Silica-supported catalysts for ring-closing metathesis: effects of linker group and microenvironment on recyclability†

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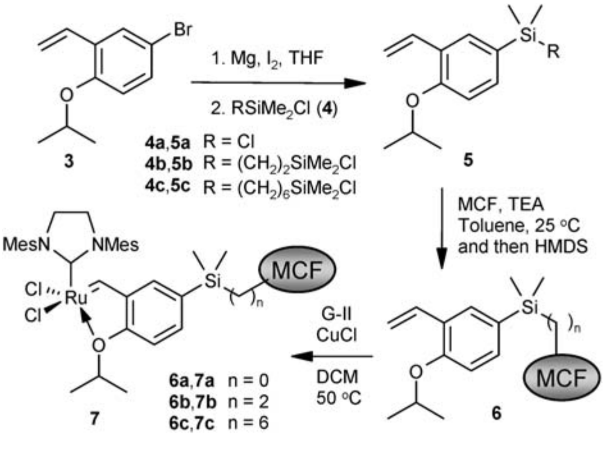
The interesting effects of the linker and microenvironment on the recyclability of well-defined silica-supported catalysts were examined, which demonstrated the excellent activity and reusability for the ring-closing metathesis (RCM) of a number of substrates.

Despite their great potential in ring-closing metathesis (RCM),[1] the well-defined ruthenium catalysts[2] suffer from some drawbacks associated with their high cost and leaching problems.[3] To address these challenges, significant efforts have been devoted towards developing heterogenized catalysts.[4,5] In particular, covalent immobilization of the catalytic species on polymer[6] and silica[7] supports has been examined. Taking advantage of siliceous mesocellular foam (MCF)[8] as a support material,[9] we have developed highly recyclable RCM catalysts by tuning the linker group and microenvironment in the heterogenized system. MCF is a stable mesoporous silica with ultralarge, cell-like pores (24–42 nm) interconnected by windows of 9–22 nm.[8] This novel support material is well-suited for fixing bulky complexes and facilitates substrate diffusion.[10] The linear alkylsilane motif is particularly attractive as a linker group with its robust and orthogonal nature. The known bromide **3**[11] was readily transformed to three types of alkylchlorosilanes **5** with a variable linker length (Scheme 1). The electron-rich aromatic nucleophile, *in situ* generated by the Grignard protocol, proceeded smoothly to form a carbon–silicon bond in the presence of excess alkyldichlorosilanes **4**. Unreacted **4** was thoroughly removed under reduced pressure prior to the immobilization of **5** onto trimethylsilyl (TMS)-precapped spherical MCF microparticles[12] in the presence of triethylamine (TEA). The remaining silanol groups in MCF were further capped by treatment with hexamethyldisilazane (HMDS) under vapor-phase conditions[12] to minimize the undesired interactions between the catalysts and the MCF surface. The overall yields of the immobilized ligands **6** were excellent (>90% in three steps). The Fourier-transform infrared (FTIR) spectrum and the cross-polarization magic angle spinning nuclear magnetic resonance (CP-MAS NMR) ^{13}C and ^{29}Si spectra indicated the formation of well-dispersed Hoveyda-type ligands on the surface of MCF (see ESI†). The green heterogenized catalysts **7** were isolated by smooth ligand exchange in refluxing dichloromethane (DCM) with the aid of Cu(I) chloride,[6a] followed by filtration, washing, and drying. Elemental analysis revealed that the ruthenium loading was *ca.* 0.22 mmol g^{-1} in all derivatives of **7**. ^{13}C CP-MAS NMR spectra also confirmed the smooth exchange process by showing a decrease in olefin peaks upon conversion of **6** to **7** (See ESI†). With a ligand loading of *ca.* 0.34 mmol g^{-1} in the corresponding **6**, this implied that ~70% of the immobilized ligands were loaded with ruthenium.

Efficient, complete RCM of diene **8** to the cyclized product **9** was achieved in 2 h over 5 mol% of **7b** or **7c** in DCM at ambient temperature (Fig. 1). Interestingly, only 30% conversion was attained with **7a** in 2 h, which did not further progress with time. It was obvious that the reaction rates were strongly influenced by the ligand flexibility, and **7a** was probably located too close to the MCF surface, rendering most ruthenium species latent in the catalytic cycle. The accessibility of the diene to the catalytic core would likely determine the initiation rate and the overall conversion rate. The short and rigid linker in **7a** deprived the ruthenium species of mobility, sandwiching it between the MCF surface and the bulky N-heterocyclic carbene (NHC) ligand. As a result, the initial complexation of substrate **8** to trigger the catalytic cycle was considerably blocked in the case of **7a**, giving rise to a low conversion rate as compared to **7b** and **7c**, which consisted of more flexible linker moieties. It appeared that a two-carbon linker was long enough to provide access of the diene to the ruthenium, as demonstrated by the efficient RCM over **7b**.

The recyclabilities of **7b** and **7c** were investigated for the RCM of **8** in DCM at 50 °C (Fig. 2). The reaction time was



Scheme 1 Synthetic pathway to the immobilized catalysts **7**.

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† Electronic supplementary information (ESI) available: Detailed experimental procedures, and NMR spectra of the novel compounds in Scheme 1 and the RCM products in Table 1. See DOI: 10.1039/b803663b

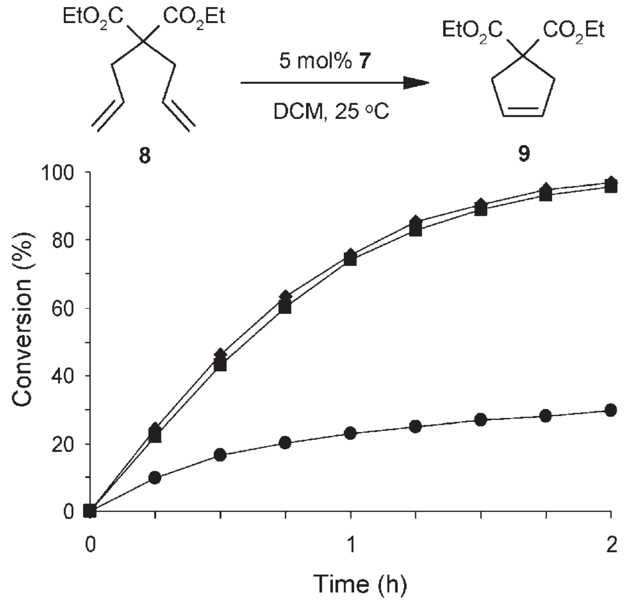


Fig. 1 RCM of **8** over catalysts (●) **7a**, (◆) **7b** and (■) **7c**.

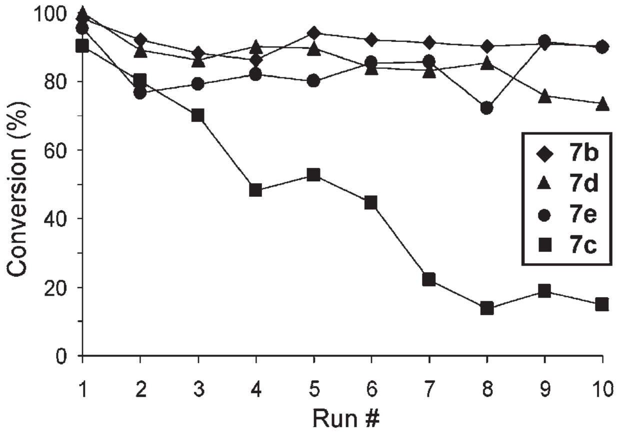


Fig. 2 RCM of **8** over catalysts **7** in DCM at 50 °C.

kept constant at 2 h to monitor the decrease in catalytic activity over multiple runs. Despite their similar conversion in the first run, the recyclabilities were dramatically different for the ethyl and hexyl derivatives. While the ethyl derivative **7b** maintained consistently high conversions ($\geq 90\%$) up to 10 runs, a significant reduction in conversion was observed in the recycling of the hexyl derivative **7c**. The gradual loss of activity could be attributed to the deactivation of the ruthenium–carbene complex,[13] possibly from the increased intermolecular interference among the neighboring ligands (and/or catalysts) associated with the flexible hexyl linker in **7c**. This might lead to permanent deactivation of the precatalysts and/or leaching of the ruthenium species. With a decreasing number of intact ruthenium–carbene complexes in the recycled **7c**, the conversions in the subsequent runs would be reduced. In contrast, the ethyl derivative **7b** could avoid intermolecular interference with its relatively short and rigid linker group. Thus, excellent recyclability was achieved by tuning the linker moiety at the two-carbon chain in our system. A comparison of the magnitude of diminished peaks in the ^{13}C CP-MAS NMR spectra of **7b** and **7c** after multiple runs confirmed that the leaching of ruthenium species was more significant in **7c** (see ESI†).

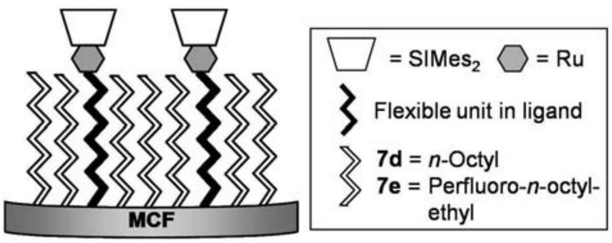


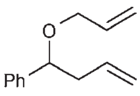
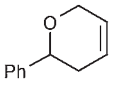
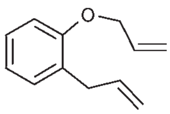
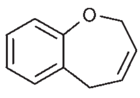
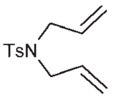
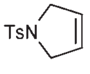
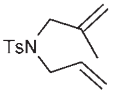
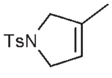
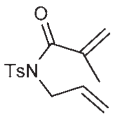
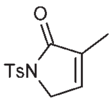
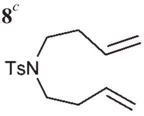
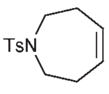
Fig. 3 The microenvironment of catalysts **7d** and **7e**.

To test our hypothesis, we have fabricated a system that surrounded the flexible hydrocarbon subunit with similarly featured precapping groups, so that the intermolecular interference among the reactive moieties could be suppressed. The beneficial role of the precapping group was well elucidated in our previous reports.[14] In this case, we simultaneously grafted precursor **5c** (the flexible catalyst precursor) and linear hydrocarbon groups (*i.e.*, *n*-octyl group for **7d** and perfluoro-*n*-octylethyl group for **7e**) onto uncapped MCF. In the course of the catalytic runs, the linear hydrophobic precapping moiety might stack along with the flexible linker group in **7c** to fixate the precatalysts on the hydrophobic surface (Fig. 3). As expected, the recyclability of catalyst **7c** was dramatically improved by tuning the microenvironment to minimize the decomposition of the reactive catalytic species **7d** and **7e**, which demonstrated excellent recyclabilities that were almost comparable to **7b** (Fig. 2). The molar ratio of the precapping group to catalyst should be *ca.* 2.6, assuming that the two alkylchlorosilanes were grafted in similar rates according to the initial amounts added.

Ruthenium leaching from **7b** and **7d** in the RCM of **8** over 10 runs was measured by inductively coupled plasma-mass spectroscopy (ICP-MS). On average, only 5 ppm and 8 ppm of ruthenium were found in the reaction solutions in each run due to the leaching from **7b** and **7d**, respectively. This low level of ruthenium leaching could be attributed to the unique structure of and synthesis scheme for **7**, which included the use of spherical siliceous MCF microparticles with well-defined, ultralarge mesopores, partial precapping of silanols on the support surface, mild and uniform ligand grafting, vapor-phase postcapping of silanols, and efficient ruthenium loading.

Given the excellent recyclability of **7b** and **7d**, these catalysts were further examined in the RCM reactions of various substrates (Table 1). The RCM of an oxygen-containing diene **10** produced the six-membered ring **11** in excellent yields for 10 consecutive runs. The typical concern of intramolecular coordination of the oxygen atom to the ruthenium–carbene intermediate[5a] did not appear to be an issue in the RCM over **7b**. Formation of the seven-membered ring **13** was also efficient, and good activities were exhibited over 7 runs. The catalyst **7b** also proved effective for cyclizing a nitrogen-containing diene **14**, although a more sterically challenging substrate **16** required an extended reaction time and the catalyst showed substantial loss of activity after the initial run. The RCM involving an electron-deficient carbonyl moiety

Table 1 RCM of several dienes over **7b** and **7d**

Catalyst	Substrate[a]	Product	Run	Conv (%)[b]
7b	 **10**	 **11**	1 4 7 10	97 97 96 97
7b	 **12**	 **13**	1 3 5 7	93 97 93 89
7b	 **14**[c]	 **15**	1 3 5 7	91 91 73 77
7b	 **16**[d]	 **17**	1 2 3	67 99[e] 45 20
7d	 **18**[c]	 **19**	1 4 7 10	83 78 89 79
7d	 **20**	 **21**	1 4 7 10	99 97 95 87

[a] Conditions: 5 mol% of **7**, 50 °C, 1 h, 0.05 M in DCM. [b] Determined by gas chromatography (GC) or liquid chromatography (LC). [c] Performed for 2 h. [d] Performed for 4 h. [e] Performed for 20 h.

(substrate **18**) was especially effective with **7d** as the catalyst. The reaction efficiency appeared sustainable, although the initial run was not performed to completion. The seven-membered ring **21** was formed more efficiently than its five-membered ring analog **15**, exhibiting good conversions up to 10 consecutive runs.

In conclusion, we have successfully developed highly active and recyclable MCF-supported ruthenium catalysts for RCM by optimizing the linker group and microenvironment. These cost-effective and environmentally benign heterogenized catalysts are of interest for industrial processes.[15] The remarkably low leaching of ruthenium species would be particularly attractive in pharmaceuticals manufacturing.

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