

Applications of metathesis in heterogeneous catalysis and separation sciences

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Abstract

During the last 15 years, the area of well-defined metathesis initiator systems was characterized by almost dramatic improvements in terms of initiator activity, stability, and selectivity. In due consequence, control over polymer properties increased and metathesis-based polymerization techniques (in particular ring-opening metathesis polymerization, ROMP) have been adapted for materials science purposes. Quite recently, metathesis-based supports have entered the fields of heterogeneous catalysis as well as separation and life sciences. In this review, both the synthesis and properties of metathesis-based well-defined catalytic supports and separations systems shall be summarized. Special consideration will be given to the particular structural features that have been made possible using ROMP.

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1. Introduction

Beaded, either regularly or irregularly shaped inorganic and organic materials are widely used in separation science and heterogeneous catalysis [1]. In separation science, packed columns represent excellent separation media for chromatographic techniques such as HPLC, capillary liquid chromatography (CLC) and capillary electrochromatography (CEC) [1]. Usually, supports with well-defined particle diameters, surface areas and pore volumes are used. Similar applies to heterogeneous catalysis. Here, catalytic systems are either prepared via fusion, (co-)precipitation, sol-gel processes or simple deposition of the catalytic species onto or within various carriers such as silica, γ -Al₂O₃ and zeolites [2]. Despite the quite obvious differences

between separation science and heterogeneous catalysis, these two important areas of chemistry are based on similar principles. Separations scientists usually think in terms of porosity, specific surface area, adsorption isotherms, mass transfer, mechanical and chemical stability of the chromatographic support. Almost the same problems are encountered in heterogeneous catalysis, yet the basically same issues are addressed by a different terminology such as catalyst bleeding, bed compressibility, diffusion and recycling. In the following, some metathesis-based solutions for both heterogeneous catalysis and separation science will be presented.

2. Heterogeneous Heck systems via ring-opening metathesis precipitation polymerization

Catalytic supports with an exactly defined and stable surface chemistry still represent an intensively

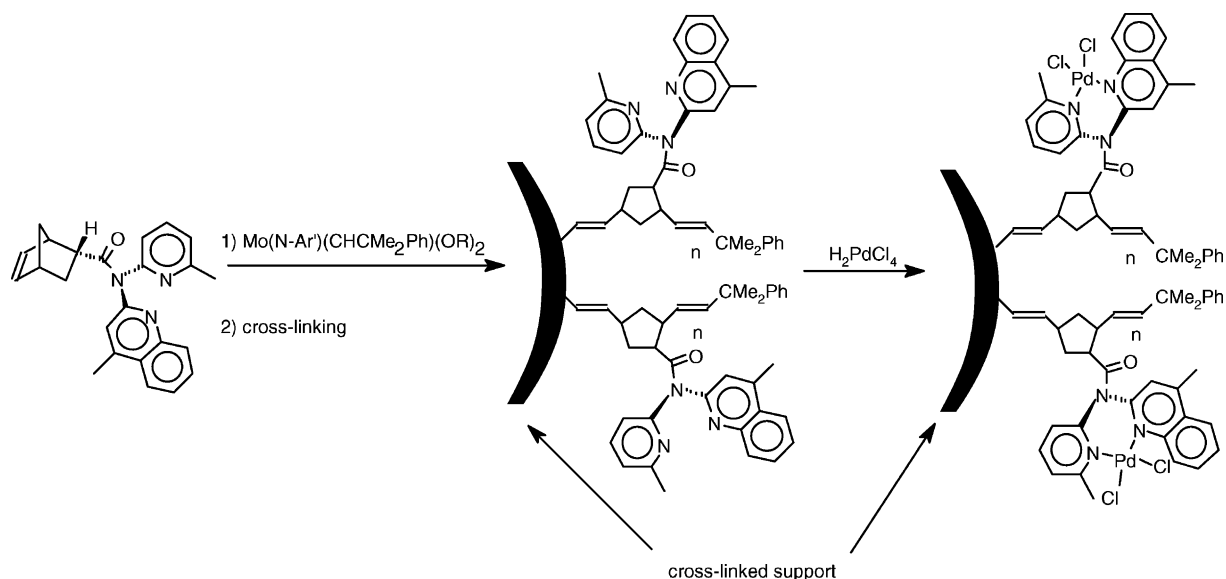
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investigated area. In order to avoid catalyst poisoning and unwanted side reactions, such high definitions are a basic requirement in any heterogeneous catalysis. Standard functionalization procedures of *organic* supports often use *divergent* synthetic approaches that entail a step by step transformation of surface-bound functional groups. Ill-defined systems result from the fact that these transformations usually do not proceed in a quantitative way. In order to avoid this, we elaborated a conceptually new approach based on metathesis precipitation polymerization [3] that allows the synthesis of such supports by a *convergent* synthetic route, starting from functional monomers.

There exist a vast variety of different Pd-based systems for the vinylation of aryl halides, commonly called Heck systems [4]. Despite the significant progress in homogeneous catalysis [5,6], the demand for highly active and stable heterogeneous systems is still high. Highly active systems may be generated from phosphine- or aminophosphine-based ligands [7], yet these are easily transformed into the corresponding phosphine oxides, which somehow limits their general applicability. Consequently, phosphane-free ligands are of particular interest [8–10]. Ligands solely based on nitrogen [11], e.g. dipyrindyl amide-based systems, are relatively rare, yet turned out to

be suitable for the synthesis of highly temperature stable and active Heck catalysts [12]. If incorporated into suitable monomers, ring-opening metathesis precipitation polymerization applying Schrock initiators may be used for the preparation of well-defined heterogeneous Heck systems based on such ligands [12]. The adherent polymerization system must fulfill a class VI living system [13]. Subsequent cross-linking of the “living” linear polymer chains by a suitable norbornene-based cross-linker in course of the precipitation polymerization leads to the formation of irregularly shaped polymer beads (Scheme 1) [14–16]. Even complex functionalities may be introduced with high reproducibility and without any change in the chemical nature, geometry and even absolute configuration of the corresponding functional group. Generally speaking, heterogeneous polymer supports prepared by this approach are characterized by an exact knowledge about the chemical structure of the actual catalytic sites and a high density of functional groups at the surface. The amount of functional monomer immobilized by this approach may be varied within a range of 0–1 mmol/g. Table 1 gives an overview over the beaded materials. The particles have a mean diameter of 20–40 μm , and are generally characterized by a low specific surface



Scheme 1. Synthesis of derivatized polymer beads, e.g. based on substituted dipyrindyl amides via ROMP [14]. Cross-linker: DMN-H6.

Table 1
Summary of poly(norbornene-5-dipyridyl carbamide) (C(O)Npy₂)-functionalized resins [14–16,71]

Catalyst	Functional group	Capacity (mmol/g)
1	<i>N,N</i> -Dipyrid-2-ylcarbamide	1.0
2	<i>N,N</i> -Dipyrid-2-ylcarbamide	0.6
3	<i>N</i> -Pyrid-2-yl- <i>N</i> -(3-methylpyrid-2-yl)carbamide	0.03
4	<i>N</i> -Pyrid-2-yl- <i>N</i> -(6-methylpyrid-2-yl)carbamide	0.05
5	<i>N</i> -(6-Methylpyrid-2-yl)- <i>N</i> -(4-methylquinolin-2-yl)carbamide	0.05
6	<i>N,N</i> -bis(Pyrimid-2-yl)carbamide	0.4

Cross-linker: 1,4,4a,5,8,8a-hexahydro-1,4,5,8-*exo-endo*-dimethanonaphthalene (DMN-H6).

area ($4 \text{ m}^2/\text{g} < \sigma < 30 \text{ m}^2/\text{g}$). As a consequence of the polymerization order, the linear polymer chains bearing the functional groups form tentacles that are attached to the surface of the cross-linked carrier (Scheme 1). This ensures a fast mass transfer with any kind of mobile phase or liquid and makes these materials highly attractive for both extraction and immobilization purposes. In due consequence, these

dipyridyl and bis(pyrimidyl)carbamide-based materials may be used as supports for heterogeneous catalysis as they represent typical small-particle catalysts [17]. Thus, the palladium-loaded chelating groups are located exclusively at the surface of the particle, they are easily accessible, diffusion plays a minor role and coupling reactions proceed within the interphase [18]. Table 2 summarizes some results that were obtained

Table 2
Summary of Heck-couplings^a, Suzuki-couplings^b, aminations^c and Sonogashira–Hagihara-couplings^d

Ar–X	H ₂ C=CHR	Product	Catalyst	Yield (%)
Iodobenzene	Styrene	<i>trans</i> -Stilbene	1	99
Iodobenzene	Styrene	<i>trans</i> -Stilbene	3	91
Iodobenzene	Styrene	<i>trans</i> -Stilbene	4	96
Iodobenzene	Styrene	<i>trans</i> -Stilbene	5	92
Bromobenzene	Styrene	<i>trans</i> -Stilbene	1	90
4-Bromobenzonitrile	Styrene	4-Cyano- <i>trans</i> -stilbene	1	83
4-Bromo-1-fluorobenzene	Styrene	4-Fluoro- <i>trans</i> -stilbene	1	58
4-Cl-acetophenone/TBAB	Styrene	4-Acetyl- <i>trans</i> -stilbene	1	95
4-Bromobenzonitrile	Styrene	4-Cyanostilbene	6	98
4-Chloroacetophenone/TBAB	Styrene	4-Acetylstilbene	6	70
Ar–B(OH) ₂ , Ar =	Ar–X			
4-MeC ₆ H ₄ -	Iodobenzene	4-Methylbiphenyl	6	83
4-MeC ₆ H ₄ -	Bromobenzene	4-Methylbiphenyl	6	74
Amine	Ar–X			
Piperidine	Chlorobenzene	<i>N</i> -Phenylpiperidine	6	80
Diethylamine	Ethylacrylate	β-(<i>N,N</i> -Diethylamino)-ethylpropionate	6	79
R–CCH	Ar–X			
Ph–CCH	Iodobenzene	Diphenylacetylene	6	98
Ph–CCH	Bromobenzene	Diphenylacetylene	6	68
Ph–CCH/TBAB	Chlorobenzene	Diphenylacetylene	6	65

TBAB: NBu₄⁺Br[−] isolated yields. For further experimental conditions refer to [12,15,16].

^a DMAc at $T = 150 \text{ }^\circ\text{C}$, $t = 6 \text{ h}$, 0.001–0.2 mol% Pd, base: Bu₃N.

^b THF at $T = 65 \text{ }^\circ\text{C}$, $t = 6 \text{ h}$, 0.005–0.2 mol% Pd, base: Cs₂CO₃.

^c THF at $T = 65 \text{ }^\circ\text{C}$, $t = 72 \text{ h}$, 0.005–0.2 mol% Pd.

^d THF at $T = 65 \text{ }^\circ\text{C}$, $t = 72 \text{ h}$, 0.007–0.04 mol% Pd, base: Bu₃N.

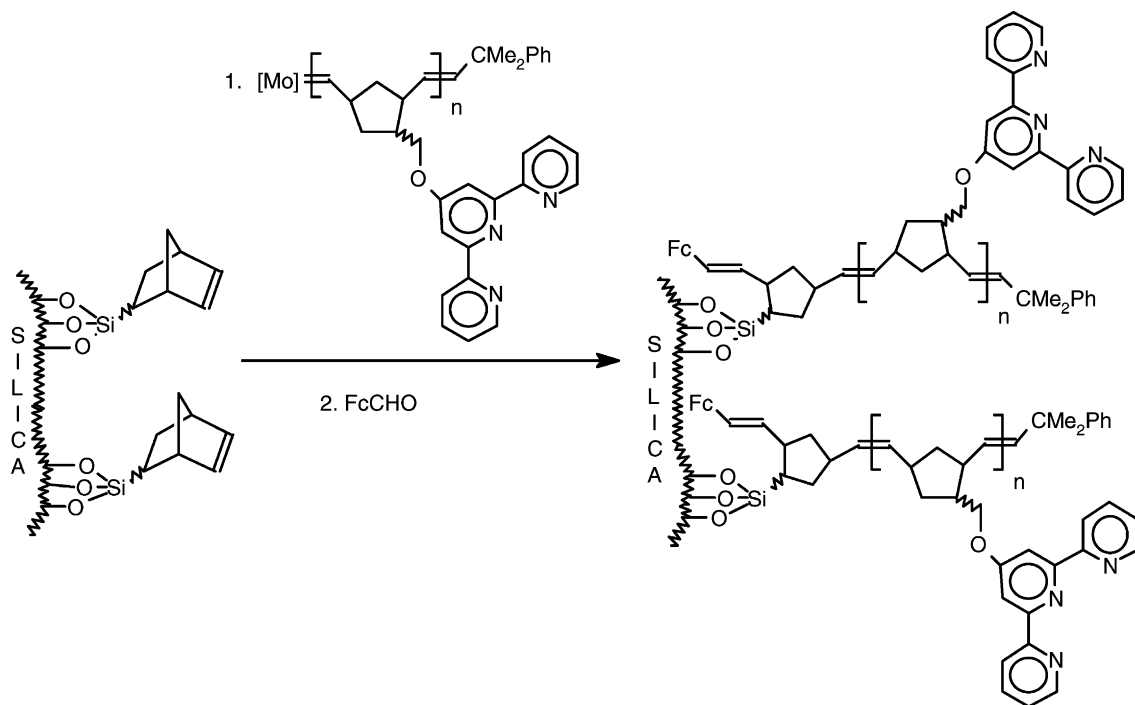
with these supports in various Heck-, Suzuki-, and Sonogashira–Hagihara-couplings, as well as amination reactions. Most reactions (in particular those carried out with aryl iodides and bromides) may be carried out with good yields (>90%). The fact that basically no Pd-leaching occurs allows the subsequent reuse of the supports. For a detailed discussion refer to literature [12,15,16].

3. Heterogeneous ATRP supports via ring-opening metathesis graft-copolymerization

Living radical polymerizations [19–21] and in particular atom transfer radical polymerization (ATRP) [22] have gained significant interest during the last years. Such polymerizations may be carried out in a “quasi-living” [13,19,23–25] manner and allow the presence of certain functionalities [26–28]. Despite the simplicity of this approach, the resulting polymers suffer from high metal contents due to the homogeneous approaches that are used in most cases. Due to

the encouraging results obtained with heterogenized Heck-coupling systems [12,29], a new ROMP-based access to well-defined, highly active heterogeneous polymer supports for ATRP was elaborated [30–33].

For these purposes, norborn-2-ene-derivatized silica-based supports were prepared by silanization employing norborn-2-ene-5-yltrichlorosilane. Surface grafting [34] of the norbornene-modified supports with a series of dipyrindylamide and terpyridine-containing chelating monomers was accomplished using ROMP (Scheme 2). Complementary, coating techniques similar to those reported previously [35] were applied. Since ATRP systems based on dipyrindylamides and terpyridines represent monoligated metal centers and the equilibrium $M^{n+} \leftrightarrow M^{n+1}$ that is involved in this type of reactions does not require any conformational changes or dissociation of a ligand, polymerization proceeds comparably fast. Thus, maximum monomer conversion is already achieved within 2 h. The general results obtained with ROMP-based heterogeneous polymerization systems may be summarized as follows: (i) both dipyrindylamide and terpyridyl-based



Scheme 2. Ring-opening metathesis graft-copolymerization [34]. Initiator: Mo(*N*-2,6-*i*-Pr₂-C₆H₃)(CHCMe₂Ph(OCMe(CF₃)₂)₂). Fc: ferrocenyl.

monoligated systems may be used in ATRP; (ii) complexes that contain the reduced species of the corresponding metal (preferably Cu) were found to work best and additionally avoid the use of a reducing agent (e.g. MAO, $\text{Al}(i\text{-OPr})_3$); (iii) poly(styrene) may be prepared up to a M_w of 80,000 in 20–30% yield. Polydispersities vary from 1.4 to 1.6. These polymers are virtually metal free as determined by atom absorption spectroscopy (metal content < 100 ng/g); (iv) polymerizations proceed fast yet level off after approximately 2 h at monomer consumption \leq 35%.

4. The concept of monolithic supports

Many attempts have been made to reduce the size of inter-particle voids of packed stationary phases by using non-porous particles with small diameters (1–2 μm). Despite the highly favorable properties of non-porous micropellicular supports, e.g. in the rapid analysis of large biomolecules, reduced inter-particle volumes lead to higher backpressures, which generally limits the useful minimum particle size to about 1.5 μm . As an alternative approach to packed columns, separation media with a high degree of continuity, such as porous disks [36–38], stacked membranes [39], rolled cellulose sheets [40] or woven matrices [41] were investigated. Since the introduction of continuous beds to separation science by Hjertén and coworkers [42–44], these materials have been further developed [45–48]. While separation efficiencies for small molecules are usually comparably low due to non-uniform velocities across these materials, continuous beds turned out to be excellent separation media for many medium and high-molecular mass biopolymers [39] and, quite recently, even for low-molecular mass analytes [49–52]. In terms of applications, these new separation media, usually referred to as monolithic columns or rigid rods [53] have already been used successfully in standard HPLC and micro-separation techniques [42,54–59], capillary electrochromatography as well as in solid phase extraction (SPE) [60], and more recently, as bioreactors [61,62]. Generally speaking, the term “monolith” applies to any uni-body structure composed of interconnected repeating cells or channels. Such media may either be metallic or prepared from inorganic mixtures, e.g. by a sintering process to form ceramics,

or from organic compounds, e.g. by a cross-linking polymerization. For this particular review, the term “monolith” or “rigid rod” shall comprise cross-linked, either inorganic or organic media which are characterized by a well-defined porosity and which are used as supports for interactions/reactions between a solid and a liquid phase. Besides advantages such as lower backpressure and enhanced diffusional mass transfer [63,64], the ease of fabrication as well as the many possibilities in structural alteration need to be mentioned. Important enough, the enhanced diffusional mass transfer allows separation scientists to run separations at comparably high flow rates of up to 10 mm/s, resulting in fast and highly efficient separations. Similarly, one can take advantage of it to design supports for fast heterogeneous catalytic reactions.

5. Monolithic media prepared by transition metal catalyzed polymerization

So far, a variety of functionalized and non-functionalized monolithic columns prepared from either organic or inorganic polymers are available. While inorganic monoliths are usually based on silica and may conveniently be prepared via sol-gel techniques [49–52], organic continuous beds are traditionally either based on methacrylates or poly(styrene-divinylbenzene) [45,47,48,65,66] and are almost exclusively synthesized by radical polymerization.

Transition metal-catalyzed polymerizations have gained significant interest due to the rapidly growing armor of well-defined, selective and active catalytic systems. Among these catalytic systems, those applicable to metathesis polymerization and related techniques are probably among the most important ones. Well-defined systems such as the highly selective and active Schrock catalysts of the general formula $\text{Mo}(N\text{-}2,6\text{-R}_2\text{-C}_6\text{H}_3)(\text{CHCMe}_2\text{Ph})(\text{OCR}')_2$ or the more robust Grubbs-type initiators of the general formula $\text{Cl}_2\text{Ru}(\text{CHPh})(\text{PR}'_3)_2$ offer access to basically every polymer architecture one might think of [3]. Among metathesis-based polymerization techniques such as acyclic diene metathesis polymerization (ADMET), alkyne polymerization and ring-opening metathesis polymerization (ROMP), the latter one appears to be the most attractive technique for the synthesis of complex cross-linked architectures. On

one hand, no volatile products as in ADMET evolve. On the other hand, a significantly broader range of monomers than in alkyne polymerization may be used. One additional advantage of ROMP is the possibility to use functional monomers. This and the controlled, “living” [13,23,25,67,68] polymerization mechanism allow a highly flexible yet reproducible polymerization setup. In course of our investigations to use ROMP [69] for the synthesis of functional high-performance materials, we already combined this polymerization technique with grafting and precipitation techniques for the synthesis of functionalized separation media [14,34,35,70–78] and catalytic supports [12,15,30,31,33]. Due to the broad applicability of ROMP and the high definition of the resulting materials, we investigated as to which extent such transition metal catalyzed polymerizations might be used for the synthesis of continuous polymeric supports [75]. In fact, this may be accomplished by generating a continuous matrix by ring-opening metathesis copolymerization of suitable monomers and a cross-linker in the presence of porogenic solvents within a device (column). In the following, the design and realization of the entire system shall be outlined more detailed.

6. Monomers and catalysts

The choice of the appropriate catalyst represents a crucial step in order to create a well-defined polymerization system in terms of initiation efficiency and

control over propagation. Only in this case the entire system may be designed on a *stoichiometric base*. This is important, since for microstructure variation the composition of the entire polymerization mixture (vide infra) needs to be varied within extremely small increments. Thus, the catalyst needs to be carefully selected from both a chemical and a practical point of view. In principle, Schrock and Grubbs systems, both highly active in the ROMP of strained functionalized olefins, may be used. Since the preparation and in particular derivatization of ROMP-based rigid rods requires some handling that may not be performed under a strict inert atmosphere, we focused on the use of the less oxygen-sensitive ruthenium-based Grubbs-type initiators of the general formula $\text{Cl}_2(\text{PR}_3)_2\text{Ru}(\text{=CHPh})$ ($\text{R} = \text{phenyl}$, Cy ($\text{Cy} = \text{cyclohexyl}$)) rather than on the use of the molybdenum-based Schrock-type initiators. Among the possible combinations of monomers and cross-linkers, e.g. norbornene (NBE), norbornadiene, dicyclopentadiene (DCPD), 1,4,4a,5,8,8a-hexahydro-1,4,5,8-*exo-endo*-dimethanonaphthalene (DMN-H6), and 1,4a,5,8,8a,9,9a,10,10a-decahydro-1,4,5,8,9,10-trimethanoanthracene (Fig. 1), various Grubbs-catalysts as well as different porogenic solvents, the copolymerization of NBE with DMN-H6 in the presence of two porogenic solvents, 2-propanol and toluene, with $\text{Cl}_2(\text{PCy}_3)_2\text{Ru}(\text{=CHPh})$ was found to work best.

In order to understand its relevance to the synthesis of monolithic supports and its influence on polymerization parameters, a brief description of the

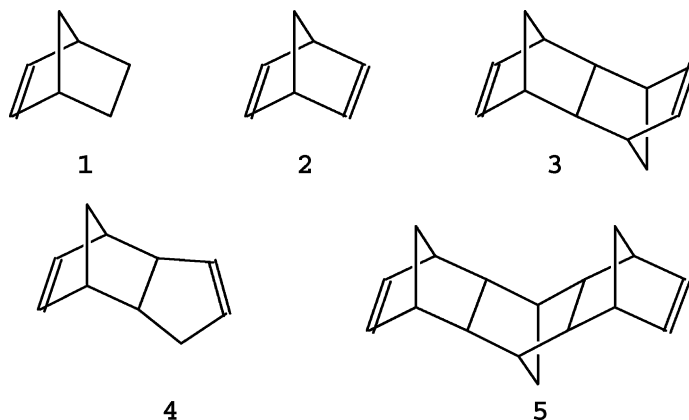


Fig. 1. Structures of monomers and cross-linkers. (1) NBE, (2) norbornadiene, (3) DMN-H6, (4) DCPD, (5) 1,4a,5,8,8a,9,9a,10,10a-decahydro-1,4,5,8,9,10-trimethanoanthracene.

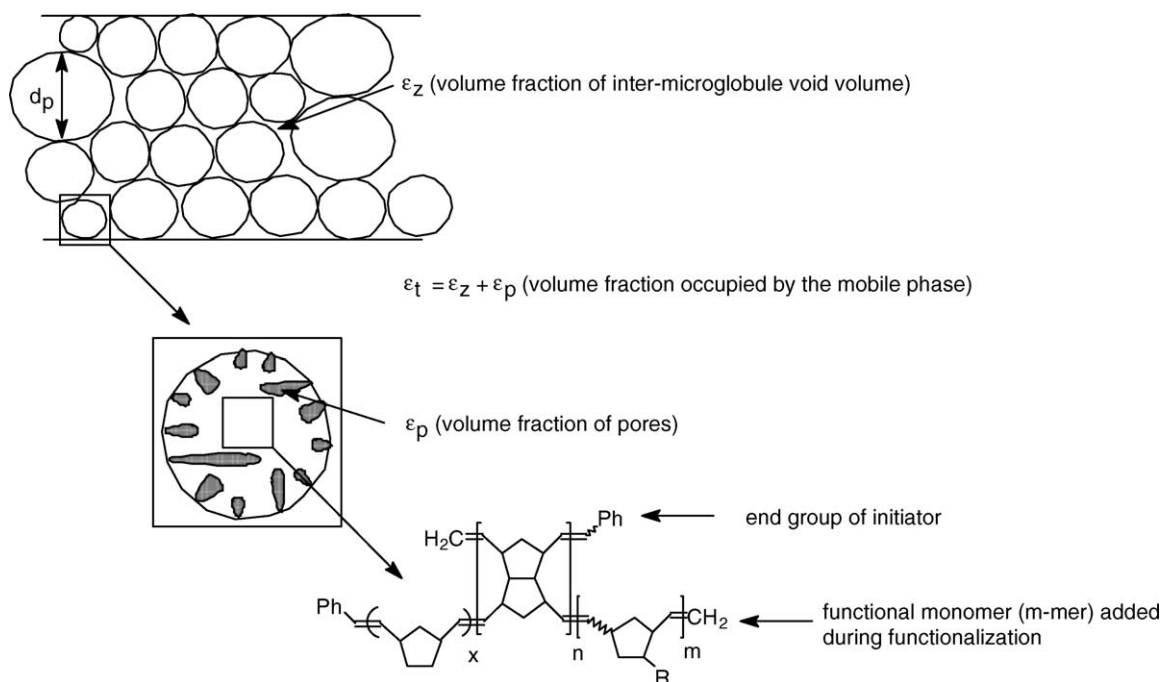


Fig. 2. Illustration of the physical meanings of d_p , ϵ_z , ϵ_p , ϵ_t and schematic drawing of the backbone structure. R: functional group.

general construction of a monolith in terms of microstructure, backbone and relevant abbreviations is given in Fig. 2. As can be deduced therefrom, monoliths consist of microstructure-forming microglobules, which themselves are characterized by a certain diameter (d_p) and microporosity (ϵ_p). This microporosity as well as the total volume of the void fraction (intermicroglobule porosity) summarizes to the total porosity (ϵ_t). Together with the pore size distribution (calculated from ISEC data), this value, representing a fraction (expressed in percentage), on one hand, directly translates into a total pore volume (V_p , expressed in milliliters), and on the other hand, allows the calculation of the specific surface area (σ , expressed in m^2/g).

7. Initiator concentration

Initiator concentrations represent a crucial point in the preparation of monoliths. Most importantly, any uncontrolled, highly exothermic reaction must be strictly avoided. Additionally, the total amount of initiator directly determines the amount of growing

nuclei that are responsible for phase separation and microglobule size. Nevertheless, in terms of a desired in situ derivatization (vide infra), higher initiator concentrations appeared favorable. In order to determine the number of active sites accessible for derivatization, the active sites were “capped” with ethylvinyl ether in order to cleave off the living termini. Surprisingly, Ru-measurement by inductively coupled plasma–optical emission spectroscopy (ICP–OES) investigations carried out with the effluent revealed that more than 98% of the initiator (!) are located at the surface of the microglobules after the structure forming process [79]. This is in accordance with a micelle-based microglobule formation, where the catalytically active sites are located at the boundary between the solid and liquid phase. Fortunately, besides some effects on the microglobule shape, no significant influences of initiator concentration within a range of 0.1–1% on the morphology in terms of pore and microglobule size of the continuous rods were observed. For experimental reasons, 0.4% of **1** were used for rod formation and found sufficient for derivatization purposes (vide infra) without changing the properties of the rods in terms of microstructure.

At this point, when dealing with transition metal catalyzed polymerizations, the efficiency of removing the metal from the rod after polymerization needs to be addressed. The fact that ruthenium-initiated polymerizations may conveniently be capped with ethylvinyl ether may be demonstrated by ICP–OES investigations on the Ru-content of the final rods. These investigations revealed Ru-concentrations $< 10 \mu\text{g/g}$, corresponding to a 99.8% removal.

8. Monomers, monomer ratios and polymerization conditions

Based on the existing knowledge about pore-formation in monolithic materials [47,60,80,81], different

mixtures of macro- and microporogens [45] were tested for their ability to form the desired, well-defined microstructures. Methanol, 2-propanol, cyclohexanol, 1-decanol, 1-dodecanol were investigated for their macropore-forming properties, dichloroethane, dichloromethane and toluene were used as microporogens. Among the many macropore-forming solvents, 2-propanol was found to possess good properties. Toluene, dichloromethane and dichloroethane were found to be capable of forming the desired microstructures in combination with 2-propanol. The choice of either toluene or methylene chloride strongly depends on the need of any subsequent derivatization (vide supra). The relative ratios of all components (i.e. NBE, DMN-H6, the porogens and the catalyst) now allow varying the microstructure of continuous media.

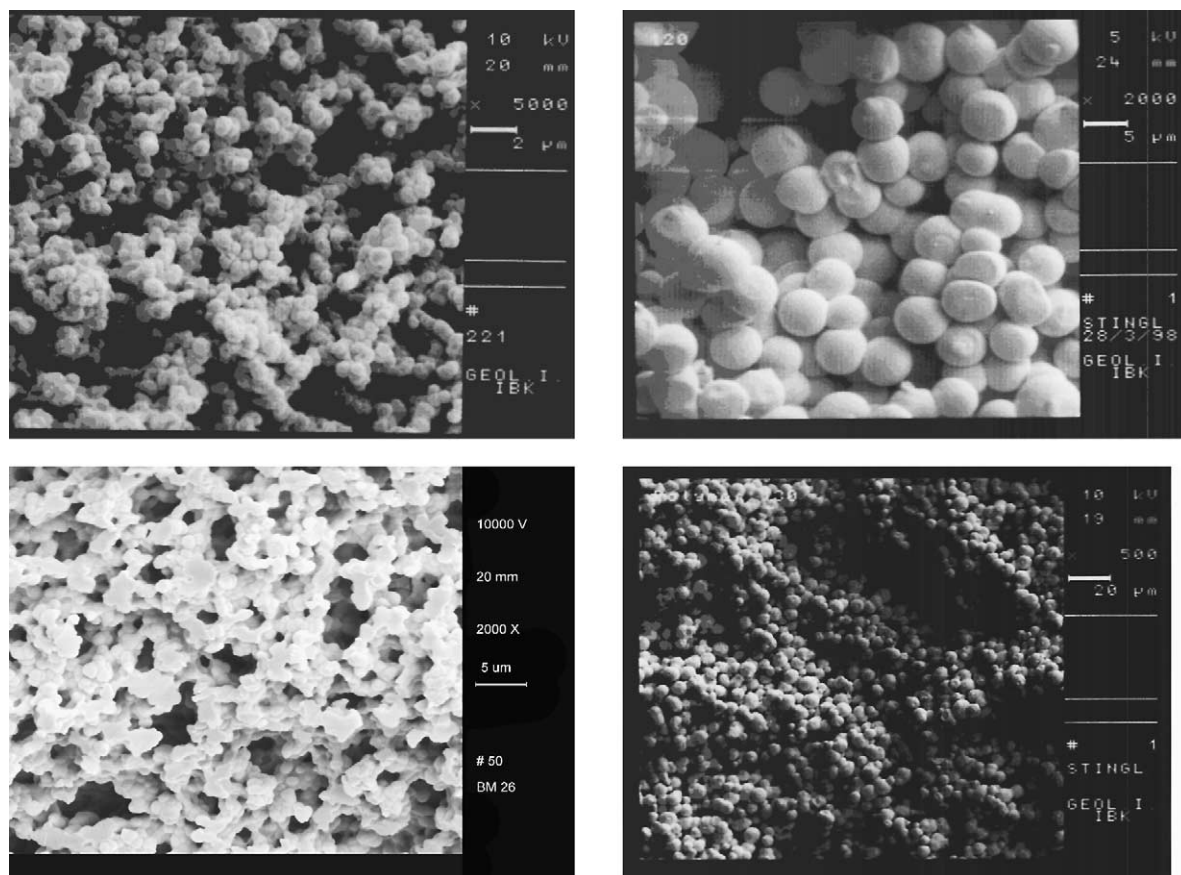


Fig. 3. Variations in microstructure of various metathesis-based monoliths in terms of intermicroglobule void volume (ϵ_z) and volume fraction of pores (ϵ_p).

Table 3
Physicochemical data for monoliths 1–5

NBE ^a (%)	DMN-H6 ^a (%)	Toluene ^a (%)	2-PrOH ^a (%)	1 ^a (%)	σ^b (m ² /g)	ε_p (%)	ε_z (%)	ε_t (%)	ρ_p (g/cm ³)	V_p (ml)	d_p (μ m)
15	15	10	60	0.4	76	43	37	80	0.27	0.31	2 \pm 1
20	20	10	50	0.4	62	43	33	76	0.31	0.31	4 \pm 1
25	25	10	40	0.4	85	48	15	63	0.40	0.34	2 \pm 1
25	25	10	40	1	86	48	14	63	0.40	0.34	4 \pm 1
30	30	10	30	0.4	191	50	5	54	0.46	0.35	8 \pm 2
30	30	10	30	1	96	50	2	53	0.46	0.36	6 \pm 2
15	15	20	50	0.4	110	39	49	89	0.25	0.28	3 \pm 1
20	20	20	40	0.4	74	44	21	65	0.36	0.31	4 \pm 1
25	25	20	30	0.4	91	47	15	62	0.42	0.33	4 \pm 1
30	30	20	20	0.4	93	65	5	69	0.50	0.46	4 \pm 1
0	50	10	40	0.4	88	44	25	69	0.32	0.31	2 \pm 1
PPh ₃ added = 20 ppm											
25	25	10	40	0.4	6	9	31	41	0.426	0.062	3 \pm 1
PPh ₃ added = 40 ppm											
25	25	10	40	0.4	6	8	33	41	0.423	0.058	2.5 \pm 2
PPh ₃ added = 80 ppm											
25	25	10	40	0.4	7	10	34	44	0.405	0.069	4.5 \pm 1

NBE: norborn-2-ene, DMN-H6: 1,4,4a,5,8,8a-hexahydro-1,4,5,8-*exo-endo*-dimethanonaphthalene, **1**: initiator, T_p : polymerization temperature = 0 °C; s : specific surface; ε_p : volume fraction of pores [82]; ε_z : volume fraction of intermicroglobule void volume [82]; ε_t : volume fraction occupied by mobile phase [82]; ρ_p : apparent density [82]; V_p : pore volume [82]; d_p : microglobule diameter [82]. For a comprehensive information refer to literature [75,77,83].

^a By weight (initiator (**1**)) = 0.4% throughout.

^b Based on PS standards (2610 Da < M_p < 1,250,000 Da).

Structural data such as microglobule diameter (d_p) may be deduced from electron microscopy (ELMI) while inverse size exclusion chromatography (ISEC) allows the determination of all porosity data (ε_z , ε_p , ε_t) as well as specific surface area (s , vide infra) [82]. Alternatively, mercury intrusion (mercury porosimetry) or BET may be used, since they represent competitive alternatives for the analysis of porous systems. Particularly mercury intrusion is capable of providing data for the (here most relevant) macropores (>1000 Å). Nevertheless, mercury intrusion turned out to be less favorable, since it requires the drying of the supports, a process that usually gives raise to significant changes in the pore size distribution, thus giving raise to ambiguous results. Since monoliths mainly consist of macropores (>1000 Å), these are identified by this method yet may complementarily be addressed by electron microscopy (Fig. 3). Nevertheless, the total porosity as obtained by this technique is in excellent agreement with the one obtained from ISEC data. Table 3 summarizes the structural variations that may

be achieved. As can be deduced therefrom, the volume fraction of the intermicroglobule void volume (ε_z) and total porosity (ε_t) may be varied within a range of 0–50% and 50–80%, respectively.

9. Applications of non-functionalized metathesis-based monoliths in separation science: structure-separation efficiency relationships

Due to the pure hydrocarbon backbone, monoliths prepared from NBE and DMN-H6 are strongly hydrophobic. Nevertheless, the resulting materials significantly differ from PS–DVB based resins, in that the latter one contains aromatic systems that are capable of forming π -stacks with analytes possessing aromatic groups. Fig. 4 shows the fast separation of 10 different biologically relevant proteins by reversed phase chromatography. At flow rates of 3 ml/min, this separation may be accomplished within 90 s. Such separation performance at high flow rates gives an illustration of the

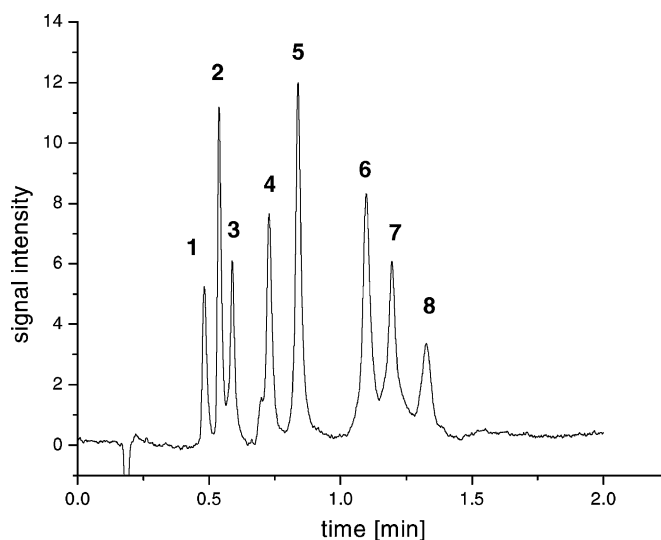


Fig. 4. RP-HPLC separation of eight proteins on a metathesis-based monolith. Mobile phase: 0.1% aqueous trifluoroacetic acid; linear gradient, 14.5–37% acetonitrile in 0.5 min, 37–46% acetonitrile in 1 min; flow rate, 3 ml/min; $T = 20^{\circ}\text{C}$; detection, UV (218 nm). (1) Ribonuclease A, (2) insulin, (3) cytochrome C, (4) lysocyme, (5) α -lactalbumin, (6) α -chymotrypsinogen A, (7) β -lactoglobulin B, (8) catalase. Inj. vol. (injection volume): 1–6:22 μg ; 7–8:44 μg .

fast mass transfer that may be achieved [75,77,83]. It should be mentioned that ongoing research focuses on the synthesis of miniaturized microcolumn systems with i.d. $\leq 300 \mu\text{m}$ [84].

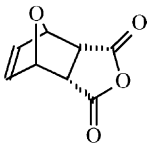
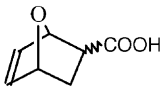
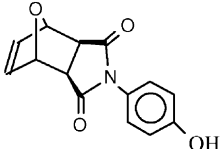
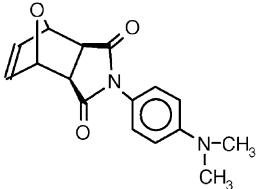
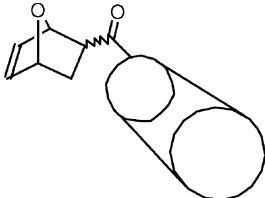
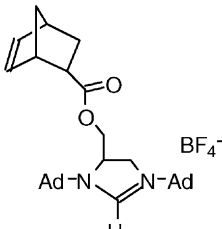
10. Functionalization

Despite the high definition in terms of microstructure (size and form of microglobules that form the rod), specific surface area and pore volume [46–48,60,80,85,86] as well as the impressive results that may be obtained in separation science with organic monolithic carriers prepared by radical polymerization, the preparation of *functionalized* monoliths is still somehow limited [45]. One synthetic protocol entails the copolymerization of the corresponding functional monomer during the synthesis of the rigid rod. Despite its simplicity, two problems have to be addressed. On one hand, a major part of the functional monomer is located at the interior of the rod. Since these rods are usually either non-porous or microporous, a major part of the functional groups is not available in course of the separation process. On the other hand, the presence

of polar functional groups located close to the surface of the microstructure-forming polymer leads to unfavorable swelling properties. An alternative approach that avoids these problems entails the copolymerization of monomers possessing active sites for post-derivatization, e.g. epoxide groups or azlactone groups. Those reactive groups that are located at the surface may in fact be conveniently transformed into standard functionalities such as sulfonic acids, amines [65,87,88] or alcohols [89,90].

In the present ruthenium-based polymerizations [19,23,25,91], one can take advantage of the “living” character and the high tolerance of the catalytic system versus different functionalities. While a grafting approach on TEMPO-capped monoliths has been proposed recently [92], the ROMP approach appears to be even more attractive in terms of functional variety. Since any living polymerization system is not immortal [13,24] and in view of the stability data for ruthenium-based initiators and in particular for **1** [93], optimum grafting conditions were elaborated in order to reduce loss of initiator activity to a minimum. For these purposes, the minimum time needed for the formation of the polymeric backbone (1 h) was determined [77]. Using the fraction of the initiator

Table 4
Capacities of functionalized ROMP monoliths

Monolith	Functional monomer	Capacity (mmol/g)
I		0.2 ^a
II		0.14 ^a
III		0.06 ^b
IV		0.26 ^b
V		^c
VI		0.06

^a Determined by titration.

^b Determined by elemental analysis (percentage of nitrogen).

^c Estimated by comparison with loading capacities and structural data of surface-grafted materials [34].

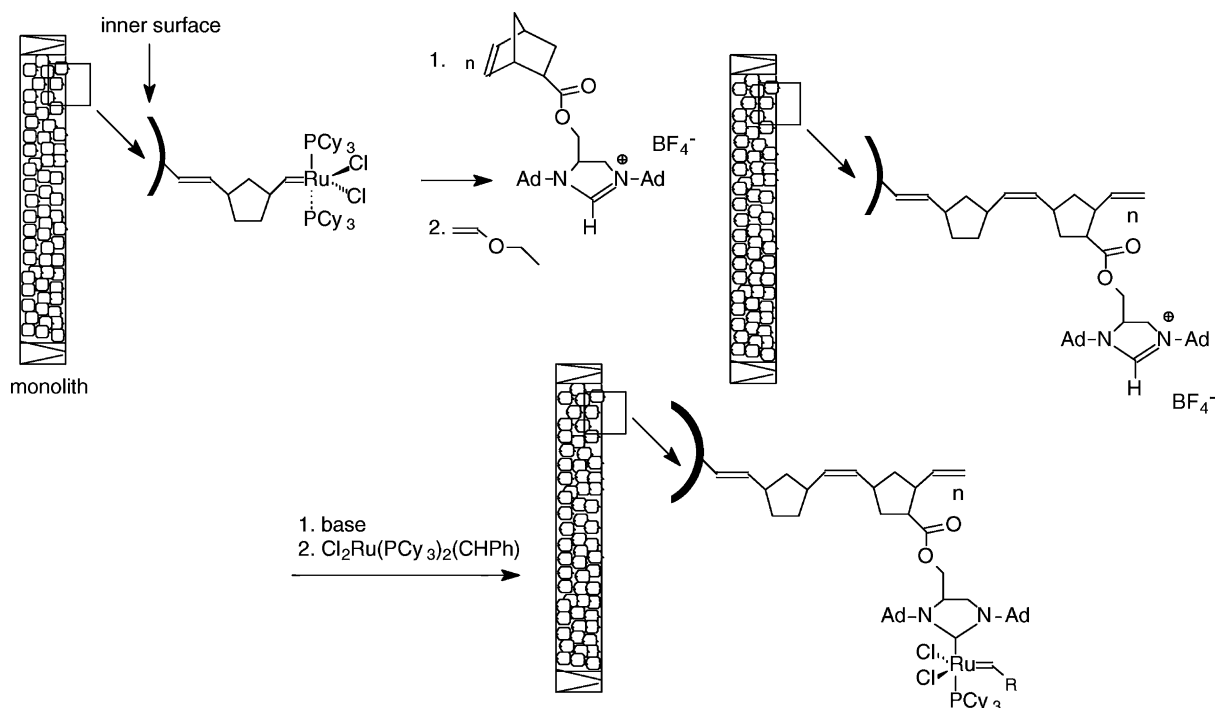
covalently bound to the surface ($\geq 98\%$, vide supra), the desired functional monomer is grafted onto the monolith surface by simply passing a solution thereof through the column/cartridge. Since there is no further possibility of cross-linking, tentacles attached to

the surface are formed. The general degree of polymerization of any functional monomer varies within almost two orders of magnitude, depending on its general ROMP activity.

Obviously, this approach offers multiple advantages. Firstly, the structure of the continuous rod is not influenced by the functional monomer and can be optimized regardless of the functional monomer used. Secondly, other solvents than the porogens toluene and methanol (e.g. methylene chloride, DMF) may be used for the “in situ” derivatization of the rod. This avoids possible limitations related to the solubility of the functional monomer in the porogens (e.g. β -cyclodextrins are only soluble in DMF). Finally, a large variety of functional monomers may be grafted onto the continuous rod. Restrictions due to a reduced polymerization activity of the initiator versus any functional monomer may be avoided by a careful monomer design. The versatility of this concept is clearly underlined by the large variety of functional monomers that may be attached to the surface of monolith. Table 4 summarizes data from different functionalized continuous rods. For purposes of convenience, all functional monomers employed are either based on norborn-2-ene or 7-oxanorborn-2-ene. The amount of functional monomer grafted onto the monolith may be determined both in a *qualitative* way by FT-IR spectroscopy and *quantitatively* by acid–base titration and elemental analysis, respectively.

11. Applications of functionalized metathesis-based monoliths in catalysis

As the ultimate goal in heterogeneous catalysis, one wants to combine the general advantages of homogeneous systems such as high definition, activity, etc. with the advantages of heterogeneous catalysis such as increased stability, ease of separation, recycling. Besides a few applications in solid phase synthesis [94,95] and enzyme immobilization [61,62], monolithic catalytic media have basically been restricted to metal oxides, porous metals [96] and certain polysaccharides [97]. The first successful use of metathesis-based monolithic media for heterogeneous catalysis was accomplished by using these supports as carriers for Grubbs-type initiators based on *N*-heterocyclic carbenes (NHC-ligands)



Scheme 3. Functionalization of metathesis-based monoliths with NHC-precursors and generation of a heterogeneous metathesis-active support.

[98,99]. In order to generate a sufficient porosity, monoliths with a suitable microporosity (40%) and microglobule diameter ($1.5 \pm 0.5 \mu\text{m}$) have been synthesized. Consecutive “in situ” derivatization was successfully accomplished using a mixture of norborn-2-ene and 1,3-di(1-adamantyl)-4-{[(bicyclo [2,2,1]hept-5-en-2-yl-carbonyl)oxy]methyl}-4,5-dihydro-1*H*-imidazol-3-ium tetrafluoroborate in methylene chloride (Scheme 3). The use of norborn-2-ene drastically enhances the graft yields for the functional monomer. Using this setup, tentacles of copolymer with a degree of oligomerization of 2–5 of the functional monomer may be generated. The free NHC necessary for recomplexation may simply be generated using 4-dimethylaminopyridine (DMAP). In the last step, excess base is removed by extensive washing and finally the catalyst is immobilized/formed by passing a solution of Cl₂Ru(CHPh)(PCy₃)₂ over the rigid rod. Loadings of up to 1.4% of Grubbs-catalyst on NHC base may be achieved. Monolith-immobilized metathesis catalysts prepared by this approach show high activity in various metathesis-based reactions

such as ROMP and RCM. The *cis/trans* ratio of polymers (90%) exactly corresponds to the one found with homogeneous systems. The use of chain-transfer agents (CTAs, e.g. *cis*-1,4-diacetoxybut-2-ene) allows the regulation of molecular mass, in particular in the case of cyclooctene. The presence of CTAs additionally enhances the lifetime of the catalytic centers by reducing the average lifetime of the ruthenium methylidenes. This allows the repetitive use of these systems. Additionally, both the tentacle-type structure and the designed microstructure of the support reduce diffusion to a minimum. This and the enhanced stability directly translate into a high average turn-over frequency (TOF) of up to 200 s^{-1} , thus exceeding even a homogeneous analogue (TOF = 0.07 s^{-1} ; 45°C) [100].

These monolith-based catalytic systems may be used as pressure stable catalytic reactors as well as one-way systems for use in combinatorial chemistry. The use of NHC-ligands successfully suppresses any bleeding leading even in RCM to virtually Ru-free products with a ruthenium-content of <0.07%.

12. Summary

It has been shown that ROMP represents a highly versatile tool in the preparation and modification of functional polymer supports. In contrast to standard binary and ternary systems, the use of well-defined initiators allows the highly reproducible preparation of tailor-made materials with regards to particle size, diameter, pore volume and functionalization. Most polymerization techniques such as precipitation graft and even bulk polymerization may be used for these purposes. Thus, even continuous rods are accessible via metathesis technology. They possess a homogeneous microstructure that may be tailored and offer the additional possibility of functionalization by using a large variety of functional groups including chiral selectors and chelating ligands. As other metathesis-based supports, these monolithic metathesis-based media therefore possesses enormous potential in catalysis as well as in the synthesis of separation media including micro-applications such as CLC.

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