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Monolithic polymer/carrier materials: Versatile composites for fine chemical synthesis

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Abstract

At our institutes composite materials were developed, which ideally allow to combine polymer functionalization utilized for organic synthesis with good mass transfer properties of monolithic carriers. Starting with a megaporous glass carrier material, a polymer is introduced into the pore volume of this support. During the precipitation co-polymerization small polymer spheres are formed, which are connected by polymer bridges, resulting in a rigid polymer monolith intruding the glass. This unique combination leads to versatile materials for organic synthesis, which can be used in a flow-through mode. Based on these monolithic materials with different polymer functionalities a wide variety of different chemical reactions was conducted such as selective reductions, Suzuki cross coupling reactions, nucleophilic substitutions and catalytic transfer hydrogenations. These reactions were performed with reactors constructed from monolithic materials of different sizes allowing to achieve production capacities ranging from the millimole range to several gramms.

Keywords: Polymer supported synthesis; Polymer/carrier composites; Structured catalysts; Organic synthesis; Fine chemicals production

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1. Introduction

Polymers as solid supports in organic synthesis are well established [1–5]. During the last years functionalized polymers have increasingly served in solution phase synthesis [6]. One reason for this development is, that polymers can easily be modified resulting in a wide variety of tailor-made materials with anchoring sites for different applications. Another reason is, that many organic solution-phase reactions are performed at modest temperatures where polymers as supports are still stable. In principal, two types of functionalized polymers can be distinguished. Either they are loaded with reagents that are stoichiometrically employed or with catalysts. In the first case the polymer acts as a reservoir for reactants or intermediates. During the chemical reaction the solid phase bound compound is consumed and ideally by products stay bound to the solid phase. Thus, a combination of chemical synthesis in solution with facile purification can be achieved. After having performed the reaction the solid phase has to be cleaned and reloaded. In the alternative case, the immobilization of catalysts on polymers, strategies of attachment, activity of the catalytic system and leaching of transition metals need to be addressed. Simple examples for this strategy are sulfonic acid sites on crosslinked polystyrenes, which have found widespread application in industrial processes like etherification of olefins yielding octane number boosters or the hydration of olefins producing alcohols. In these large scale applications ion exchange resins in the shape of small spheres are used. Due to the small dimensions inside the reactor pressure drop can be a problem. This can be solved by structured packings filled with the resin. A typical example is their use in reactive distillation columns [7].

From a chemical point of view, polymers are ideal supports, from an engineering point of view, they are not. Polymers are sensitive to mechanical forces, they change

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volume and properties by swelling and shrinking phenomena, particle size is limited to a narrow range of a few millimetres and their thermal stability is a restriction.

To circumvent some of these disadvantages we developed composite materials consisting of inorganic carrier materials with incorporated polymers. This concept has the advantage, that the well-known properties of structured reactors [8] are now available for organic fine chemical production in a broad sense.

2. Experimental

2.1. Preparation of polymer/carrier composites

The preparation of the composite materials has been described in detail [9]. In brief, carrier materials with pores in the micrometer range up to millimetre range were chosen as supports. Thus, mass transport is no longer limited by diffusion and convection can now contribute to mass transfer. This carrier material is immersed in a homogeneous solution of monomers in a non-polar solvent. By radical induced polymerization polymer precipitation occurs in the pore volume of the carrier, forming micrometer sized small spheres. The spheres are connected to each other by polymer bridges. By this method a second monolithic material is created, intruding the inorganic support. The concentration of the solvent is chosen in such a way, that pores with diameters in the micrometer range are formed. Thus, the composites are very porous materials, allowing good penetration by liquids at low-pressure drop. This property makes them well suited for flow-through reactors. Previously we demonstrated, that small reactors in the shape of a chromatographic monolithic column equipped with sulfonic acid sites can perform chemical synthesis with simultaneous separation by chromatography [10]. To broaden the applicability to more sophisticated organic reactions we extended our polymerization method to other monomers [11]. Now we are able to introduce sulfonic acid groups, vinylbenzylchloride groups, quarternary aminonium groups, amino groups, vinylpyridine and imidazol moieties, just to mention the most important ones. These groups allow anchoring of reactants by ion exchange or of metal catalysts by complexation. In this work attachment of metal catalysts was achieved by ion exchange of transition metal salts, which was followed by reduction. This leads to bifunctional catalysts with the ionic site in intimate contact to the catalytically active metal particle.

2.2. Preparation of reactors with composite materials

(a) For rod-shaped reactors several methods for the pressure resistant housing were investigated. One method is to cover the monolithic composite rod by a double layer shrinking hose. The inner layer is made of hot melt glue; the outer layer consists of polytetrafluorethylene. Upon heating the outer layer shrinks and the hot melt glue is pressed firmly onto the outer surface of the rod. This results in a gap free encapsulation, avoiding any by-pass during reactor operation. Then, a fibre reinforced epoxy resin casing is created to achieve pressure resistance. During the shrinking process metal connectors are integrated. This method has the advantages that the preparation of the rods (polymerization, functionalization) can be carried out before setting up the housing. Many rods can be functionalized in one batch. However, this procedure is not well suited for temperature sensitive functionalities so that damage caused by thermal treatment during shrinking the polytetrafluorethylene hose can occur.

(b) High pressure resistant casings can be made from stainless steel tubes. Here the carrier material rod is first inserted into a metal cartridge. To avoid a gap between the wall and the rod two different techniques were successfully employed. In the first method the tube is expanded by slight heating prior to insertion of the rod into the tube. After cooling the rod is firmly fixed inside the metal tube. For softer carrier materials like ceramic foams, which cannot withstand the force during the metal shrinking process, the carrier is just inserted into the tube and the gap is closed by polymerization. In any case the reactor is then filled with the mixture of monomers and can be polymerized by heating in an oven. After this step functional groups can be introduced by successive steps. This method has the advantage that temperature sensitive functionalities can smoothly be incorporated. A disadvantage is that each reactor needs to be functionalized individually under flow-through conditions.

(c) Reactors with ring shaped composites can be prepared as irregular beds as well as regularly structured arrangements. This reactor concept is well suited for larger scales or for very small scales (only one ring). Rings in large quantities can be prepared in batches of many litres, making the preparation much cheaper than rod shaped reactors.

Single ring reactors have a scale, which is sufficient for many organic chemist's laboratory purposes. This design can handle one or several rings, so variation of catalyst amount by keeping the flow conditions constant can easily be achieved. Just the change of active rings with inert rings is necessary. The casing can be made of stainless steel, glass or of polymers like PEEK. The latter materials allow to use these reactors under microwave irradiating conditions in order to speed up reaction rates.

The single ring reactor can be modified by using a porous filter cartridge fixed to a glass tube. Equipped with a simple glass bottle (laboratory screw bottle) a very cheap flow-through reactor is obtained. This is valuable if disposable reactors are needed for example in pharmaceutical synthesis where contaminations have to be avoided.

Fig. 1. Different polymer/carrier composites: Rings (upper left), rings in an arranged ordered structure (middle), flow pattern inside arranged rings (right), size of the arranged packing is about 20 cm in length.

In addition to these reactors, monolithic materials in the shape of honey combs were also prepared. In Figs. 1–3 examples of different materials and reactor designs are presented.

3. Results and discussion

The properties of these materials were studied in different applications. First rod-shaped reactors were used to

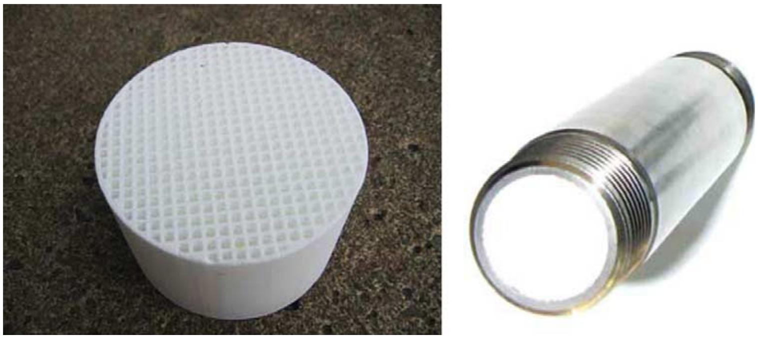


Fig. 2. Honeycomb monolithic composite (left), monolithic porous composite rod inserted into stainless steel tube (right). Diameter of the honeycomb monolith is 7.5 cm. Diameter of the stainless steel reactor is 2.4 cm, length of the inserted porous monolith is 11 cm.

Fig. 3. Flow-through reactor with single ring shaped composites. Rings are aligned on a perforated tube. Gaskets between the rings prevent bypass. Housing is made of PEEK polymer. The flow streams from an annular gap through the ring walls and leaves through the perforated inner tube. Nine millimeters ring diameter.

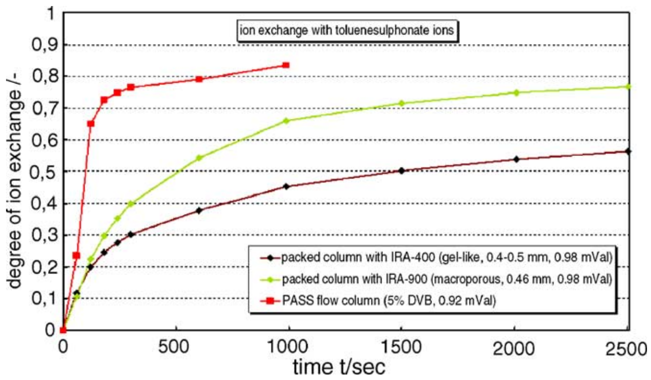


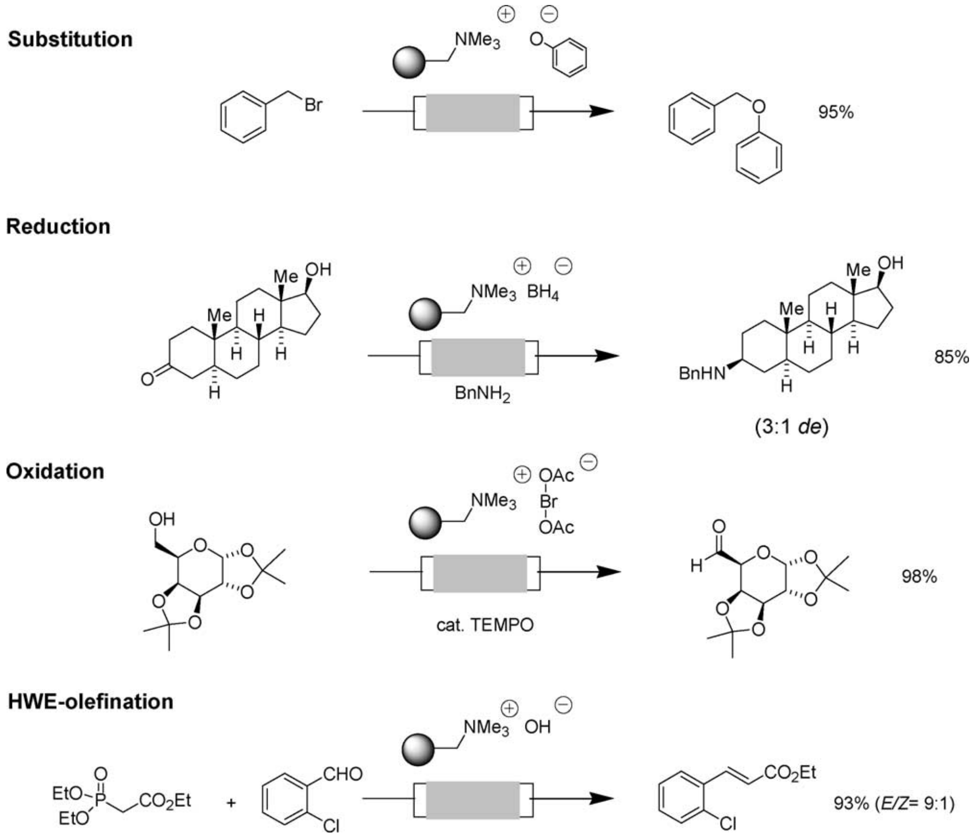
Fig. 4. Comparison of ion exchange rate, ion exchange sites are quarternary ammonium chloride, exchange is done with toluenesulphonate ions.

investigate internal mass transfer effects. For this purpose a fast reaction was chosen. As suitable test reaction ion exchange was considered because ion exchange is governed by the moving of ions, the attachment by charging effects is very fast. Only charges have to be transferred but not molecules. By dynamic ion exchange experiments we could demonstrate, that mass transport is enhanced by convective flow through our reactors. In these experiments an anion exchange resin was exchanged with different counter ions. The concentration of chloride ions set free was measured by an electrode selective for chloride ions. In Fig. 4 results are listed, demonstrating that the composite filled reactors are much faster with respect to ion exchange processes [12].

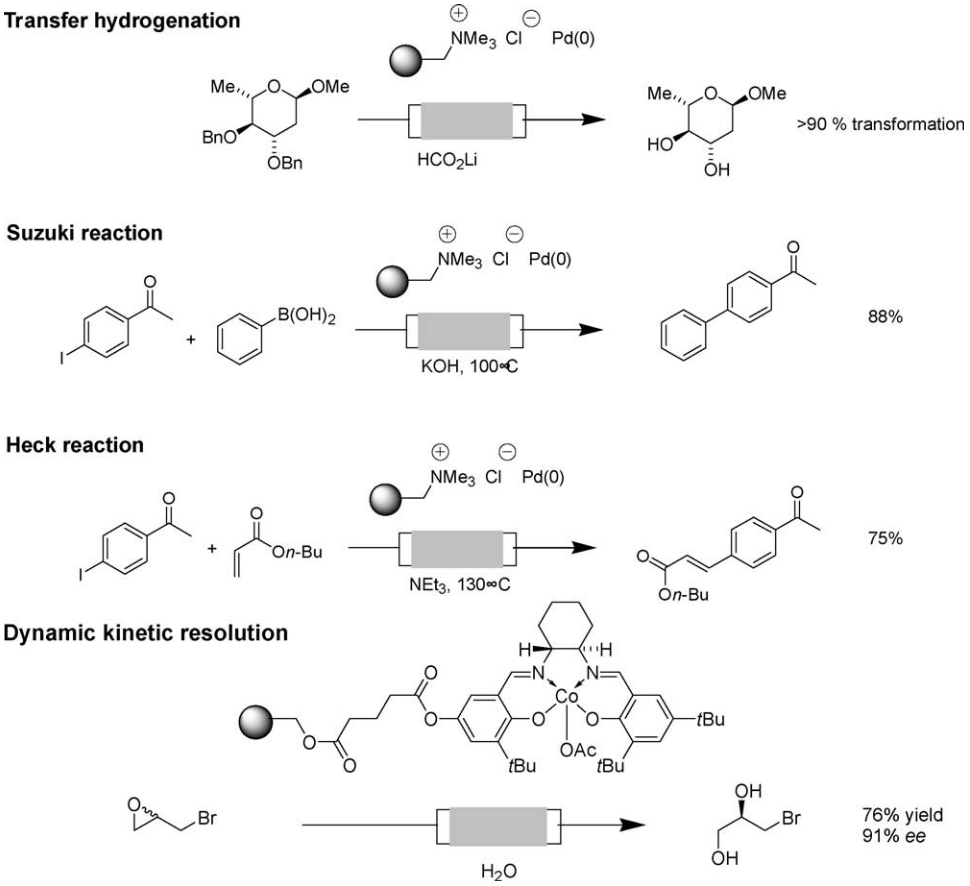
In a next step the reduction of benzaldehyde with borohydride loaded reactors was studied. In this selective reduction the observed rate was much higher for the composite materials compared to packed bed reactors with commercial resin beads. This indicates that internal mass transfer effects limit the observed rate if commercial resin particles are used. The reasons for the enhanced mass transfer are the smaller (2–3 orders of magnitude) resin particles inside the composites and the forced convective flow through the pore volume of the composite materials. This reaction was performed in a batch-recycle mode with the reactor as described earlier [13].

Other synthetic transformations carried out with these continuous flow reactors are stoichiometric transformations (Scheme 1) as well as transition metal catalysts (Scheme 2). All of these transformations are important examples with potential applications in building block synthesis for pharmaceutical research as well as for fine chemical synthesis in an industrial context. Commonly pure products were collected without the necessity of extensive purification steps.

Examples for catalytic applications are transfer hydrogenations, Suzuki-Miyuara and Heck, coupling reaction using Pd(0) sources as catalysts. For this purpose a basic ion



Scheme 1. Transformations with stoichiometric bound reactants.



Scheme 2. Transformations with transition metal catalysts.

exchange resin loaded monolith was used. In this case the intimate neighborhood of ionic sites and noble metal sites is beneficial. The ionic site first immobilizes and activates the boronic acid on the resin and the Pd(0) sites catalyse the formation of the coupling product. The formation of Pd(0) sites can be influenced by the reduction power of the reducing agent. For our purposes the reduction with sodium borohydride was most beneficial [14,15]. Finally, an example of an asymmetric kinetic resolution is given, which relies on Jacobsen's cobalt sal en complex covalently anchored to the solid support inside the reactor.

The single ring reactors developed are valuable tools to study internal mass transfer phenomena in catalytic applications. Rings with ionic sites can be loaded by two different methods: (a) Impregnation of the rings by immersion in an appropriate solution of the noble metal salt or (b) by convective loading, that means by pumping a noble metal solution through the ring wall. The first method leads to shell like catalysts with the noble metal located in the outer layers of the rings. The second method results in homogeneous distribution of the noble metal all through the ring. In Fig. 5 samples of the two methods are given. The dark outer colour indicates the noble metal.

The protocol of preparation of Pd(0) catalysts have an impact on the metal particle diameter. In order to investigate this aspect two sets of experiments were performed. In the first one the rings were loaded with sodium tetrachloropalladate solution by impregnation, that means only diffusion controls the deposition of the noble metal. In the second one the rings were loaded by forced convective flow through the ring wall. In the following sodium borohydride mediated reduction was carried out. This was performed by diffusion as well as by forced flow. Transmission electron microscopy pictures were prepared for the diffusive loading and reduction as well as for the convective loading and reduction (Fig. 6).

Both methods lead to Pd nanoclusters. The difference of the two methods can be seen if metal particle size distributions are calculated from the TEM pictures. This was done by measuring the particle diameters on the pictures. The particle size distributions are given in Fig. 7.

Fig. 5. Noble metal loaded rings by impregnation (only diffusion driven, left) and by convective forced flow through the ring wall (right).

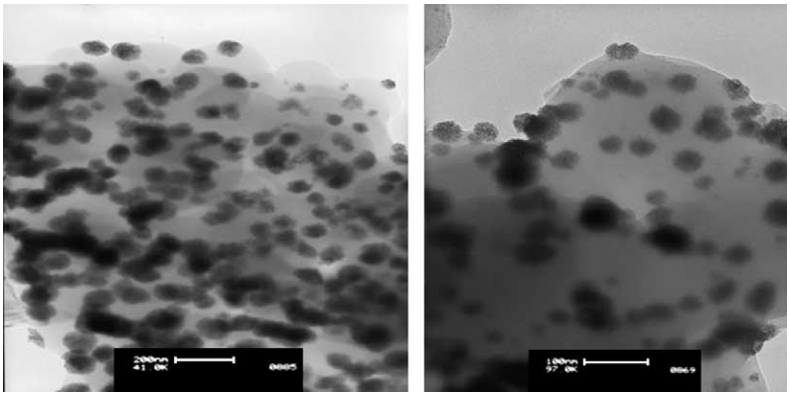


Fig. 6. TEM pictures of diffusive loading method (left) and convective loading method (right). The scale bar is 200 nm (left) and 100 nm (right).

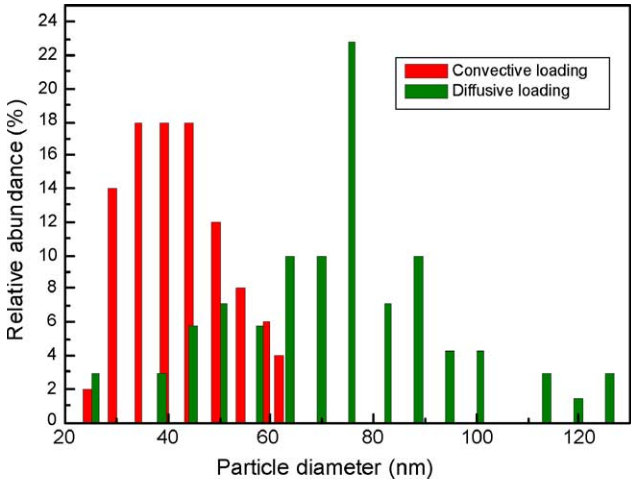


Fig. 7. Particle size distribution for diffusive loading calculated from 70 particles taken from Fig. 6 and particle size distribution for convective loading calculated from 50 particles taken from Fig. 6.

Fig. 7 shows that 90% of the particles are in a particle diameter range from 44 to 100 nm if diffusion loading was used whereas with convective loading the same percentage is in the range from 30 to 55 nm. In addition, the average value of the particle diameter is 75 for the diffusive method and 40 for the convective method.

These measurements indicate that catalyst morphology is influenced by the flow conditions during catalyst preparation. The more uniform catalyst particles with smaller diameters can be prepared by convective methods. The reason for this could be the concentration of borohydride inside the pores of the composite materials during reduction. With convective flow this concentration is always at a high level, resulting in a steeper concentration gradient and a faster transition metal reduction. The faster the reduction is the smaller the particles become.

4. Conclusions and outlook

Composite polymer/carrier materials in various shapes are a valuable tool for the organic chemist's laboratory as well as for the production of fine chemicals. The concept of monolithic composite flow through reactors can contribute to a more efficient continuous production of fine chemicals instead of batch wise production, which is state of the art today. The benefits of reactors made with these composites will lead to added value by replacing laborious work of batch processes with continuously operated smart apparatuses. Safety is improved by handling smaller volumes under reaction conditions. These reactors can easily be connected to existing laboratory equipment like automated HPLC pumps [13]. The combination of the composite based flow-through reactors with other enabling techniques like microwave heating may contribute to new standard equipment for the organic chemist's laboratory, replacing Erlenmeyer flasks and beakers [16].

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