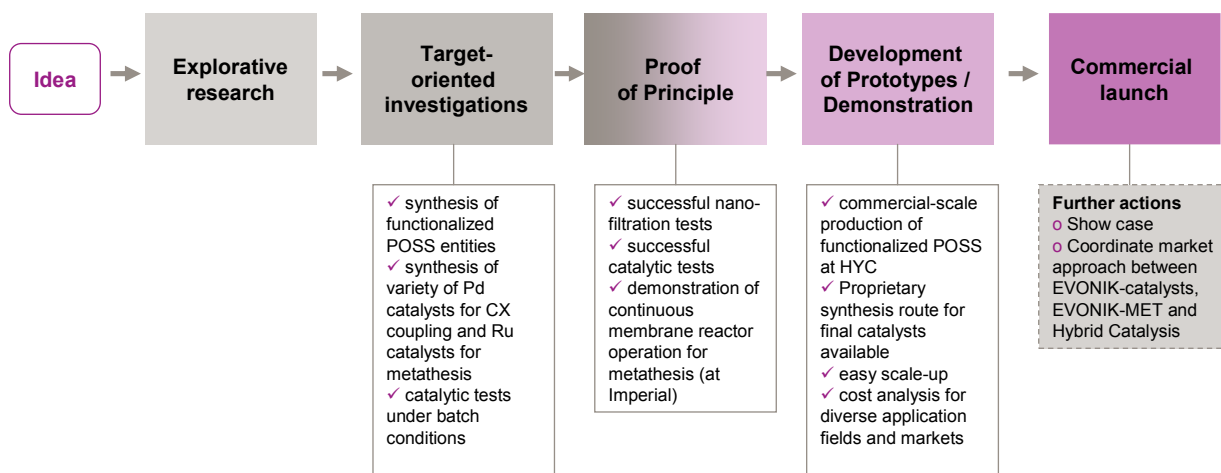


Figure 19