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Heterogeneous C–C Coupling and Polymerization Catalysts Prepared by ROMP

Michael R. Buchmeiser*

Institute of Analytical Chemistry and Radiochemistry, University of Innsbruck, Innrain 52 a, A-6020 Innsbruck, Austria

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Abstract—This contribution summarizes the latest developments in the area of catalytic supports prepared via ring-opening metathesis polymerization (ROMP). In particular, the synthesis of heterogeneous catalytic systems active in Pd-mediated C–C coupling reactions such as Heck, Sonogashira–Hagihara and Suzuki couplings, as well as in ruthenium-mediated olefin metathesis reactions will be summarized. The general concept for the synthesis of these supports will be outlined in detailed. © 2002 Elsevier Science Ltd. All rights reserved.

Heterogeneous Pd Systems Prepared Via Ring-Opening Metathesis Precipitation Polymerization

The demand for highly potent systems capable of forming C–C bonds started an intense research on Pd-catalyzed reactions such as the vinylation of aryl halides, commonly called Heck systems.[1] Despite the impressive progress in homogeneous catalysis,[2,3] there is growing interest in highly active and stable *heterogeneous* systems. Phosphine- or aminophosphine-based ligands[4] are widely used, yet easily oxidized. This necessitates comparably high catalyst loadings or an excess of ligand. Consequently, phosphane-free ligands are of particular interest.[5–7] Ligands solely based on nitrogen,[8] (e.g., dipyridyl amide-based systems) are relatively rare, yet suitable for the synthesis of homogeneous highly temperature stable and active Heck catalysts.[9] If attached to appropriate polymerizable groups, analogous *heterogeneous* systems are accessible.[9–11] Generally, metathesis-based polymerizations have gained significant interest due to the rapidly growing armor of well-defined, selective and active catalytic systems. Well-defined systems such as the highly selective and active Schrock catalysts of the general formula $Mo(N\text{-}2,6\text{-}R_2\text{-}C_6H_3)(CHCMe_2Ph)(OCR')_2$ or the more robust Grubbs-type initiators of the general formula $Cl_2Ru(CHPh)(PR''_3)_2$ offer access to basically every polymer architecture one might think of.[12] Ring-opening metathesis precipitation polymerization is an attractive technique for the synthesis of complex cross-linked architectures for various reasons. On one hand, it comprises the possibility to polymerize functional monomers. On the other hand, the controlled, 'living'[13] polymerization mechanism allows a highly flexible yet reproducible polymerization setup.

For a reproducible synthesis that can be carried out on a stoichiometric base, the adherent polymerization of the ligand-containing monomer must fulfill a class VI living system.[14] Subsequent cross-linking with 1,4,4a,5,8,8a-hexahydro-1,4,5,8-*exo*-*endo*-dimethanonaphthalene (DMN-H6) 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).[15]

By this approach, the functional group (i.e., the ligand) can be introduced without any change in its chemical nature, geometry. Consequently, polymer-supported Pd-catalysts prepared by this approach are characterized by an exact knowledge about the chemical structure of the actual catalytic sites. Due to a tentacle-type structure, a large amount of functional groups are located at the surface. This also ensures a fast mass transfer within the interphase. Typical amounts of ligand immobilized by this approach are within a range of 0–1 mmol/g. Particles have a mean diameter of 20–40 μm, and are generally characterized by a low specific surface area ($4<\sigma<30\,m^2/g$). This size guarantees the convenient removal of the catalyst at the end of the reaction by means of filtration. After loading with

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*Corresponding author. Tel.: +43-512-507-5184; fax: +43-512-507-2677; e-mail: michael.r.buchmeiser@uibk.ac.at

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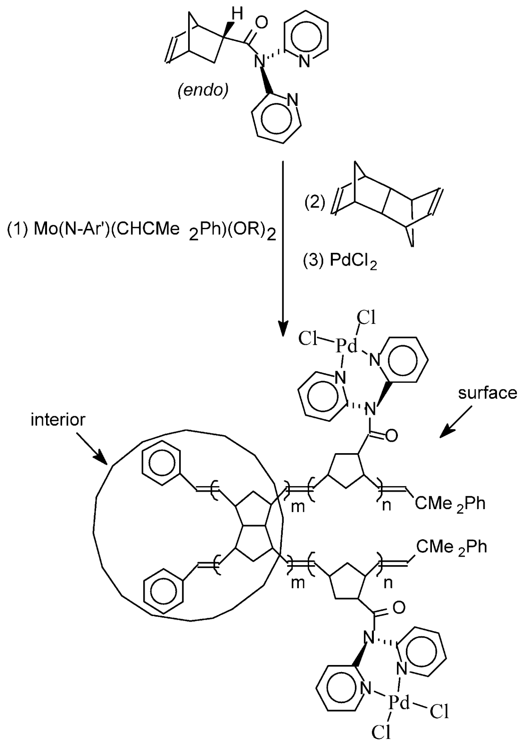
$PdCl_2$, the parent dipyridylamide-based system can be used in Heck as well as Sonogashira–Hagihara couplings of aryliodides and bromides. Reactions catalyzed by such heterogeneous systems are characterized by high turn-over numbers, typically in the range of 100,000–500,000. Amounts of Pd as low as 0.0003 mol%, corresponding to roughly 1 mg of resin can be used. The demand for such low amounts of polymer-immobilized catalyst additionally offers access to applications in the area of high-throughput screening. In order to increase reactivity for aryl chlorides, alkyl-substituted dipyridylamides as well as bis(pyrimidyl)amides based ligands were used (Table 1). Disappointingly, alkyl-substitution results in a decrease of reactivity due to reduced complexation and complex stability.[11] Nevertheless, bis(pyrimidine) ligands show an increased reactivity.[11] Heck couplings can be carried out with both aryliodides and bromides in quantitiatve yields. Similar to the parent system, coupling reactions with activated chloroarenes can be carried out in the presence of tetrabutylammonium bromide, known to promote Pd-mediated couplings.[16] Nevertheless, these reactions result in higher yields, typically 60–70%. Sonogashira–Hagihara couplings are quantitative with aryl iodides and result in yields of 50–70% with aryl chlorides. Suzuki couplings[17–20] represent an interesting yet still comparably expensive alternative to Heck couplings. With the bis(pyrimidine)-based ligand, reaction of aryl boronic acids with iodoarenes in THF proceeds smoothly with yields >80%. Nevertheless, coupling reactions with bromoarenes require comparably high amounts of Pd (up to 0.2 mol%) in order to obtain acceptable yields.



Scheme 1. Synthesis of catalytic supports via ring-opening metathesis precipitation polymerization.

For such reactions, ligand systems recently reported by Fürstner appear the most suitable ones.[23] The major difference between dipyridyl- and bis(pyrimidyl)-based ligands is reactions kinetics. Thus, pyrimidyl-based ligands exceed the dipyridylamide-based analogues in terms of turn-over frequency.[11]

Monolith-Immobilized Ruthenium-Based Systems for Metathesis

Olefin metathesis and in particular cross-metathesis (CM), and ring-closing metathesis (RCM), are nowadays among the most important C–C bond forming reactions. Consequently, these techniques are more and more used in industrial and pharmaceutical chemistry as well as chemical technology. Numerous well-defined homogenous systems are available for the above-mentioned purposes.[12,24] In contrast, only few reports exist on analogous, stable, permanently immobilized heterogeneous systems prepared by a molecular approach.[25–27] Instead, most relevant heterogeneous catalysts are either based on metal oxides and suffer from comparably ill definition.[28] Besides a recent report on a PS-DVB-immobilized second-generation Grubbs initiator,[25] there are no further reports on permanently immobilized metathesis systems.

The concept of heterogenization

In order to gain access to well-defined heterogeneous catalysts, synthetic transformations on heterogeneous supports should be avoided to a maximum extent. Therefore the synthesis of these systems must be accomplished in a way that a catalyst precursor, which may be transformed into the final catalytic system by a few simple synthetic steps, is attached to the carrier using a convergent rather than a divergent synthetic approach. Additionally, in order to provide high catalyst loadings, an approach that consists of the grafting of catalyst precursor-carrying polymer chains appeared favorable. This approach may only be accomplished by a few of the existing 'living' polymerization techniques.[29] For chemical reasons, polymerization of suitable *N*-heterocyclic carbene (NHC) precursors cannot be carried out be ionic polymerization techniques, since these precursors are usually cationic. Nevertheless, polymerization can be accomplished in a living manner via ROMP using $Cl_2Ru(CHPh)(PCy_3)_2$, where Cy = cyclohexyl. The fact that these polymerization systems fulfill the criteria of a class VI living system offer access to grafting chemistry, in particular to a 'grafting from'

Table 1. Summary of functionalized resins[9,11,21,22]

Functional group	Ligand (mmol/g)
N,*N*-Dipyrid-2-ylcarbamide	1.0
N,*N*-Dipyrid-2-ylcarbamide	0.6
N-Pyrid-2-yl-*N*-(3-methylpyrid-2-yl)carbamide	0.03
N-Pyrid-2-yl-*N*-(6-methylpyrid-2-yl)carbamide	0.05
N-(6-Methylpyrid-2-yl)-*N*-(4-methylquinolin-2-yl)carbamide	0.05
N,*N*-bis(pyrimidyl) carbamide	

approach. In principle, three different supports appear suitable for grafting. The first group comprises (the widely used) PS-DVB-based materials. Despite the ease of fabrication and the comparably broad range of particle size, the high-surface candidates with a low degree of cross-linking (typically $<10\%$) appear less favorable in terms of swelling properties and mechanical stability. Thus, heterogeneous phosphine- or NHC-based ruthenium metathesis catalysts immobilized onto Merrifield type supports described by Grubbs et al. as well as Blechert et al. were reported to suffer from diffusion controlled reactions.[25,26] This severely aggravates their successful use both in ROMP as well as in ring-closing metathesis (RCM). Alternatively, monolithic media can be used. Such materials are usually prepared via free radical polymerization and have been studied extensively by Svec, Fréchet and co-workers.[30–33] They are generally known under the term 'monoliths'. Generally speaking, the term 'monolith' applies to any uni-body structure composed of interconnected repeating cells or channels. Besides advantages such as lower back-pressure and enhanced mass transfer,[34,35] the ease of fabrication as well as the many possibilities in structural alteration need to be mentioned. Due to the broad applicability of ROMP and the high definition of the resulting materials, we applied this technique to the synthesis of continuous polymeric supports.[36]

Monolithic media prepared by ROMP

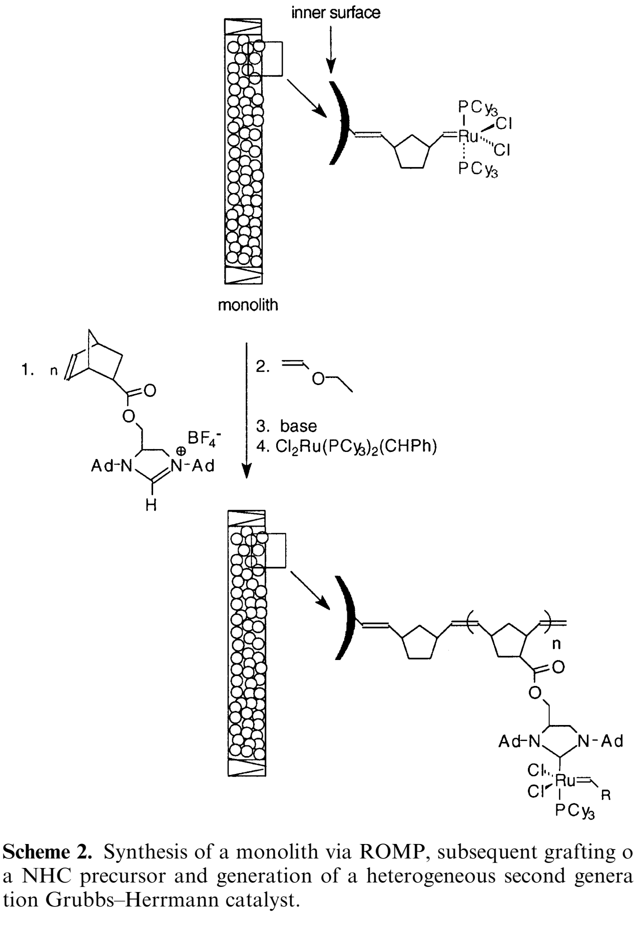
Based on the existing knowledge about pore-formation in monolithic materials,[32,37–39] norbornene (NBE) and DMN-H6 were copolymerized in the presence of two porogenic solvents, 2-propanol and toluene, using $Cl_2(PCy_3)_2Ru(=CHPh)$. In order to determine the amount of 'living' initiator sites after rod formation available for grafting, 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.[40] This is in accordance with a micelle-type microglubule formation, where the catalytically active sites are located at the boundary between the solid and liquid phase. This also allows an efficient removal of basically all the ruthenium after derivatization. Ruthenium-initiated polymerizations may conveniently be capped with ethylvinyl ether. ICP-OES investigations on the Ru content of the final rods revealed Ru concentrations $<10\,\mu g/g$, corresponding to a 99.8% removal.

Functionalization: grafting of NHC precursors

Following the above-mentioned concept, metathesis-based monolithic media may successfully be used for heterogeneous metathesis. In order to generate a sufficient porosity, monoliths with a suitable microporosity (40%) and microglobule diameter ($1.5\pm0.5\,\mu m$) were 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. The use of norborn-2-ene significantly 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 were generated. The free NHC necessary for recomplexation can be generated using 4-dimethylaminopyridine (DMAP). In a last step, excess base is removed by extensive washing and finally the catalyst is immobilized/formed by passing a solution of $Cl_2Ru(CHPh)(PCy_3)_2$ over the rigid rod. A summary of the entire procedure is shown in Scheme 2. Catalyst loadings up to 1.4 were 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 was found to be 90% and corresponds exactly to the one found with homogeneous systems.

The use of chain-transfer agents (CTAs, e.g., *cis*-1,4-diacetoxybut-2-ene, diethyldiallyl malonate, 2-hexene) allows the regulation of molecular mass, in particular in the case of cyclooctene. Typical values for the molecular weight and polydispersity (PDI) of poly(cyclooctene) were in the range of 1500–2500 and 1.2–1.9, respectively. The corresponding values for poly(norbornene) are 12,000 and 1.2. The presence of CTAs additionally enhances the lifetime of the catalytic centers by reducing



Scheme 2. Synthesis of a monolith via ROMP, subsequent grafting of a NHC precursor and generation of a heterogeneous second generation Grubbs–Herrmann catalyst.

the average lifetime of the ruthenium methylidenes. In particular *cis*-1,4-bisacetoxybut-2-ene turned is well suited for these purposes. This allows the repetitive use of these systems, particularly important in RCM. In terms of reaction kinetics, both the tentacle-type structure and the designed microstructure of the support reduce diffusion to a minimum. Thus, these systems behave as predicted by theory and must therefore be considered as successful alternatives to the above-mentioned PS-DVB supports. The fast kinetics as well as an enhanced stability quantitatively translate into a high average turnover frequency (TOF) in RCM of up to 25 min^{-1}, thus exceeding even the homogeneous analogue (TOF = 4 min^{-1}; 45 °C).[25] Maximum turnover numbers are around 60 (homogeneous ≤ 20). The catalytic systems presented here 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 less than 0.07%.

Acknowledgements

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