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Silica Immobilized Second Generation Hoveyda-Grubbs: A Convenient, Recyclable and Storageable Heterogeneous Solid Catalyst

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Abstract: The second generation Hoveyda–Grubbs metathesis catalyst was successfully immobilized on silica in pellet and powder form following a practical and fast synthesis procedure. The activity of the solid system is truly heterogeneous, efficient in various metathesis reaction types and stable for at least 4000 TON. Ru contamination of the products was very low (ppb levels). The successful use of the robust system has been demonstrated in a continuous reactor set-up.

Keywords: heterogeneous catalysis; immobilization; metathesis; N-heterocyclic carbenes; ring-opening polymerization; ruthenium

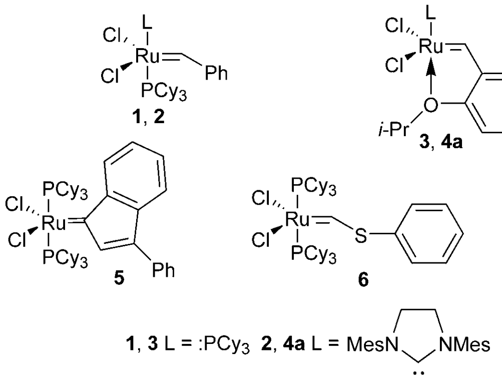


Figure 1. Commercial ruthenium-metathesis catalysts **1**–**6**; Cy = cyclohexyl and Mes = 2,4,6-trimethylphenyl.

Olefin metathesis has since its discovery left a mark on organic synthesis, polymer chemistry and catalyst development, making metathesis a key reaction of the last decade. The discovery of Grubbs' ruthenium catalyst **1** inspired the development of a new family of metathesis catalysts (**2**–**6**, Figure 1) with high activity and remarkable tolerance towards functional groups, air and moisture.[1,2] Taking into account Ru cost and high end-product purity, straightforward catalyst separation, recyclability and minimal complex leaching become decisive criteria for widespread applications of metathesis in organic synthesis.

Various immobilization strategies for metathesis catalysts have been recently reviewed.[3] Anchoring of stable ruthenium alkylidenes **3** and **4a** *via* phosphine or halogen exchange, *via* the N-heterocyclic carbene ligand, or *via* alkylidene exchange (boomerang-type catalysts) has been performed most frequently on insoluble organic polymers and silica supports.[4] Whereas immobilization of homogeneous catalysts combines advantages of homogeneous and heterogeneous catalysis,[5] most reports on supported metathesis catalysts describe a loss of activity as a result of immobilization. Moreover, many catalysts barely survive a few recycles, while only a handful of systems guarantee fully recyclable activity. Unfortunately, despite ingenious organic syntheses, their preparation often consists of multiple steps or requires additional reagents and modified Ru complexes, consequently making them less accessible for general use. A practical, inexpensive immobilization strategy for recyclable and reusable catalysts, compatible with organic and combinatorial chemistry and with large-scale potential remains thus challenging.

In our search for immobilizing metathesis catalysts, we were attracted by the recovery experiments of Hoveyda et al.[6a] and later Fogg et al.[6b] They recycled catalyst **4a** and related aryl oxide catalysts simply by silica gel column chromatography. While a chromatographic recovery is time-, solvent- and material-consuming, sometimes with metal losses of 5% Ru per cycle and more,[3c] we envisioned that the silica-bound catalyst could potentially be used as a heterogeneous catalyst by playing with solvent polarity.

However, it is not clear how the Ru catalyst was anchored to the silica, whether the silica supported catalyst would retain its activity, and even if so, whether its activity is truly heterogeneous.

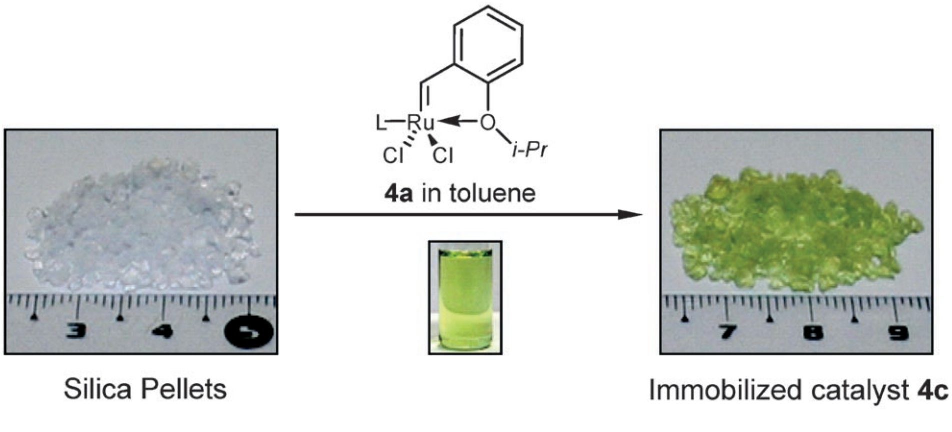
The silica immobilized metathesis catalyst in this report is prepared in an easy and straightforward manner, taking advantage of the high affinity of silica gel (Fluka) for the stable catalyst **4a**. In a typical example, 0.2 g silica gel[8] is contacted with **4a** (5 mL, 0.5 mM in toluene), and the suspension is stirred at 293 K for two hours to acquire the bright greenish powder **4b** (0.1 wt% Ru) after a single wash (hexane) and dry step. Higher loadings (up to 0.06 μmol m^{-2} or 0.6 wt% Ru) are easily achieved upon increasing the initial Ru complex concentration in the preparation solution and by using high surface silica material of the MCM-41 and SBA-15 types. For potential combinatorial usage, silica pellets (WR Grace) instead of silica powders were loaded identically with **4a** resulting in catalyst **4c** (Scheme 1). We found that the silica source has no important impact on the catalyst performance, as long as it is free of impurities such as Al or Ca. The use of impure silica results in inactive brown solids.[9]

As a first test, cyclooctene **7** was polymerized using 0.5 mol% of catalyst **4b** (0.05 wt% Ru loading) at 293 K in undistilled, reagent-grade hexane with quantitative conversion within 3 h (Table 1, entry 1). As expected, **7** is converted much faster upon using higher Ru loadings (0.1 and 0.2 wt% Ru, entries 2 and 3). Interestingly, catalyst pellets **4c** show a comparable activity with the powder, despite shaking the reaction instead of stirring to avoid mechanical damage (entry 4). As expected, higher ROMP activities were measured with a higher concentration in **7** (entry 6). Catalysts **4b** and **4c** were stored for days at 293 K in a glass container (not shown) or for several months at 248 K without loss of activity (entry 7).

The activity of catalyst **4c** has been evaluated in various metathesis reactions. Next to **7**, other cyclic olefins (**8** and **9**) were polymerized with success (entries 8 and 9). The potential of **4c** was also tested for self-metathesis (entry 10–13). Remarkably, complete conversion of 1-octene **10** is obtained within short time using a low Ru concentration (0.18 mol%). Even the less reactive ether functionalized styrenes **11** and **12** are converted selectively and almost quantitatively into the corresponding stilbenes **17** and **18** in reflux conditions. As expected from the bulky aromatic moiety, *trans* isomers are mainly formed. The catalyst **4c** is also active in the self-metathesis of **13** to the 1,20-diester **19**, a potential monomer for polyester and polyamide synthesis. Finally, catalyst pellets **4c** also proved to be active in the ring-closing metathesis of silanes (**14** and **15**) (entries 14 and 15), albeit with incomplete product yield for the bulky diphenylsilane **21**.

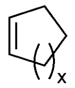
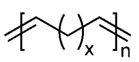
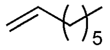
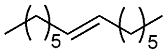
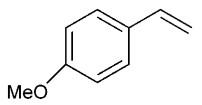
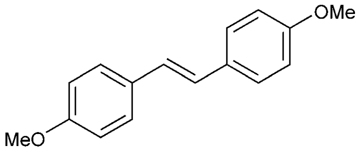
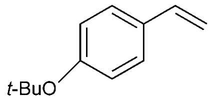
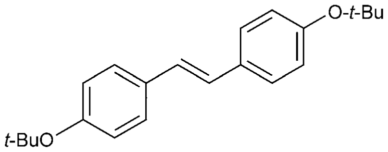
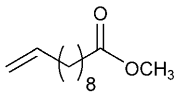
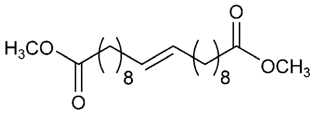
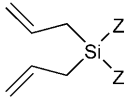
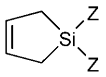
While the powdered silica-based catalyst **4b** has to be separated from the products by filtration, work-up with pellets **4c** simply involves decantation of the product mixture. Its ease of handling and isolation offers the pellet-based catalyst **4c** potential use in fast screening experiments and combinatorial applications. The recovered solid catalysts appear remarkably stable. Even with filtration in air and usage of undistilled reagent grade solvent in a batch recycling experiment, no diminution of activity for ROMP of **7** (conditions of entry 4; stable initial TOF of 220 h^{-1}) was observed after four cycles, each to full conversion, corresponding to 400 TONs (see Supporting Information, Table SI1).

To exclude any contribution of homogeneous activity, we employed a more decisive experiment, the so-called split test. A standard ROMP reaction with **7** (conditions of Table 1, entry 4) was set up, and after 50% consumption of **7**, 10 vol% of supernatant was transferred into another reactor. Both reactions were continued under identical conditions, and sampled after 1 hour. As derived from Figure 2, ROMP in the presence of **4c** went to completion, while the removed



Scheme 1. Schematic of the preparation of catalyst pellets **4c**.

Table 1. Various metathesis reactions (ROMP, CM and RCM) utilizing immobilized catalysts **4b** and **4c**.[7]

No.	Substrate [M]	Product[c]	Ru (mol%)	*t* [min] (*T* [K])	Yield [%] (TOF [h^{-1}])[d]
					
	7	x = 4			
1[a]	[0.05]		0.5	180 (293)	98 (170)
2[a]	[0.05]		1	80 (293)	95 (218)
3[a]	[0.05]		1.5	50 (293)	97 (240)
4	[0.05]		1	80 (293)	98 (222)
5[b]	[0.05]		1.1	120 (293)	98 (390)
6	[0.2]		0.22	25 (293)	98 (3610)
7	[0.05]		1	80 (293)	97 (220)
8	**8** [0.05]	x = 8	1.5	180 (293)	97 (30)
9	**9** [0.05]	x = 3	1.5	300 (293)	96 (27)
					
10	**10** [0.3]	**16**	0.18	240 (293)	95 (913)
					
11[e]	**11** [0.15]	**17**	3	300 (333)	90 (36)
					
12[e]	**12** [0.15]	**18**	3	300 (333)	67 (21)
					
13[e]	**13** [0.05]	**19**	1	300 (333)	90 (190)
					
14	**14** [0.05]	**20** (Z = Me)	1	240 (318)	80 (106)
15	**15** [0.05]	**21** (Z = Ph)	2	600 (318)	44 (6)

[a] Catalyst **4b**.
[b] Silica pre-dried at 700 °C.
[c] Determined by GC-MS and ^{1}H NMR.
[d] After 10 min.
[e] Isolated yields (89% for entry 11, 65% for entry 12, 85% for entry 13)

supernatant was free of activity. These data nicely illustrate a true heterogeneous activity of immobilized **4a**, when carried out in hexane. As a comparative example, when an identical test was carried out in diethyl ether (see Supporting Information, Figure SI2), active Ru species were leached in the solution. Use of non-polar solvents is thus recommended to prevent Ru leaching. While Ru leaching free metathesis of functionalized substrates such as **11, 12** and **13** is possible, the use of highly polar substrates such as alcohols and acids should obviously be avoided to assure true heterogeneous metathesis. All reactions summarized in Table 1 have passed successfully the aforementioned leaching split test.

To explore the stability limits of **4c**, we performed long-run reactions by continuously feeding a cyclooctene solution over a fixed bed. Again, no precautions were undertaken to avoid traces of air or to purify the chemicals. Strikingly, continuous experiments appear rarely in Ru-based metathesis literature to evaluate the robustness of the heterogeneous catalyst. In one example, a more pronounced catalyst deactiva-

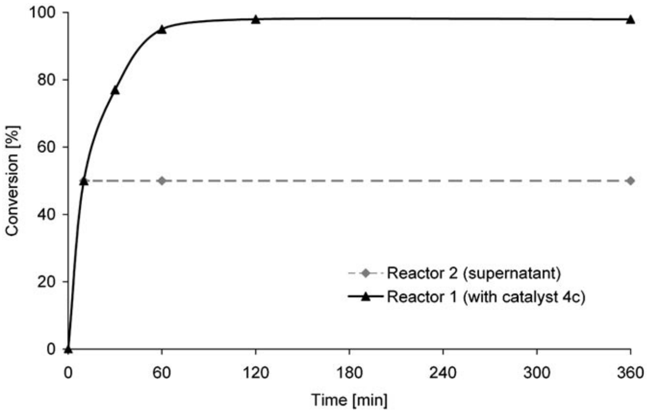


Figure 2. Example of split-test for entry 4, Table 1.

tion of **4a** and metal leaching was found compared to the corresponding batch experiments.[4e] Yet, stable catalytic performance under continuous flow could offer a great leap forward to metathesis applications. The data of our continuous experiments are summarized in Figure 3. In one example (▲), **7** (0.05 M in hexane), dosed at 50 mL $gcat^{-1}$ h^{-1}, was fully converted at a TOF of 90–100 h^{-1} during the first ten hours. When more concentrated **7** (0.2 M) was fed at 150 mL $gcat^{-1}$ h^{-1}, more than 4000 TONs were obtained (■). To the best of our knowledge, this is one of the highest numbers reported for immobilized **4a** for metathesis carried out in unprotected and non-purified circumstances.[3] Along with the activity, metal (complex) leaching was carefully monitored with ICP during the course of the continuous reaction. For collected samples of the continuous experiment, the Ru content was below the detection limit of 7 ppb (see Supporting Information). Interestingly, the Ru contamination is substantially lower than many reported values, typically around 10 ppm and more.[3]

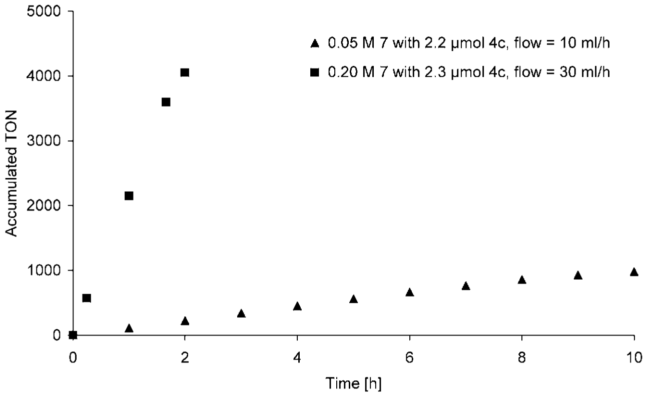


Figure 3. Continuous flow reactions of cyclooctene **7** with catalyst **4c**.

Moreover, when a bed of pure white silica was placed behind the catalyst bed in the continuous reaction set-up, no coloration of this silica loading was observed. As no Ru displacement occurs along the catalyst bed and no detectable Ru is found in the end product, the active Ru species stay firmly anchored to the silica. To have an idea of the interaction of the Ru complex with the silica support, we carried out FT-IR and ^{29}Si MAS NMR. As there is a clear decrease of the isolated O–H vibration stretch at 3745 cm^{-1} (see Supporting Information, Figure SI5) and of the Q3 and Q2 signals at −101 and −93 ppm (Supporting Information, Figure SI6) upon contacting the silica with the Ru complex **4a**, we propose a direct chemical interaction of the Ru center with the silanols of the surface instead of a weak physisorption.

We conclude that the second generation Hoveyda–Grubbs catalyst **4a** is successfully immobilized on commercial silica in pellet and powder form according to a practical one-step procedure. The activity is truly heterogeneous, efficient in various metathesis reaction types and stable for up to at least 4000 TON. The successful use of the robust system in a continuous reactor has been demonstrated. While the anchoring mechanism is under further investigation, we propose a direct attachment of Ru to the surface silanols *via* ligand exchange.

Experimental Section

All chemicals were commercially available and used as received.

Typical Procedure for Metathesis Reaction

Batch reactions: The respective substrate, in 5 mL undistilled reagent-grade hexane, was added to a small reactor vessel containing 0.2 g of catalyst **4b** or **4c**. Reactions with catalyst **4b** were stirred magnetically at 1000 rpm, while those using catalyst **4c** were shaken. Reactions were conducted at room temperature, unless stated otherwise, and sampled at regular time intervals. The crude mixture was analyzed with GC and GC-MS using toluene as the internal standard. When ethylene was formed during reaction, an argon balloon was used to avoid major pressure build up in the reactor.

Continuous reaction: A solution of hexane containing the substrate was fed continuously with a syringe pump over a catalyst bed (0.2 g catalyst **4c** pellets in a quartz tube), which was placed between quartz wool. A picture of the reactor set-up is presented in the Supporting Information. The outlet of the reactor was sampled at regular time intervals. The crude mixture was analyzed with GC and GC-MS using toluene as internal standard.

Typical Procedure for Split Test

The reaction has been carried out according to the aforementioned standard procedure. Here, after ±50% consumption of substrate, 10 vol% supernatant (without solid catalyst) was transferred into another reactor. Removal of the catalyst has been carried out at the corresponding reaction temperature in order to avoid retrapping of the catalyst. Both reactions were continued under identical conditions, and both sampled at various times. In order to prove the heterogeneous nature of the catalytic reaction, all reactions in Table 1 were subjected to this heterogeneity test.

Supporting Information

Experimental details of the batch and continuous experiments, split and Ru leaching tests and characterization data are given in the Supporting Information.

Acknowledgements

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References

[1] R. H. Grubbs, *Handbook of Metathesis*, Vol. 1, Wiley-VCH, Weinheim, **2003**, pp 61–67.

[2] For selected reviews: a) R. H. Grubbs, S. Chang, *Tetrahedron* **1998**, 54, 4413–4450; b) T. M. Trnka, R. H. Grubbs, *Acc. Chem. Res.* **2001**, 34, 18–29; c) R. R. Schrock, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2003**, 42, 4592–4633.

[3] For selected reviews: a) C. Copéret, J.-M. Basset, *Adv. Synth. Catal.* **2007**, 349, 78–92; b) A. H. Hoveyda, D. G. Gillingham, J. J. Van Veldhuizen, O. Kataoka, S. B. Garber, J. S. Kingsbury, J. P. A. Harrity, *Org. Biomol. Chem.* **2004**, 2, 8–23; c) H. Clavier, K. Grela, A. Kirschning, M. Mauduit, S. P. Nolan, *Angew. Chem. Int. Ed.* **2007**, 46, 6786–6801.

[4] a) Q. Yao, Y. Zhang, *Angew. Chem. Int. Ed.* **2003**, 42, 3395–3398; b) S. T. Nguyen, R. H. Grubbs, *J. Organomet. Chem.* **1995**, 497, 195–200; c) X. Elias, R. Pleixats, M. W. Chi Man, J. J. E. Moreau, *Adv. Synth. Catal.* **2006**, 348, 751–762; d) L. Li, J.-L. Shi, *Adv. Synth. Catal.* **2005**, 347, 1745–1749; e) A. Michrowska, K. Mennecke, U. Kunz, A. Kirschning, K. Grela, *J. Am. Chem. Soc.* **2006**, 128, 13261–13267; f) J. O. Krause, O. Nuyken, K. Wurst, M. R. Buchmeiser, *Chem. Eur. J.* **2004**, 10, 777–784; g) F. Michalek, W. Bannwarth, *Helv. Chim. Acta* **2006**, 89, 1030–1037; h) T. S. Halbach, S. Mix, D. Fischer, S. Maechling, J. O. Krause, C. Sievers, S. Blechert, O. Nuyken, M. R. Buchmeiser, *J. Org. Chem.* **2005**, 70, 4687–4694; i) J. Lim, S. S. Lee, S. N. Riduan, J. Y. Yinga, *Adv. Synth. Catal.* **2007**, 349, 1066–1076; j) X. Elias, R. Pleixats, M. W. C. Man, J. J. E. Moreau, *Adv. Synth. Catal.* **2006**, 348, 751; k) F. Michalek, D. Mädge, J. Rühe, W. Bannwarth, *J. Organomet. Chem.* **2006**, 691, 5172.

[5] D. E. De Vos, M. Dams, B. F. Sels, P. A. Jacobs, *Chem. Rev.* **2002**, 102, 3615–3640.

[6] a) J. S. Kingsbury, J. P. A. Harrity, P. J. Bonitatebus, A. H. Hoveyda, *J. Am. Chem. Soc.* **1999**, 121, 791–799; b) J. C. Conrad, H. H. Parnas, J. L. Snelgrove, D. E. Fogg, *J. Am. Chem. Soc.* **2005**, 127, 11882–11883.

[7] Active metal leaching and thus contribution of homogeneous catalysis is excluded for all entries, based on the *split-test*.

[8] The silica support is pre-dried in an oven overnight at 120 °C before contacting with **4** in toluene, except in entry 5, where it was pre-dried at 700 °C under vacuum.

[9] Immobilization attempts with silica-alumina Siral 1/Siral 40 (Sasol) and Redco $CaO{\cdot}SiO_2{\cdot}6H_2O$ resulted in inactive brown powders.