Inorganica Chimica Acta 409 (2014) 179–184

Contents lists available at SciVerse ScienceDirect

Inorganica Chimica Acta

journal homepage: www.elsevier.com/locate/ica

Note

Hyperbranched polyglycerol supported ruthenium catalysts for ring-closing metathesis

Venkatakrishnan S. Thengarai, Juliane Keilitz, Rainer Haag *

Department of Chemistry and Biochemistry, Freie Universität Berlin, Takustraße 3, 14195 Berlin, Germany

ARTICLE INFO

Article history:
Available online 28 June 2013

Metallodendrimers Special Issue

Keywords:
Ring-closing metathesis
Immobilization
Hyperbranched polyglycerol
Ruthenium leaching
Recycling

ABSTRACT

Immobilization of Hoveyda–Grubbs type I and II metathesis catalysts onto hyperbranched polyglycerol has been achieved via two distinct synthetic routes. The catalytic units were either placed at the periphery or the interior of the polymer and catalyst loadings between 0.166 and 0.517 mmol g^{-1} were achieved. The activity of the catalysts in ring-closing metathesis of variously substituted dienes and the ruthenium leaching into the product was investigated. It was found that the supported second-generation Hoveyda–Grubbs catalyst displayed higher activity than the first-generation analogues and achieved high conversions in only two hours. After the first run, however, longer reaction times were required to reach a reasonable conversion. Ru-leaching was determined by ICP-MS and found to be in the range of 0.2–7.8% of the initial ruthenium content, which corresponds to 28–288 ppm of Ru in the products. Additional treatment with activated charcoal after dialysis was found to be beneficial for Ru-removal.

1. Introduction

Since its discovery [1], olefin metathesis has been significantly developed and now plays an important role in organic synthesis [2,3]. A number of well-defined ruthenium based metathesis catalysts are known, which display very high activity in the metathesis reactions of several organic substrates [4,5]. Removal of the ruthenium residues from the final product is very tedious when homogeneous molecular catalysts are used and therefore is the subject of extensive research [6,7]. One means to facilitate the separation between catalyst and product is the immobilization of the homogeneous catalyst onto a polymeric scaffold which enables the use of simple separation techniques [8]. In order to enhance catalyst stability while retaining the high activity of the homogeneous catalyst, there has been a continuing interest to immobilize homogeneous analogues onto various polymeric supports [9]. Our group successfully employed hyperbranched polyglycerol (**hPG**) [10] as a support for a variety of catalysts [11].

The importance of olefin metathesis in organic synthesis [3] and the difficulties of the removal of metal residues from the products [5,7] motivated us to investigate the ability of **hPG** to function as a scaffold for metathesis catalysts with the long-term goal of an application in continuous flow membrane reactors. Here we present the synthesis and characterization of hPG-supported metathesis catalysts, their performance in ring closing metathesis (RCM) of differently substituted diolefins, and our results on the Ru-leaching into the final products.

* Corresponding author. Tel.: +49 30 838 52633; fax: +49 30 838 53357.
E-mail address: haag@chemie.fu-berlin.de (R. Haag).

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http://dx.doi.org/10.1016/j.ica.2013.06.031

2. Experimental and methods

All reactions were performed under dry and air-free conditions using standard Schlenk techniques or dry box procedures. Dry solvents were taken from a solvent purification system MB SPS-800 from MBraun and were used after three vacuum-nitrogen cycles. Hyperbranched polyglycerol has a Mw of 10 kDa and 13.5 mmol OH per gram of polymer. 4-Isopropoxy-3-vinylbenzyl alcohol [12], Grubbs II catalyst [13], and diethyl-allylmethallyl malonate [14] were synthesized according to literature procedures. All other chemicals were purchased from commercial sources and used as received. Ultrafiltration was performed under Nitrogen (or Argon) pressure in a solvent-resistant stirred cell with regenerated cellulose membranes (molecular weight cut-off 1000 or 5000), both from Millipore. Dialysis was performed with benzoylated cellulose membrane tubing purchased from SIGMA Aldrich with a MWCO 1000. ICP-MS measurements were carried out on an Element 2 (Thermo Fisher) at low resolution (sample gas 0.863 L/min; plasma power 1350 Watt). NMR spectra were recorded on a Bruker AMX 500, an Avance 700 instrument, or a Jeol 400 MHz instrument. IR spectra were recorded as thin film on KBr or diamond anvil using Avatar 320 FT-IR spectrometer. Ring closing metathesis (RCM) reactions were performed in regular NMR tubes.

2.1. Synthesis of 4-isopropoxy-3-vinylbenzyl-2-bromoacetate (*1*)

To a solution of 4-isopropoxy-3-vinylbenzyl alcohol (0.25 g, 1.30 mmol) in THF (5 mL) at 0 °C, solid DMAP (0.16 g, 1.30 mmol, 1 equiv) was added in one portion and the mixture was stirred

for 5 min. Bromoacetyl chloride (0.21 g, 1.30 mmol, 1 equiv) was added at 0 °C over a period of 2 h. The cold bath was removed and the reaction mixture was stirred at ambient temperature for 1 h. The reaction mixture was then cooled to 0 °C and quenched with ice. It was transferred to a separating funnel, saturated $NaHCO_3$ and water (50 mL each) were added and the product was extracted with dichloromethane (3 × 50 mL). The organic extracts were washed with water, dried over Na_2SO_4, filtered and dried in vacuo to obtain the product as a light yellow oil. Compound **1** was used for the next step without further purification. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.46 (d, J = 2.4 Hz, 1H, aromatic), 7.20 (dd, J = 8.0, 2.4 Hz, 1H, aromatic), 7.01 (dd, J = 6.8, 2.4 Hz, 1H, $ArCHCH_2$), 6.84 (d, J = 8.8 Hz, 1H, aromatic), 5.73 (dd, J = 16.0, 1.6 Hz, 1H, $ArCHCH_2$), 5.24 (dd, J = 11.2, 1.6 Hz, 1H, $ArCHCH_2$), 5.12 (s, 1H, $ArCH_2OC(O)$), 5.11 (s, 1H, $ArCH_2OC(O)$), 4.53 (septet, 1H, $ArOCHMe_2$), 3.85 (s, 1H, $BrCH_2C(O)$), 3.84 (s, 1H, $BrCH_2C(O)$), 1.33 (d, J = 6.0 Hz, 6H, $ArOCHMe_2$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 167.4, 155.5, 131.5, 129.6, 127.5, 127.4, 126.9, 114.7, 114.0, 71.0, 68.1, 41.1, 22.2 ppm. IR ($\nu_{C=O}$ cm^{-1}): 1742 (s), 1651 (vs).

2.2. Synthesis of hPG-(OAc)$_{30\%}$ **2**

A well-dried sample of hyperbranched polyglycerol (2.67 g, 36.10 mmol OH) was placed in a double-necked, round-bottom flask equipped with a condenser and dissolved in dry pyridine (30 mL). Acetic anhydride (1.1 mL, 11.91 mmol, 0.33 equiv per OH) was added and the reaction mixture was heated to 55 °C for 18 h. After cooling to ambient temperature, the mixture was cooled to 0 °C and quenched by adding ice. The volatiles were evaporated by cryo-distillation and the product was purified by dialysis using methanol. The extent of acylation was determined from the relative integral intensities of the acyl-methyl group protons (3H at 2.08 ppm; see below) against the combined integrals (5H, 5.25–4.95 and 4.45–3.45 ppm; see below) from polyglycerol. Yield: 2.60 g (83%, degree of functionalization: 30%). ^{1}H NMR (CD_3OD, 500 MHz): δ = 5.25–4.95 (m, 0.27, secondary protons of polymer), 4.45–3.45 (m, 14.79, primary protons of polymer), 2.08 (s br, 3H, $OC(O)CH_3$) ppm. ^{13}C NMR (CD_3OD, 125.8 MHz): δ = 171.4 (s), 78.7 (s), 72.3 (s), 71.3 (s br), 71.2 (br), 69.8 (br), 68.3 (br), 65.6 (s), 63.2 (s), 19.7 ppm. IR ($\nu_{C=O}$ cm^{-1}): 1731 (s), 1646 (s).

2.3. Synthesis of hPG-supported ligand 3

A well-dried sample of hyperbranched polyglycerol (0.40 g, 5.40 mmol OH) was placed in a double-necked, round-bottom flask fitted with dropping funnel and dissolved in dry DMF (4 mL). The solution was then cooled to 0 °C. A solution of KO^{t}Bu (0.24 g, 2.16 mmol, 0.4 equiv) in a 1:2 mixture of DMF/THF (6 mL) was transferred into a dropping funnel and added drop-wise to the cold DMF solution during 15 min leading to the formation of a white suspension and was stirred for ½ h at that temperature. The above-prepared styrene isopropoxy derivative **1** (345 mg, 1.10 mmol, 0.2 equiv) was dissolved in THF (15 mL), transferred to the dropping funnel and added dropwise for 30 min to the white suspension at 0 °C. The solution turned bright yellow and turned more intense during the addition; a red–orange colored solution and a white precipitate was obtained. The cold bath was removed and the reaction mixture was stirred overnight. The reaction mixture was cooled to 0 °C and quenched with ice. The volatiles were evaporated under vacuum to obtain an orange-red residue, which was dissolved in methanol, filtered through a cotton plug, and subjected to ultrafiltration (MeOH) until the washings were colorless. The hPG-supported ligand **3** was obtained as a yellow sticky compound. Yield: 0.31 g (65%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.37 (m br, aromatic), 7.10 (m br, aromatic), 6.93 (m br, $Ar–CH=CH_2$), 6.77 (m br, aromatic), 5.65 (m, $Ar–CH=CH_2$), 5.13 (m, $Ar–CH=CH_2$+$ArCH_2OC(O)$), 4.48 (m, $CHMe_2$), 4.00–3.20 (m br, primary protons of polymer + polymer–$OCH_2C(O)$), 1.25–1.15 (m br, $CHMe_2$) ppm. IR ($\nu_{C=O}$ cm^{-1}): 1646 (m br), 1601 (m br).

2.4. Synthesis of hPG-(OAc)$_{30\%}$-supported ligand **4**

The ligand was prepared by a similar procedure as ligand **3**. A well-dried sample of hPG-(OAc)$_{30\%}$ **2** (0.10 g, 0.81 mmol OH) was placed in a double-necked, round-bottom flask equipped with a dropping funnel and dissolved in dry THF (10 mL). The solution was then cooled to 0 °C. A solution of KO^{t}Bu (1.34 mL, 0.15 g, 1.3 mmol, 1.6 equiv; 1 M solution in THF) in THF (5 mL) was transferred into a dropping funnel and added dropwise to the cold THF solution over 15 min resulting in the formation of a white suspension which was stirred for another 30 min at that temperature. The above-prepared styrene isopropoxy derivative **1** (1.30 mmol, 1.60 equiv) was dissolved in THF (10 mL), transferred to the dropping funnel, and added dropwise over 30 min to the white suspension at 0 °C. The resulting red–orange colored solution and a white precipitate was allowed to warm to ambient temperature and stirred overnight. The reaction mixture was cooled to 0 °C and quenched with ice. The volatiles were evaporated under vacuum to obtain an orange-red residue. The residue was dissolved in methanol, filtered through a cotton plug and subjected to ultrafiltration in the same solvent until the filtrates were colorless. The supported ligand **4** was obtained as yellow sticky oil which was further subjected to dialysis in methanol. Yield: 0.26 g (60%). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.45 (m br, aromatic), 7.15 (m br, aromatic), 7.00 (m br, $Ar–CH=CH_2$), 6.80 (m br, aromatic), 5.75 (br, $Ar–CH=CH_2$), 5.10 (m br, $Ar–CH=CH_2$ + $ArCH_2OC(O)$), 4.48 (m, $CHMe_2$), 4.00–3.20 (m, primary protons of polymer + polymer–$OCH_2C(O)$), 1.25–1.15 (m br, $CHMe_2$). IR ($\nu_{C=O}$ cm^{-1}): 1731 (s), 1645 (m sh), 1625 (m).

2.5. Synthesis of hPG-supported Hoveyda–Grubbs I catalyst **5**

In a glove box, the hPG-supported ligand **3** (0.14 g, 94.85 μmol styrenyl ligand) was suspended in dry dichloromethane (5 mL) in a Schlenk flask. Solid Grubbs I catalyst (0.16 g, 0.19 mmol) was added and the Schlenk flask was capped, taken out of the glove box and the mixture was heated at 40 °C for 15 h. The reaction mixture was then subjected to dialysis in dichloromethane to obtain the supported catalyst **5** as a brownish-pink solid that was stable under air. Yield: 0.16 g (85%). ^{1}H NMR ($CDCl_3$, 400 MHz): 17.40 (s, br, Ru=CH), 7.75–7.30 (m, aromatic), 7.20–6.70 (m, aromatic), 6.60 (m br, aromatic), 5.25 (br, $ArCH_2OC(O)$) 4.30 (m, $CHMe_2$), 4.00–3.30 (m, primary protons of polymer + polymer-$OCH_2C(O)$), 1.80–1.40 (m br, PCy_3 protons + $CHMe_2$). ^{31}P NMR ($CDCl_3$, 162 MHz): 61.8 (s, br). IR ($\nu_{C=O}$ cm^{-1}): 1728 (s br), 1628 (m br). ICP-MS: 0.517 mmol g^{-1} Ru, 0.572 mmol g^{-1} P; catalyst loading: 0.517 mmol g^{-1}; degree of functionalization: 3.85%.

2.6. Synthesis of hPG-(OAc)$_{30\%}$-supported Hoveyda–Grubbs I catalyst **6**

In a glove box, the hPG-supported ligand **4** (20 mg, 3.29 μmol styrenyl ligand) was dissolved in dry dichloromethane (0.5 mL) in a Schlenk flask. Solid Grubbs I catalyst (9 mg, 11.24 μmol) was added and the Schlenk flask was capped, taken out of the glove box and the mixture was heated at 40 °C for 15 h. The reaction mixture was then subjected to dialysis in dichloromethane to obtain the air stable pinkish brown hPG-(OAc)$_{30\%}$-supported catalyst **6**. Yield: 19 mg (50%). ^{1}H NMR ($CDCl_3$, 400 MHz): 17.38 (s, br, Ru=CH), 7.80–7.40 (m, aromatic), 7.10–6.60 (m, aromatic), 7.10–6.60 (m br, aromatic), 5.10 (br, $ArCH_2OC(O)$), 4.50 (m, $CHMe_2$), 4.25–3.20 (m, primary protons of polymer + polymer–$OCH_2C(O)$), 2.05 (br, $OC(O)CH_3$) 1.80–1.40 (m br, PCy_3

protons), 1.30–1.20 (m br, $CHMe_2$). IR ($\nu_{C=O}$ cm^{-1}): 1728 (s), 1683 (m), 1625 (m). ICP-MS: 0.166 mmol g^{-1} Ru, 0.162 mmol g^{-1} P; catalyst loading: 0.166 mmol g^{-1}; degree of functionalization: 1.23%.

2.7. Synthesis of hPG-$(OAc)_{30\%}$-supported Hoveyda–Grubbs II catalyst 7

In a glove box, the hPG-supported ligand **4** (25 mg, 4.11 μmol styrenyl ligand) was dissolved in dry dichloromethane (0.5 mL) in a Schlenk flask. Solid Grubbs II catalyst (12 mg, 14.05 μmol) was added and the Schlenk flask was capped, taken out of the glove box and the mixture was heated to 40 °C for 15 h. The reaction mixture was then subjected to dialysis in dichloromethane to obtain the supported catalyst **7** as an air-stable bright green compound. Yield: 25 mg (55%). ^{1}H NMR ($CDCl_3$, 400 MHz): 16.50 (s, br, Ru=CH), 7.60–7.30 (m, aromatic), 7.10–6.80 (m, aromatic), 6.80–6.50 (m br, aromatic), 4.80–4.50 (m br, $ArCH_2$-OC(O) + $CHMe_2$), 4.00–3.30 (m, primary protons of polymer + polymer–$OCH_2C(O)$), 2.50–2.15 (m br, mesityl-Me), 2.00 (br, $OC(O)CH_3$) 1.80–1.40 (m br, PCy_3 protons), 1.30–1.20 (m br, $CHMe_2$). IR ($\nu_{C=O}$ cm^{-1}): 1730 (s), 1632 (m). ICP-MS: 0.298 mmol g^{-1} Ru; catalyst loading: 0.298 mmol g^{-1}; degree of functionalization: 2.21%.

2.8. General procedure for ring-closing metathesis

In an NMR tube, the catalyst was dissolved in $CDCl_3$. The substrate was added, everything was mixed well and then placed in a pre-heated oil bath at 55 °C for the indicated period of time. The product formation and disappearance of the diene were monitored by ^{1}H NMR. The conversion of substrates **S1** and **S3** was determined according to a literature procedure [15]. In the case of **S3**, the conversion was determined by comparing the integrals of the methylene protons of the product [4.48 (m, 2H), 4.36 (m, 2H)] [16] with those of the starting material [3.99 (m, 4H)].

3. Results and discussion

In order to understand the influence of the polymer on the catalytic performance we sought to incorporate the catalytic sites either predominantly at the periphery or at the interior of the polymer (Fig. 1). Hyperbranched polyglycerol (**hPG**) can be easily obtained by anionic ring-opening, multi-branching polymerization (ROMBP) of glycidol and contains interior secondary monohydroxy and terminal dihydroxy functional groups, which can be easily converted by standard synthetic methods [10]. These different types of hydroxyl groups offer a handle to distinguish between the interior and exterior of the polymer by utilizing the appropriate synthetic route.

The introduction of catalytic sites at the periphery can be achieved by simply reacting **hPG** with the ligand **1** followed by metal complexation. Since the outer hydroxyl groups are most easily accessible, those will be functionalized primarily. In order to functionalize the interior of **hPG**, the outer hydroxyl groups have to be blocked before ligand coupling and metal complexation can take place.

Several strategies have been employed for the immobilization of ruthenium-based metathesis catalysts onto polymer supports, among which immobilization via benzylidene has gained wide attention [9,17–20]. In order to achieve a stable coupling, an ether linkage was used to bind ligand **1** to **hPG** (Scheme 1).

For the synthesis of catalyst **5** with Grubbs I catalytic sites mainly at the periphery, **hPG** (Mw 10 kDa, 13.5 mmol OH g^{-1}) was first reacted with ligand **1** to obtain the hPG-supported ligand **3** with approximately 20% functionalized hydroxyl groups. Due to their easy accessibility, the outer hydroxyl groups will react first. Purification of **3** is achieved by simple ultrafiltration.

In order to obtain a catalyst with the catalytic sites in the interior of the polymer, the exterior hydroxyl groups have to be blocked first, which is achieved by reaction with acetic anhydride. hPG-$(OAc)_{30\%}$ **2** was obtained with a degree of functionalization of about 30% and then reacted with ligand **1** to give hPG-$(OAc)_{30\%}$-supported ligand **4** in moderate yield (60%).

Complexation with Grubbs I or II proceeds via a similar reaction to the one described for the analogous non-supported, homogeneous Hoveyda–Grubbs catalysts [21]. The treatment of hPG-supported ligand **3** with Grubbs I catalyst and purification by dialysis gave the hPG-supported first-generation Hoveyda–Grubbs catalyst **5** in good yield of 85%. Catalyst **5** was characterized by ^{1}H and ^{31}P NMR and IR spectroscopy. The ^{1}H NMR of **5** shows a resonance at 17.40 ppm for the benzylidene, which is in the range usually observed for first-generation Hoveyda–Grubbs catalysts [21]. Similarly, the ^{31}P chemical shift of ruthenium-bound tricyclohexyl phosphine is observed at 61.8 ppm [21]. The catalyst loading of **5** was analyzed by ICP-MS and it was found that 0.517 mmol g^{-1} of metathesis catalyst were bound, which corresponds to a degree

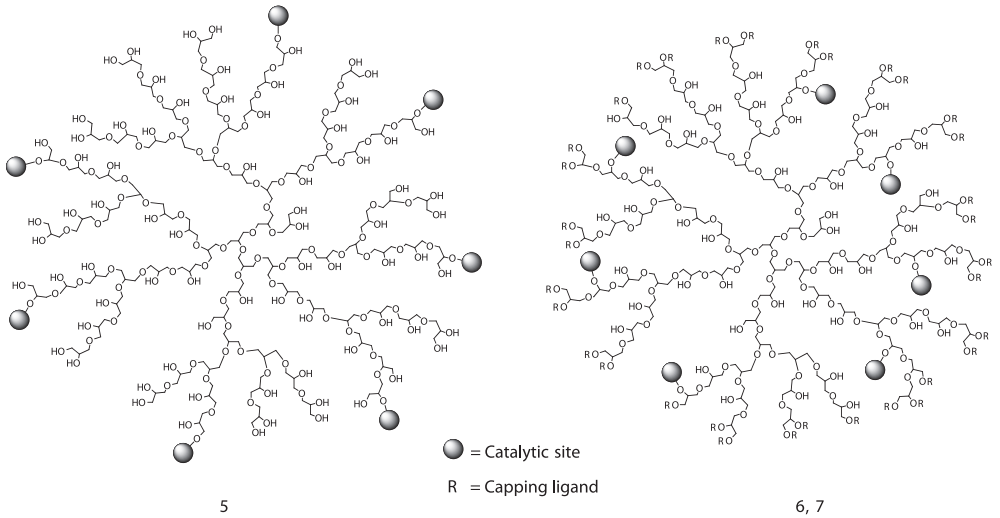
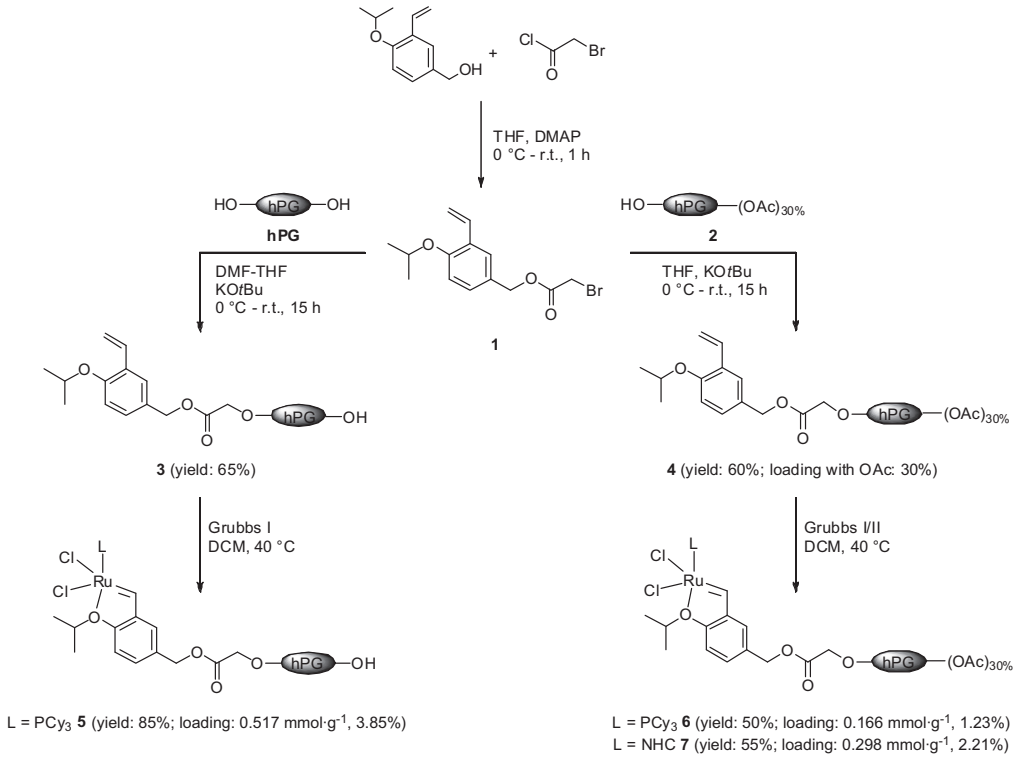


Fig. 1. Schematic representation of the supported catalysts with the active catalytic sites located at the periphery (left) or the interior (right). The polyglycerol scaffold shows an idealized structure of hPG.



Scheme 1. Synthesis of hPG-supported ligands **3** and **4** and catalysts **5**–**7**.

of functionalization of 3.85%. It is worth mentioning that the ruthenium to phosphorus ratio in the supported catalyst is 0.9 which confirms the nature of the supported catalyst.

Catalyst **6** was obtained in moderate yield (50%) by the same synthetic procedure and the ^{1}H NMR and IR spectroscopic data is similar to that of catalyst **5**. However, since the catalytic units in **6** are bound to the interior hydroxyl groups of **hPG**, the loading is significantly reduced. By ICP-MS a catalyst loading of 0.166 mmol g^{-1} is measured, which is approximately three times lower than the loading of **5**. The ruthenium to phosphorus ratio in **6** (see Table 1) is 1.02, again confirming the nature of the supported catalyst.

The second generation of metathesis catalysts bear strongly nucleophilic N-heterocyclic carbenes and is known to be highly active in ring-closing metathesis [5,17,22,23]. Since the removal of phosphorus compounds from organic products is often difficult, the use of these phosphine-free catalysts is attractive. In order to support the second-generation catalyst, hPG-supported ligand **4** is reacted with Grubbs II to afford the hPG-supported Hoveyda–Grubbs II catalyst **7** in moderate yield (55%). The benzylidene proton in **7** is observed at 16.50 ppm in the ^{1}H NMR spectrum. This chemical shift is in agreement with non-supported catalysts [17,22]. The loading of the catalyst on the polymer was found to be 0.298 mmol g^{-1}, which corresponds to a degree of functionalization of 2.21%.

Table 1
Ruthenium and phosphorus content and the loading of catalysts **5**–**7**.[a]

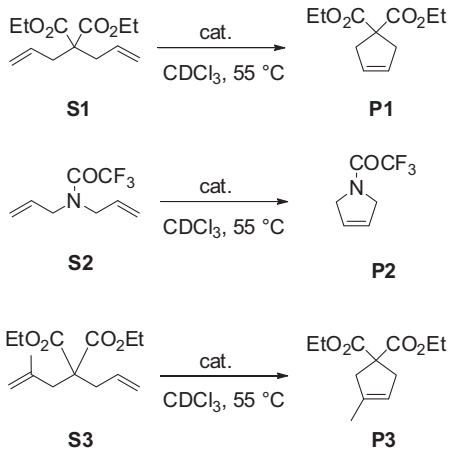
Entry	Catalyst	Ru (mmol g^{-1})	P (mmol g^{-1})	DF (%)	Ru/P
1	**5**	0.517	0.572	3.85	0.90
2	**6**	0.166	0.162	1.23	1.02
3	**7**	0.298	0.184	2.21	1.62

[a] Results obtained from ICP-MS measurements.

3.1. Catalytic ring-closing metathesis

With the supported catalysts **5**–**7** in hand, we investigated their activity in ring-closing metathesis reactions (Scheme 2). Initial experiments were performed on the benchmark substrate diethyldiallyl malonate (**S1**). Substrate **S2** was chosen to investigate the tolerance of the supported catalysts towards N-heterocycles and substrate **S3** was chosen to investigate the efficacy of the catalysts in the synthesis of tri-substituted cycloalkenes. The results are shown in Table 2.

As can be seen from Table 2, substrate **S1** undergoes quantitative conversion to the corresponding cycloalkene P1 in the presence of all three catalysts **5**–**7** (entries 1–3, 1st run). However, the phosphine-free catalyst **7** is obviously significantly more active



Scheme 2. Catalytic ring-closing metathesis reactions of substrates **S1**–**S3** using hPG-supported catalysts **5**–**7**.

Table 2
Results of ring-closing metathesis reactions of substrates **S1**–**S3** using catalysts **5**–**7**.

Entry	Subst.	Cat.	S/C[a]	Conversion (%)[b] (time (h))			TON	Ru-leaching[c]
				Run 1	Run 2	Run 3	(1st run)	(ppm) ((%))
1	S1	**5**	20	99 (20)	28 (20)	–	20	283 (2.4)
2	S1	**6**	77	97 (17)	37 (20)	–	75	288 (7.3)
3	S1	**7**	47	>99 (2)	82 (18)	83 (20)	47	224 (7.8)
4	S2	**5**	55	87 (13)	59 (2)	75 (66)	48	150 (5.2)
5	S2	**6**	105	>99 (17)	63 (20)	–	104	2884 (98.9)[d]
6	S2	**7**	60	86 (2)	34 (18)	25 (3)	52	134 (6.0)
7	S3	**5**	15	63 (20)	–	–	9	–
				80 (39)	–	–	12	64 (0.2)
8	S3	**6**	106	85 (17)	33 (20)	–	90	173 (6.0)
9	S3	**7**	40	91 (2)	80 (18)	63 (3)	36	28 (0.8)[e]

[a] Valid for the first run.
[b] Determined from the relative integral intensities in the crude ^{1}H NMR spectrum.
[c] Results obtained after the last run by ICP-MS after purification by dialysis.
[d] Since the leaching accounts to 99% of the initial Ru-content of the reaction mixture, it is most likely that a leak in the dialysis tube during purification is responsible for this leaching value.
[e] Results obtained by ICP-MS after purification by dialysis and subsequent treatment with activated charcoal.

(entry 3) affording the cycloalkene **P1** in less time than required with catalysts **5**and **6** (entries 1, 2). Similarly, catalysts **5**–**7** also transform substrate **S2** to **P2** with high conversions (entries 4–6, 1st run). Again, catalyst **7** displays a higher activity, giving 86% conversion in two hours. In the case of the sterically demanding substrate **S3** a significant difference in activity between the three catalysts is observed (entries 7–9). The overall activity trend is similar to the one observed for substrates **S1** and **S2**: catalyst **7** displays superior activity compared to **5** and **6**, affording 91% conversion in only two hours. Catalyst **5** shows poor activity in the formation of the tri-substituted olefin **P3**, requiring 39 h to achieve 80% conversion of **S3** whilecatalyst **6** needs only 17 h to reach 85% conversion. However, the activity of **7** is comparable to those of corresponding non-supported catalysts [17,21,22] and other second generation catalysts [23]. For substrates **S1** and **S2** the monomeric second generation metathesis catalyst usually achieves up to 99% yield within a few hours reaction time [23a,b]. In comparison to other supported second-generation Hoveyda–Grubbs catalysts, **7** shows comparable activity [19,20,24–26].

3.2. Catalyst recycling and ruthenium leaching into theproduct

Initial experiments on catalyst recycling were performed with the following procedure: the organic product was separated from the supported catalyst by dialysis and additional ligand **4** was added to re-form the catalyst. However, upon addition of another equivalent of substrate and subjection to the standard reaction conditions, no conversion was observed.

Therefore, we decided to use sequential addition of substrate without intermediate product purification to increase the total turnover numbers and to determine the overall activity of **5**–**7**. After the first addition of the substrate and heating, the conversion was monitored by ^{1}H NMR every two hours to ensure complete conversion. Upon complete consumption of the starting material, another equivalent of substrate was added and the NMR tube was heated again. The reactions wereusually stopped after two or three runs and the mixture was then subjected to dialysis to isolate the ring-closing metathesis product.

Two protocols were employed for ruthenium removal: (a) dialysis only and (b) dialysis followed by treatment with activated charcoal for 12 h [16]. The organic product obtained after dialysis was found to be free of polymer by ^{1}H NMR. However, the presence of trace amounts of ruthenium was determined by inductively coupled plasma mass spectrometry (ICP-MS). The results are shown in Table 2. The amount of ruthenium found in the organic products ranges from 28 to about 288 ppm. Purification by dialysis was able to reduce the amount of ruthenium to as low as 64 ppm. However, supplementing dialysis with activated charcoal treatment reduced theruthenium level to as low as 28 ppm. When the leaching values are calculated in per cent of the original amount of Ru used, values between 0.2 and 7.8% are obtained. The amount of ruthenium leaching found in this work is comparable to the leaching found for other supported metathesis catalysts immobilized on polystyrene [27], poly(ethylene glycol) [28], poly(ethylene) [26], poly(divinyl benzene) [29], porous silica [25,30], silica-based cationic exchange resins [20], or sol–gel monoliths [12].

4. Conclusion

In conclusion we successfully synthesized hPG-supported metathesis catalysts **5**–**7** with the catalytic moieties either located at the periphery or interior of the dendritic polymer. They are quite robust and air stable at ambient temperature for at least six weeks. The second-generation catalyst exhibiting an N-heterocyclic carbene ligand is significantly more active than the immobilized first generation Hoveyda–Grubbs catalysts, leading to the formation of both di- and trisubstituted olefins in good to high conversions. The analysis of ruthenium levels in the final products shows a ruthenium contamination in the range of 64–288 ppm which corresponds to a loss of ruthenium of 0.2–7.8% based on the initial metal content. A further reduction of the contamination was achieved by complementary treatment with activated charcoal after dialysis which reduced the Ru-content of the product to 28 ppm.

Acknowledgements

The authors thank Mr. Thomas Wons for ICP-MS measurements. This work is part of the Cluster of Excellence "Unifying Concepts in Catalysis." Financial support by the Deutsche Forschungsgemeinschaft (DFG) (EXC 314) is gratefully acknowledged. We are grateful to Dr. Pamela Winchester for proofreading this manuscript.

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