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A PS-DES immobilized ruthenium carbene: a robust and easily recyclable catalyst for olefin metathesis

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Abstract—The butyldiethylsilyl polystyrene (PS-DES) supported ruthenium carbene **7** is a robust, practical and easily recyclable catalyst for olefin metathesis of substituted olefins. © 2002 Published by Elsevier Science Ltd.

During recent years, olefin metathesis has gained a position of increasing significance. The development of well-accessible metathesis catalysts combining high activity with an excellent tolerance to a variety of functional groups has been key to the widespread application of olefin metathesis in organic synthesis and polymer chemistry (Fig. 1). The most notable examples of such catalysts are ruthenium carbenes with bulky electron-rich phosphine (**1a**) or heterocyclic carbene ligands (**1b**–**c**).[1] Despite the major advantages offered by this group of catalysts, they share some disadvantages.

Since metathesis reactions are expected to be used in pharmaceutical processes, the most undesirable feature of these complexes is that they decompose to form highly colored ruthenium byproducts, which are difficult to remove from the reaction products.[2] From the point of view of the chemical-economy recyclability is another important attribute. In this respect, immobilized or heterogeneous catalysts offer inherent operational and economic advantages over their homogeneous counterparts.[3]

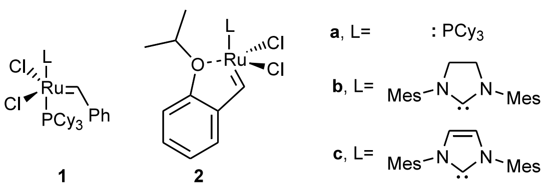

Figure 1. Ruthenium olefin metathesis catalysts.

Several attempts have been made to immobilize Grubbs-type carbenes **1a**–**c** on solid supports. Endeavors to prepare catalysts *permanently* immobilized on solid supports has met with only limited success and the resulting polymer-supported carbenes were found to be less reactive than their homogeneous analogues.[4] Moreover, their recovery and reuse led to significant losses in activity.

Barrett[5a] reported a 'boomerang' catalyst, in which the carbene precatalyst becomes soluble during the course of the reaction and can be recaptured by the polymer once the substrate in solution has been consumed.[5] Recently Hoveyda established **2a**–**b** as remarkably robust complexes promoting olefin metathesis by a similar 'release/return' mechanism.[6] Carbenes **2a**–**b** were subsequently attached to a dendrimer,[6b] glass,[7a] a soluble polyethylene glycol resin[7b] and to cross-linked insoluble polystyrene polymers[7c,d] as well as hydrophilic PEGA–NH_2 resin.[7e]

Although these systems give very promising results, this area is far from being fully explored. The need for further developments led us to try another approach to efficiently immobilize a metathesis catalyst. From numerous resins known, we selected butyldiethylsilyl polystyrene (PS-DES, **3**),[8] due to its advantages, such as availability, stability, high loading capacity and good swelling characteristics in solvents commonly used for metathesis. We envisaged that the butylsilyl fragment could be used for attachment of the phenol–ether part of **2b** to a solid support. The C–Si bond is perfectly stable under metathesis conditions, but is cleaved quantitatively under the action of fluoride.

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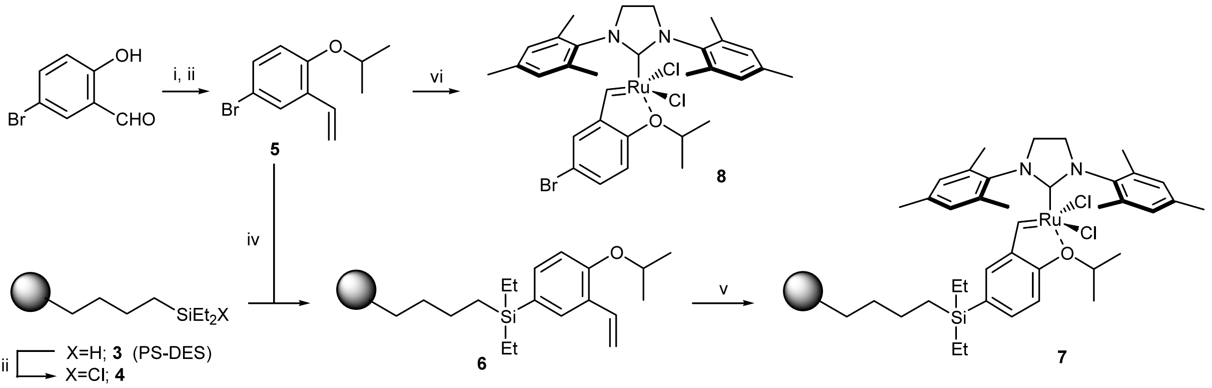


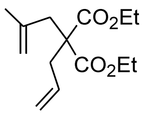
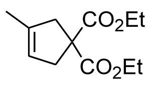
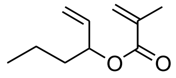
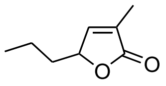
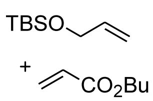
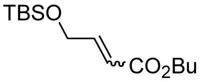
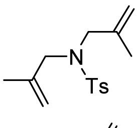
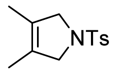
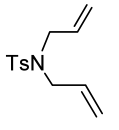
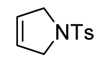
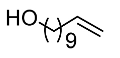
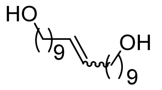
Scheme 1. *Reagents and conditions*: (i) NaH, *i*PrI, DMF, rt, 24 h; (ii) $Ph_3P{=}CH_2$, THF, −78°C to rt, 1 h, 69% over two steps; (iii) 1,3-dichloro-5,5-dimethylhydantoin, CH_2Cl_2, rt, 5 h; (iv) **5**, *t*BuLi, Et_2O, −78°C then **4**, THF, −78°C to rt, 24 h; (v) **1b**, CH_2Cl_2, rt, 24 h, four times; (vi) **1b** **5**, CuCl, CH_2Cl_2, 45°C, 1 h, 93%.

Quick and reliable determination of ruthenium loadings on insoluble supports is sometimes a difficult task.[9] Various techniques have been used for this purpose, and in many cases ruthenium loadings were calculated only from indirect measurements, such as elemental analysis of other elements, mass increase which accompanies functionalization of the polymer surface, etc.

Our approach allows a more direct and easy method of ruthenium loading determination based on the cleavage of the carbene complex from the PS-DES resin with TBAF and further spectroscopic Ru measurement in solution.

The use of the longer butylsilyl linker increases the distance between the metal centre and the polymer and,

Table 1. Olefin metathesis using **7**

Entry	Substrate **9**	Product **10**	Conversion, time[a]	
			Supported Catalyst **7**	Reference Catalyst
a			41%, 3h quant., 8h[b]	**8**: 90%, 3h quant., 8h[b]
b			78%, 16h[b]	**8**: 86%, 16h[b] **1b**: 98%, 2h[b]
c			quant., 8h[b,c]	**8**: quant., 8h[b,c] **1b**: quant., 8h[c]
d			0%, 16h	**8**: 45%, 16h **1c**: 95%, 5h[d]
e			95%, 7h[e]	
f			quant., 4h	**8**: quant., 4h

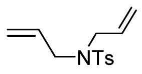
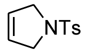
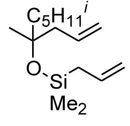
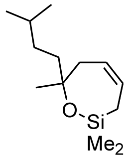
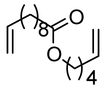
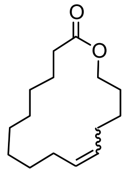
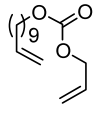
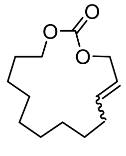
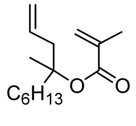
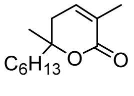
[a] GC yield. General conditions: catalyst (5.0 mol%), c_{diene} =0.02M, CH_2Cl_2, 45 °C. [b] with 2.5 mol% of catalyst. [c] Reaction was performed in the presence of 2 eq. of *n*-butyl acrylate. [d] Ref. 10. [e] Performed at rt.

therefore should result in an improvement in catalyst reactivity and recyclability. The easy three steps method of preparation renders additional advantages to the PS-DES system.

Preparation. The PS-DES resin **3** was first activated to form the silyl chloride **4** by treatment with 1,3-dichloro-5,5-dimethylhydantoin.[8b] The reactive silyl chloride derivative was then used immediately for coupling with an organolithium, prepared from 2-isopropoxy-5-bromostyrene **5** and 2 equiv. of *tert*-butyllithium. The support-bound ruthenium complex **7** was then prepared from **6** by washing of the resin with four successive portions of 25 mol% of **1b** (Scheme 1). The catalyst was obtained after filtration as deep-green beads showing ruthenium loading of 0.22–0.35 mmol/g (as determined from the inductively coupled plasma mass spectrometry (ICP-MS) analysis of Ru). Samples of resin **7** did not lose activity after three months of storage in air at room temperature.[11]

Activity study. PS-DES supported complex **7** (2.5–5.0 mol%) was then tested for activity using representative substrates for ring-closing metathesis leading to the formation of different carbo- and heterocycles (Table 1).[12] It is notable, that the rates of reaction were somewhat slower than those obtained using the soluble analogue **8**, e.g. when the diene **9a** was treated with 2.5 mol% of catalyst **7** for 3 h at reflux, the reaction was only 41% complete, compared to the 90% conversion when 2.5 mol% of **8** was used. However, after an additional 5 h the diene **9a** was converted cleanly by supported catalyst **7** to the cyclic olefin **10a** in greater than 99% conversion (Table 1, entry a).

Table 2. Recyclability study using **7**

Entry	Substrate **9**	Product **10**	Cycle	Conversion time [a]
e			1	95%, 7h [b]
g			2	quant., 5h
h			3	quant., 5h
i			4	79%, 4h
j			5	30%, 6h 95%, 24h

[a] GC yield. General conditions: catalyst (5.0 mol%), c_{diene}=0.02M, CH_2Cl_2, 45 °C. [b] Performed at rt.

Ring-closing metathesis of other challenging substrates goes cleanly, with typically high conversion, as determined by GC–MS and ^1H NMR analysis, leading to α,β-unsaturated lactone (entry *b*) and products containing a trisubstituted double bond (entries *a*, *b*); however, the tetrasubstituted olefin was not formed (entry *d*). We have also demonstrated the ability of **7** to perform cross-metathesis (CM) of *n*-butyl acrylate (entry *c*) and a substrate having an unprotected hydroxy function (entry *f*). The catalyst **7** can be readily recovered by simple filtration and washing with dichloromethane. The resulting unpurified products were pure according to GC–MS and ^1H NMR analyses.

Recyclability study. As we demonstrated with model substrate **9e**, the same batch of PS-DES catalyst can be used for up to 5–6 cycles of metathesis and gave similarly high conversions with only a slight loss of activity. It was also possible to perform metathesis using the PS-DES supported carbene **7** in reagent-grade non-degassed dichloromethane under air, but in this case the resin cannot be recycled more than three times without almost complete loss of activity.

More importantly, the same batch of a recycled catalyst can be used sequentially in different reactions (Table 2), as the catalyst from the metathesis of **9e** was subsequently used for the metathesis of the silicon-tethered diene **9g**.[13] The same batch of recovered catalyst was then used for the formation of macrocyclic musk-odored ester **10h** (cycle 3) and carbonate **10i** (cycle 4). Finally, in cycle 5 the substrate[13] **9j** was converted to the α,β-unsaturated lactone **10j** in 95% conversion with recycled resin **7**. In this experiment we did not observe contamination from a previous reaction substrate/product, as the crude reaction mixtures consist of only the substrate and cyclized product **10g–j** (GC–MS analyses). We have additionally checked the ruthenium content in selected crude products and found only low levels of ruthenium contamination (≤0.1 wt%, ICP–MS analysis of Ru).[12]

In summary, we have reported a robust, stable and easy to (re)use supported catalyst for olefin metathesis, which can be easily prepared in three steps from commercial butyldiethylsilyl polystyrene. The possibility of instant ruthenium determination renders additional advantages of this PS-DES system. Detailed studies regarding preparation and recycling of other PS-DES bound ruthenium carbenes are in progress.

Acknowledgements

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References

1. Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012–3043.
2. For approaches where ruthenium impurities are removed by addition of various scavengers, see: (a) Maynard, H. D.; Grubbs, R. H. *Tetrahedron Lett.* **2000**, *40*, 4137–4140; (b) Paquette, L. A.; Schloss, J. D.; Efremov, I.; Fabris, F.; Gallou, F.; Mendez-Andino, J. Yang, J. *Org. Lett.* **2000**, *2*, 1259–1261; (c) Ahn, Y. M.; Yang, K.; Georg, G. I. *Org. Lett.* **2001**, *3*, 1411–1413.
3. Yet another 'green-chemistry' approach is the use of supercritical CO_2 as the reaction medium. The ruthenium carbenes **1a** and **1c** act as *heterogenous* catalysts in this environmentally benign medium: (a) Fürstner, A.; Koch, D.; Langemann, K.; Leitner, W.; Six, C. *Angew. Chem., Int. Ed.* **1997**, *36*, 2466–2469; (b) Fürstner, A.; Ackermann, L.; Beck, K.; Hori, H.; Koch, D.; Langemann, K.; Liebl, M.; Six, C.; Leitner W. *J. Am. Chem. Soc.* **2001**, *123*, 9000–9006.
4. (a) Nguyen, S. T.; Grubbs, R. H. *J. Organomet. Chem.* **1995**, 195–200; (b) Schürer, S. C.; Gessler, S.; Buschman, N.; Blechert, S. *Angew. Chem., Int. Ed.* **2000**, *39*, 3898–3901; (c) Melis, K.; De Vois, D.; Jacobs, P.; Verpoort, F. *J. Mol. Catal. A: Chem.* **2001**, *169*, 47–56; (d) Mayr, M.; Mayr, B.; Buchmeiser, M. R. *Angew. Chem., Int. Ed.* **2001**, *40*, 3839–3842.
5. (a) Ahmed, M.; Barrett, A. G. M.; Braddock, D. C.; Cramp, S. M.; Procopiou, P. A. *Tetrahedron Lett.* **1999**, *40*, 8657–8662; (b) Ahmed, M.; Arnauld, T.; Barrett, A. G. M.; Braddock, D. C.; Procopiou, P. A. *Synlett* **2000**, 1007–1009; (c) Jafarpour, L.; Nolan, S. P. *Org. Lett.* **2000**, *2*, 4075–4078.
6. (a) Kingsbury, J. S.; Harrity, J. P. A.; Bonitatebus, P. J.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 791–799; (b) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168–8179.
7. (a) Kingsbury, J. S.; Garber, S. B.; Giftos, J. M.; Gray, B. L.; Okamoto, M. M.; Farrer, R. A.; Fourkas, J. T.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2001**, *40*, 4251–4256; (b) Yao, Q. *Angew. Chem., Int. Ed.* **2000**, *39*, 3896–3898; (c) Dowden, J.; Savovic, J. *Chem. Commun.* **2001**, 37–38; (d) Randl, L.; Buschmann, N.; Connon, S. J.; Blechert, S. *Synlett* **2001**, 1547–1550; (e) Connon, S. J.; Blechert, S. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1873–1876.
8. (a) PS-DES is available from Argonaut Technologies and from Aldrich Chemical Co; (b) For a general reference, see: Hu, Y.; Porco, J. A., Jr.; Labadie, J. W.; Gooding, O. W.; Trost, B. M. *J. Org. Chem.* **1998**, *63*, 4518–4521.
9. For example: cf. footnote 16 in Ref. 7a.
10. Fürstner, A.; Ackermann, L.; Gabor, B.; Goddard, R.; Lehmann, C. W.; Mynott, R.; Stelzer, F.; Thiel, O. R. *Chem. Eur. J.* **2001**, *7*, 3236–3253.
11. *Butyldiethylchlorosilane polystyrene PS-DES-Cl (**4**).* To a 5 mL solid-phase synthesis flask (equipped with a glass-frit) were added PS-DES silane resin (131 mg, 0.21 mmol) and 1,3-dichloro-5,5-dimethylhydantoin (124 mg, 0.63 mmol) in CH_2Cl_2 (2.5 mL). After 5 h, the mixture was filtered and washed with CH_2Cl_2 (4×2 mL) and dry THF (4×2 mL). The resin was used immediately after washing. The chlorination reaction can be monitored by examination of the Si–H stretch (IR: 2100 cm^{-1}).

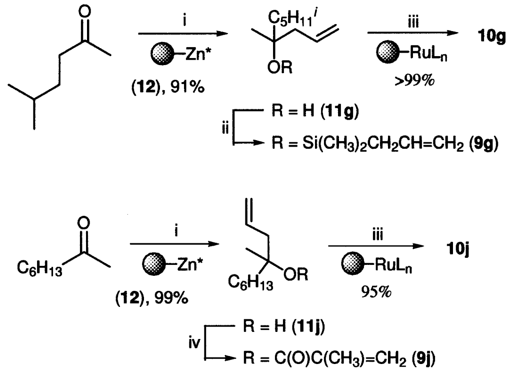
    *Butyldiethyl(4-isopropoxy-3-vinylphenyl)silane polystyrene (**6**).* To a stirred solution of *t*-BuLi (1.0 mL, 1.70 mmol, 1.7 M in pentane) at −78°C was added a solution of **5** (202 mg, 0.84 mmol) in dry Et_2O (5 mL). After stirring for 15 min the clear yellow solution was transferred via syringe to a cooled (−78°C) suspension of **4** (0.21 mmol) in THF (1 mL). The reaction mixture was stirred at −78°C for 3 h, and was then gently agitated at rt for 24 h. The mixture was filtered and washed with THF (4×2 mL), a THF–MeOH 2:1 v/v mixture (2×2 mL) and CH_2Cl_2 (2×2 mL) and dried in vacuo to give **6** as a white solid (169 mg).

    *PS-DES polymer-bound ruthenium complex (**7**).* A 5 mL solid-phase synthesis flask was charged with the resin **6** (169 mg) and a solution of Grubbs' carbene **1b** (0.05 mmol, 0.25 equiv.) in CH_2Cl_2 (2 mL) was added. The flask was gently agitated at rt for 24 h. The resin was then washed with CH_2Cl_2 (1 mL) and the cycle of reaction and washing was continued a further three times. From this point, all manipulations were carried out in air with reagent-grade CH_2Cl_2. The polymer was washed with CH_2Cl_2 until the filtrate was clear (4×1 mL) affording **7** as dark green beads, showing loading of 0.22 mmol Ru/g (ICP–MS analysis). Samples of resin **7** (loadings of 0.22–0.35 mmol/g) did not lose activity after 3 months of storage in air at rt.

    General procedure for ICP–MS determination of Ru. A solution of TBAF (0.5 mL, 1 M in THF) was added to the resin **7** (20 mg). The mixture was stirred at rt for 2 h. The resin was filtered and washed with THF (4×2 mL) and MeOH (2×2 mL). The combined filtrate was analyzed by ICP–MS using standard procedure.
12. *General procedure for metathesis utilizing **7**.* The substrate **9a**–**i** (0.1 mmol) was dissolved in CH_2Cl_2 (5 mL) and added to a solid-phase synthesis flask charged with resin **7** (2.5–5 mol%). The suspension was gently agitated at rt or 45°C. The product **10a**–**j** was obtained as a colorless oil or solid after filtration and concentration. The products were identified by GC–MS comparison with authentic samples and ^1H NMR analysis. Selected data for **10g**: colorless oil, purity $\geq 98\%$ (GC–MS analysis, HP5972A MSD, column HP-5); Ru-content 0.07 wt% (ICP–MS analysis, Perkin–Elmer Elan 6100DRC); R_f 0.20 (*c*-Hexane); ^1H NMR (500 MHz, CD_2Cl_2, ppm): 0.066, 0.069 (2s, 6H), 0.88, 0.89 (2d,

6H, $J = 6.8$ Hz), 1.13 (s, 3H), 1.15–1.28 (m, 2H), 1.41–1.61 (m, 5H), 2.25 (dd, 1H, $J = 8.0$, 14.0 Hz), 2.37 (dd, 1H, $J = 8.0$, 14.0 Hz), 5.57 (dtt, 1H, $J = 8.0$, 7.0, 1.0 Hz), 5.91 (dt, 1H, $J = 7.0$, 10.0 Hz); ^{13}C NMR (125 MHz, CD_2Cl_2, ppm): 0.97, 18.7, 22.8, 22.9, 27.8, 29.0, 33.7, 40.1, 41.4, 53.4, 96.5, 125.9, 129.9; IR (film, cm^{-1}) 3023, 2957, 2935, 2871, 1635, 1465, 1372, 1250, 1066, 1025, 840, 751; MS (EI): 226 (4, $M^{+\bullet}$), 211 (5), 183 (40), 171 (21), 155 (47), 142 (18), 129 (57), 116 (9), 113 (14), 97 (31), 75 (100), 59 (6); HRMS (EI) $C_{13}H_{26}OSi$ 226.1753. Found: 226.1754.

13. Homoallylic alcohols **11g** and **11j** can be conveniently obtained, using poly(ethylene)-supported activated zinc (**12**), which has been developed in our laboratory: Mąkosza, M.; Nieczypor, P.; Grela, K. *Tetrahedron* **1998**, *54*, 10827–10836.



Reagents and conditions: (i) PE-Zn* (**12**), allyl bromide, THF, rt, 2 h; (ii) $ClSi(CH_3)_2CH_2CH{=}CH_2$, imidazole, DMF, rt, 6 h; (iii) **7**, 5 mol.%, CH_2Cl_2, 45 °C, 5–24 h; (iv) methacryoyl chloride, pyridine, 0 °C to rt, 6 h.