Synthesis and application of a new polystyrene-supported ruthenium carbene catalyst for alkene metathesis

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Abstract—A ruthenium carbene complex was permanently immobilised on a functionalised polystyrene resin by reaction with a supported silver salt of a carboxylic acid. The catalyst thus prepared was active in the self-metathesis of internal alkenes as well as in ring-closing metathesis. It was easily separated from the reaction products, which were almost free from ruthenium contamination, and also recycled. © 2001 Elsevier Science Ltd. All rights reserved.

During recent years impressive progress has been made in the development of homogeneous olefin metathesis catalysts.[1] This has mainly been due to the synthesis of new ruthenium carbene catalysts, such as Ru(=CHPh)-(Cl)$_2$(PCy$_3$)$_2$ (**1**)[2] and Ru(=CHPh)(Cl)$_2$(PCy$_3$)L (where L is an *N*-heterocyclic carbene ligand).[3] Immobilisation of these catalysts on solid supports will facilitate the work-up and make the metathesis reaction more attractive for practical applications. Nguyen and Grubbs[4] presented the first example of immobilising a well-defined ruthenium carbene on a solid support. Complex Ru(=CH-CH=CPh$_2$)(Cl)$_2$(PPh$_3$)$_2$ (**1a**) was tethered to a series of phosphine-functionalised polystyrene–divinylbenzene (PS-DVB) solid supports by phosphine exchange, e.g. complex **2**. These supported catalysts brought about the ring-opening metathesis polymerisation (ROMP) of norbornene and cyclooctene, as well as the self-metathesis of *cis*-2-pentene, although at a much slower rate than catalyst **1a**.

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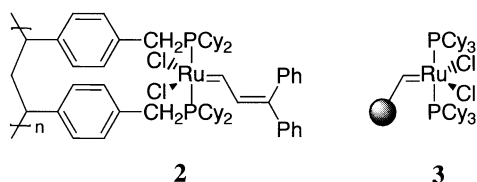
Recently, several publications have appeared describing new approaches to immobilise ruthenium carbene complexes. In most cases, the carbene unit is used as the connection to the solid phase,[5] e.g. the so-called 'boomerang' polymer-supported catalyst **3**.[5b] During metathesis the catalyst is released to the reaction medium, acts as a homogeneous catalyst, and is then recaptured by the support once the substrate has been consumed. This approach is actually not suited for continuous processes or for a metathesis reaction with thermodynamical equilibrium between substrate(s) and product(s), as for example in the self-metathesis of internal alkenes. There is one report where a ruthenium carbene is bound to a Merrifield resin functionalised with an *N*-heterocyclic carbene ligand, producing an immobilised catalyst that is active for ring-closing metathesis (RCM) and ene-yne metathesis.[6]

In our group we devised a different approach for the immobilisation of ruthenium carbenes. We anticipated that the anionic ligands, which would remain bonded to the ruthenium throughout the entire catalytic cycle, were the most suitable groups to form a covalent link between the Ru(II) centres and a support. Therefore, we have replaced the chloride ligands in **1** with carboxylic groups to produce six coordinate dimeric complexes of the type [Ru$_2$(=CHR)$_2$(R′CO$_2$)$_2$(μ-R′CO$_2$)$_2$-(PCy$_3$)$_2$(μ-H$_2$O)], where R′ is a strongly electron-withdrawing group (e.g. CF$_3$, C$_2$F$_5$, CCl$_3$).[7] These ruthenium carbene complexes were found to be highly active metathesis catalysts. Consequently, to obtain the desired supported ruthenium carbene complex, we have developed a straightforward procedure illustrated in

Scheme 1. We used a polystyrene resin as the support because of its chemical neutrality and presumed site isolation that would prevent deactivation of the catalyst by clustering.

A polystyrene resin (1% DVB) functionalised with hydroxyethyl groups (1.48 mmol OH/g) was transformed into a carboxylic-acid-functionalised resin by reaction with hexafluoroglutaric anhydride. Upon treatment with sodium bis(trimethylsilyl)amide, followed by ion exchange with silver nitrate, a silver salt of the immobilised carboxylic acid was obtained. Finally, the ruthenium complex 1 was reacted with the resin, producing the supported ruthenium carbene 4 as dark brown coloured beads. Based on our studies of the reaction with soluble silver carboxylates,[7] we believe that at least one chlorine atom in 1 was substituted with the carboxylic group. The ruthenium loading on the resin, as determined by ICP-AES analysis, was equal to 0.35 ± 0.05 wt% (~0.035 mmol/g). Thus, in the procedure employed, complex 1 substituted ca. 3% of the functional groups with respect to the starting resin.[8] In the MAS ^{1}H NMR spectrum the carbene signal was observed at 19.86 ppm as a broad singlet, which is slightly up-field with respect to complex 1 (20.02 ppm).[2a] In the MAS ^{31}P NMR spectrum two peaks were observed: a broad one at 52.6 ppm and a narrow one at 51.2 ppm in the ratio of 2:1.[9]

Our polymer-supported catalyst 4 is a highly active and versatile metathesis catalyst (Table 1). It was applied in self-metathesis of internal alkenes, such as *trans*-4-decene and methyl oleate (methyl *cis*-9-octadecenoate). Catalyst 4 converted 39 and 45% of the respective alkenes in 4 h, which is even slightly better than for the homogeneous catalyst 1 (36 and 40%, respectively)[10]

under similar reaction conditions. After an additional few hours, both reactions reached their thermodynamic equilibrium ($\sim50\%$ conversion), while the selectivity was still $\geq98\%$. Catalyst 4 is much more productive in the metathesis of internal alkenes ($TOF=54$ and 60 h^{-1} for *trans*-4-decene and methyl oleate, respectively) than catalyst 2 ($TOF=2$ h^{-1} for *cis*-2-pentene).[4] To the best of our knowledge, no other examples of self-metathesis using an immobilised homogeneous catalyst are reported in the literature.

Catalyst 4 was also tested in the RCM of diethyl diallylmalonate and exhibited 94% conversion in 2 h, which is better than for example the supported homogeneous catalyst of Dowden and Savovic (43% in 1.5 h).[5g] It is also of importance that when using 1 mol% of 4, nearly the same conversion was obtained as in the case of 5 mol% of 4 (see Table 1).

A major advantage of catalyst immobilisation is that the metathesis products are, in an ideal case, free from polluting and often difficult-to-remove ruthenium residues. Using our immobilised catalyst 4 for the metathesis of diethyl diallylmalonate (100 equiv.), we could reduce the ruthenium level in the product to 0.80 ± 0.04 µg/mg of product. In the case of *trans*-4-decene (550 equiv.) the product contamination with ruthenium was 0.156 ± 0.008 µg/mg of the product mixture after just a simple catalyst filtration. These values are comparable, or lower, than values obtained in the purification procedures reported by Maynard and Grubbs,[11] using a water-soluble coordinating phosphine, and by Paquette and co-workers[12] employing lead acetate to remove the ruthenium residues from the metathesis products. Barrett and co-workers[5b] reported similar contamination levels for their 'boomerang' sys-
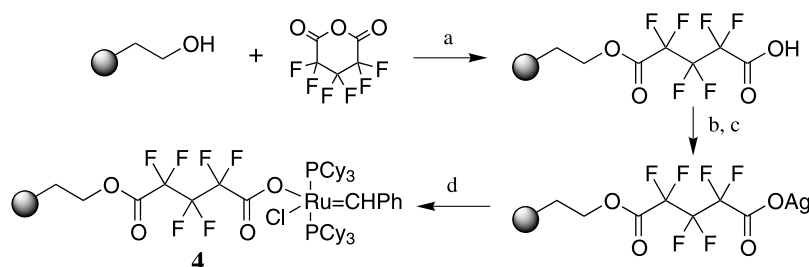
Scheme 1. Synthesis of 4: (a) THF, 1.5 h; (b) (SiMe$_3$)$_2$NNa, THF, 2 h; (c) AgNO$_3$, THF/EtOH, 12 h; (d) 0.5 equiv. 1, THF/Hex, 15 h.

Table 1. Activity of catalyst 4 for the metathesis of selected substrates[a]

Substrate	Time (h)	Conversion (%)	Ru content (µg/mg product)
trans-4-Decene[b]	4	39	0.156 ± 0.008
Methyl oleate[b]	4	45	n.d.
Diethyl diallylmalonate[c]	2	94	3.76 ± 0.12
Diethyl diallylmalonate[d]	2	93	0.80 ± 0.04

[a] In CH$_2$Cl$_2$ at rt.
[b] Ratio alkene:4 = 550:1.
[c] 5 mol% of 4.
[d] 1 mol% of 4.

tem (ca. 0.50 µg/mg product when no chromatography was performed).

We also assessed the recyclability of catalyst **4** in the RCM of diethyl diallylmalonate. The diene was allowed to undergo metathesis for 2 h, then the solution was drained off, the resin washed and a new batch of a dichloromethane solution of the substrate was added. Table 2 shows the activity of catalyst **4** upon recycling.

We observed a substantial decrease in activity after the first cycle, which can be attributed to catalyst leaching (up to 19% ruthenium loss from the resin, as measured by ICP-AES). In the following cycles the catalyst activity dropped down more slowly, and in the 6th cycle 23% conversion was reached after 2 h. The leaching of ruthenium in these cycles was less than 3% of the initial Ru loading per cycle. Product contamination by ruthenium residues was then very low: less than 0.58 ± 0.02 and 0.124 ± 0.006 µg/mg of product for 5 mol% and 1 mol% of catalyst **4**, respectively. The recycled catalyst drove the reaction to completion after prolonged reaction time (24 h), demonstrating its long-term stability. The shelf life of catalyst **4** was also good. It was stored for more than six months under a protective atmosphere of nitrogen and did not show any sign of a decrease in catalytic activity.

In conclusion, we have reported a new simple approach for permanent immobilisation of ruthenium carbene complexes on a polymeric support using carboxylate ligands as linking groups. The supported catalyst performed well in self-metathesis of internal alkenes and in RCM. It was easily separated from the metathesis products and reused without the addition of any stabilising agents, although some leaching and deterioration of the catalyst was observed. We are currently working on the improvement of the catalyst performance in order to prevent leaching of the ruthenium from the solid support. We are also expanding the scope of this procedure to other homogeneous ruthenium metathesis catalysts.

Table 2. Recycling of catalyst **4** in RCM of diethyl diallylmalonate[a]

Cycle	1	2	3	4	5	6
Conversion (%)	94	64	41	37	30	23

[a] All runs using 5 mol% of **4** in CH_2Cl_2 for 2 h at rt.

References

1. For reviews, see: (a) Ivin, K. J.; Mol, J. C. *Olefin Metathesis and Metathesis Polymerization*; Academic Press: San Diego, 1997; (b) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413; (c) *Alkene Metathesis in Organic Synthesis*; Fürstner, A., Ed. Topics in Organomet. Chem.; 1998, Vol. 1, pp. 1–231; (d) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012.
2. (a) Schwab, P.; France, M. B.; Ziller, J. W.; Grubbs, R. H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2039; (b) Schwab, P.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1996**, *118*, 100.
3. (a) Huang, J.; Stevens, E. D.; Nolan, S. P.; Petersen, J. L. *J. Am. Chem. Soc.* **1999**, *121*, 2674; (b) Weskamp, T.; Kohl, F. J.; Hieringer, W.; Gleich, D.; Herrmann, W. A. *Angew. Chem., Int. Ed.* **1999**, *38*, 2416; (c) Scholl, M.; Trnka, T. M.; Morgan, J. P.; Grubbs, R. H. *Tetrahedron Lett.* **1999**, *40*, 2247; (d) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953; (e) Fürstner, A.; Thiel, O. R.; Ackermann, L.; Schanz, H.-J.; Nolan, S. P. *J. Org. Chem.* **2000**, *65*, 2204.
4. Nguyen, S. T.; Grubbs, R. H. *J. Organomet. Chem.* **1995**, *497*, 195.
5. (a) Barrett, A. G. M.; Cramp, S. M.; Roberts, R. S. *Org. Lett.* **1999**, *1*, 1083; (b) Ahmed, M.; Barrett, A. G. M.; Braddock, D. C.; Cramp, S. M.; Procopiou, P. A. *Tetrahedron Lett.* **1999**, *40*, 8657; (c) Ahmed, M.; Arnauld, T.; Barrett, A. G. M.; Braddock, D. C.; Procopiou, P. A. *Synlett* **2000**, 1007; (d) Yao, Q. *Angew. Chem., Int. Ed.* **2000**, *39*, 3896; (e) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168; (f) Jafarpour, L.; Nolan, S. P. *Org. Lett.* **2000**, *2*, 4075; (g) Dowden, J.; Savovic, J. *Chem. Commun.* **2001**, 37.
6. Schürer, S. C.; Gessler, S.; Buschmann, N.; Blechert, S. *Angew. Chem., Int. Ed.* **2000**, *39*, 3898.
7. (a) Buchowicz, W.; Mol, J. C.; Lutz, M.; Spek, A. L. *J. Organomet. Chem.* **1999**, *588*, 205; (b) Buchowicz, W.; Ingold, F.; Mol, J. C.; Lutz, M.; Spek, A. L. *Chem. Eur. J.* **2001**, *7*, 2842.
8. From elemental analyses of the resins obtained in each step of the procedure we conclude that the esterification was practically quantitative. The rather low ruthenium loading resulted mainly from considerable cleavage of the ester link upon treatment with sodium bis(trimethylsilyl)amide.
9. At this time assignment of these two peaks is not certain. We tentatively assign the broad peak to an Ru carbene linked to the support by two carboxylic groups and the narrow one to an Ru carbene linked by one carboxylic group. Alternatively, it could be that these peaks correspond to complexes with unidentate and bidentate coordination modes of the carboxylic group to the ruthenium centre.
10. Buchowicz, W.; Mol, J. C. *J. Mol. Catal. A: Chem.* **1999**, *148*, 97.
11. Maynard, H. D.; Grubbs, R. H. *Tetrahedron Lett.* **1999**, *40*, 4137.
12. Paquette, L. A.; Schloss, J. D.; Efremov, I.; Fabris, F.; Gallou, F.; Méndez-Andino, J.; Yang, J. *Org. Lett.* **2000**, *2*, 1259.