Supported Ru Olefin Metathesis Catalysts via a Thiolate Tether

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Thiolate-coordinated ruthenium alkylidene complexes can give high Z-selectivity and stereoretentivity in olefin metathesis. To investigate their applicability as heterogeneous catalysts, we have successfully developed a methodology to easily immobilize prototype ruthenium alkylidenes onto hybrid mesostructured silica *via* a thiolate tether. In contrast, the preparation of the corresponding molecular complexes appeared very challenging in solution. These prototype supported complexes contain small thiolates but still, they are slightly more Z-selective than their molecular analogues. These results open the door to more active and selective heterogeneous catalysts by supporting more advanced thiolate Ru-complexes.

Olefin metathesis is a very powerful reaction for the construction of carbon-carbon bonds in organic chemistry.¹ However, the implementation of olefin metathesis in pharmaceutical and specialty-chemicals manufacturing is still far from reaching its full potential.² Some of the drawbacks that have hampered industrial uptake may be overcome by immobilizing molecular complexes.³ For example, heterogenization can: i) prevent some deactivation pathways, ii) increase the stability of the intermediates, iii) ease the separation of the catalysts from the products, and iv) facilitate recycling of the catalyst. The anchoring of Ru olefin metathesis catalysts on solid supports has been accomplished through three different parts of the catalyst:³ a) the alkylidene moiety, b) a neutral ligand or c) an anionic ligand. The few reports on the latter strategy exclusively employ carboxylate anions as replacement for chloride.⁴ However, in recent years, several homogeneous Ru-olefin metathesis catalyst containing thiolate ligands have been reported (Figure 1).^{5,6,7} These compounds

Figure 1. Reported homogeneous thiolate Ru olefin metathesis catalysts.

display reasonable activities, and some of them are Z-selective (**1** and **2**) or highly stereoretentive (**4**).⁸ Our group has already reported the anchoring of olefin metathesis Ru complexes onto silica materials through the NHC ligand.⁹ Besides obtaining highly active Ru olefin metathesis catalysts, we demonstrated the beneficial interaction and stabilization of the Ru complex with the silica surface.¹⁰ Herein, we report the immobilization of Ru-olefin metathesis catalysts on mesostructured silica via an anionic exchange with a thiolate-supported ligand.

The supported catalysts were prepared *via* a two-step approach commonly employed in our group.^{9,11} First, we prepare a hybrid mesostructured silica matrix containing homogeneously distributed thiolate tethers on its pore-surface. Then, a selective surface organometallic reaction between a molecular organometallic complex and the surface ligands gives the immobilized complexes.¹²

For this study, we developed two materials differing by the nature of the silica-supported thiols (Scheme 1): material **Mat-PrSH** contains a flexible mercaptopropyl linker¹³ and **Mat-PhSH** a more rigid and bulkier mercaptophenyl group. These hybrid silica materials were prepared by sol-gel process using a templating route.¹⁴ This route involved co-hydrolysis and co-

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condensation of tetraethoxysilane and the corresponding thiol-containing organo-triethoxysilane precursor in the presence of Pluronic® P-123 as the structure-directing agent. This method offers control of the loading and distribution homogeneity of the organic groups along the silica pore channels. Furthermore, to be able to perform the catalyst immobilization, the surface had to be passivated, first by hydrolyzing all remaining surface ethoxy- groups into silanols and then converting those silanol groups into trimethylsiloxanes. However, in this latter step, the thiol groups were also silylated, requiring an extra step to selectively deprotect them. The intermediates were characterized by ^1H MAS SS NMR, ^{13}C CP-MAS SS NMR, elemental analysis, and nitrogen adsorption-desorption analyses (see Supplementary Information). Materials **Mat-PrSH** and **Mat-PhSH** displayed the expected physical features of a SBA-15 type mesostructured silica: a BET specific surface area of 593 and 574 m^2g^{-1} and a mean pore diameter (D_{pBJH}) of 7 and 8 nm, respectively. The ^{13}C SS NMR spectra exhibited a dominating signal at $\delta \approx 0$ ppm, corresponding to the trimethylsilyl groups on the surface and the expected peaks from the propyl chain in **Mat-PrSH** ($\delta = 28$ [broad signal] and 11 ppm) and the aromatic moiety in **Mat-PhSH** ($\delta = 133$ and 126 ppm).

Reaction conditions: a) 40 equiv. $\text{Si}(\text{OEt})_4$, pH = 1.5, Pluronic 123, NaF, 45 °C, 3 days; b) HCl (2 M), 45 °C, 2 h; c) TMSBr, Et_3N , toluene, 25 °C, 24 h; d) K_2CO_3 , MeOH, 25 °C, 16 h; e) KHMDS, toluene, 25 °C, 2 h; f) **HG-II**, toluene, 25 °C, 20 h.

Scheme 1. Synthesis of materials **Mat-PrSH** and **Mat-PhSH** and catalyst immobilization.

In order to incorporate the Ru complex, the surface thiol group was first deprotonated with a strong base and then reacted with the Ru precursor for ligand anionic exchange (Scheme 1). Potassium hexamethyldisilazide (KHMDS) was chosen for its compatibility with silica materials.⁹ However, treatment of Hoveyda-Grubbs 2nd generation (**HG-II**) with one equivalent of KHMDS in C_6D_6 showed a slow decomposition of the complex by ^1H NMR. Thus, to avoid base-induced decomposition of the Ru precursor, the thiolate-containing material was thoroughly washed with toluene to remove any KHMDS excess before adding the Ru precursor. The Ru anchoring was carried out under inert atmosphere by addition

of a toluene solution of **HG-II** to the thiolate-containing material under stirring. The S/Ru ratios of the final solids (by elemental analysis) showed a 50% grafting for **Mat-A** (containing the propanethiolate linker) and a 74% grafting for **Mat-B** (containing the phenylthiolate linker). These grafting degrees are much higher than the 20% reported in literature precedents when grafting Ru olefin metathesis catalysts through the NHC moiety.^{9,13} ^{13}C SS NMR showed the appearance of signals in the aliphatic region ($\delta = 10\text{--}20$ ppm), corresponding to methyl groups present in **HG-II**, and in the aromatic region ($\delta = 120\text{--}140$ ppm), attributed to aromatic carbon atoms of the mesityl and the alkylidene moieties (see ^1H and ^{13}C spectra in Supplementary Information). As expected from the fact that ^{13}C labels were not used, the carbenic signal was not observed, even using cutting edge NMR techniques like dynamic nuclear polarization.^{9,11d} This can be explained by the inherent large CSA for this type of complexes¹⁵ and absence of close protons around the carbenic carbon.

Molecular analogues of supported stereogenic-at-metal complexes **Mat-A** and **Mat-B** in which only a single chloride has been exchanged with the corresponding thiolate, were very challenging to obtain (Figure 2). Reaction of **HG-II** with a small excess of propanethiolate (for **A**) or phenylthiolate (for **B**) renders the monosubstituted complex within a mixture of complexes (starting material, bis-thiolate and others). Isolation and purification of these complexes turned out to be particularly challenging because they decompose on silica gel and co-precipitate along with other complexes. However, a few milligrams of the pure complexes could be obtained after several time-consuming recrystallizations (see ESI). In this case, the advantage of supporting a catalyst becomes clear, since it is not possible to form the bis-substituted complexes and the remaining unreacted material can be easily washed away, thus giving much higher yields.

Figure 2. Isolated and characterized molecular analogues **A** and **B**.

To investigate the nature of the surface Ru-NHC active sites, we studied the stereoselectivity of **Mat-A** and **Mat-B** in the self-metathesis of methyl oleate. This reaction gives four products: *E/Z*-9-octadecene (**P1'**) and dimethyl *E/Z*-9-octadecene-1,18-dioate (**P1**). The cross metathesis between the two products leads back to the formation of methyl oleate (MO, *Z*-**S1**) and methyl elaidate (ME, *E*-**S1**). The initial selectivity (i.e. the initial *E/Z* ratio) of a Ru-olefin metathesis complex can be considered as a finger-print of the catalyst, and depends on the metal, its coordination sphere, and the stability of the metallacyclobutane intermediate.^{9,16} For that reason, by plotting the *E/Z* ratios of the diester product versus the *E/Z* ratios of the reactants (ME/MO), we can extrapolate

the initial *E/Z* values (at 0% conversion) of a given catalyst (Table 1 and Supplementary Information). The results for different molecular complexes and supported catalysts show that all initial *E/Z* ratios are around 2.0 - 2.5 (Table 1), which indicates that all complexes, including those of **Mat-A** and **Mat-B**, are truly Ru-NHC complexes, and that no degradation happened during immobilization.

Table 1. Stereoselectivities of different catalysts in the self-metathesis of methyl oleate.

#	Catalyst ^a	<i>E/Z</i> of P1 at 0% conv
1	5	2.1 ^b
2	Mat-5	1.8 ^b
3	6	2.0 ^b
4	Mat-6	2.0 ^b
5	7	2.0 ^c
6	Mat-7	2.0 ^c
7	HG-II	2.5 ^b
8	A	2.6
9	Mat-A	2.1
10	B	2.8
11	Mat-B	2.5

^a See below the corresponding structure of the Ru catalysts. ^b Values from Ref. 9. ^c Values from Ref. 10.

For sake of comparison, the *E/Z* ratios observed for relevant literature precedents describing silica-supported Ru-NHC complexes *via* different organic tethers (a flexible propyl chain for **Mat-5**, a semi-rigid benzyl group for **Mat-6** and a rigid phenyl-mesityl unit for **Mat-7**) are shown in table 2. While **Mat-5** has a lower *E/Z* ratio than its homogeneous equivalent (**5**), this tendency is not observed for **Mat-6** and **Mat-7** when compared to their molecular analogues (**6** and **7**). This difference was proven to arise from interactions of the active site with the silica surface in **Mat-5**, made possible by the

flexible propyl linker.¹⁰ Similarly, the short and flexible linker of **Mat-A** might explain its lower *E/Z* ratio (at 0% conversion) compared to **Mat-B**, **HG-II**, **A** and **B**. These results suggest that the flexibility of the organic tether influences the catalytic properties of the resulting supported complex, generating a surface active site different from that of the molecular complex in solution or from a supported analogue complex isolated from the silica surface by a more rigid tether.

Table 2. Homometathesis of 1-hexene (**S2**) and 4-phenyl-1-butene (**S3**).

Cat.	Isom. (%) ^{a,b}	Yield P2 (%) ^b	TON to P2	<i>E/Z</i> of P2 ^b
HG-II	2.7	36.4	3640	5.3
A	2.9	0.3	30	n.d.
Mat-A	0.8	4.6	460	2.7
B	1.0	14.6	1460	2.2
Mat-B	1.2	2.5	250	1.4

Cat.	Isom. (%) ^{a,b}	Yield P3 (%) ^b	TON to P3	<i>E/Z</i> of P3 ^b
HG-II	15.1	43.1	4310	3.8
A	60.0	0.2	20	n.d.
Mat-A	3.3	1.0	100	1.8
B	8.9	12.8	1280	1.3
Mat-B	1.7	0.8	80	0.9

^a isomerization of **S** + metathesis of the isomers. ^b Calculated by GC using dodecane as internal standard. n.d. = not determined due to the low yield.

Catalysts **Mat-A** and **Mat-B** were further tested in the homometathesis of two terminal olefins (Table 2): 1-hexene (**S2**) and 4-phenyl-1-butene (**S3**). When comparing the two supported catalysts, **Mat-A** displayed a better activity than **Mat-B** with both substrates, while **Mat-B** gave a lower *E/Z* ratio. The higher *Z*-selectivity can be explained by the higher bulkiness around the Ru in **Mat-B** compared to **Mat-A**.⁵ For molecular analogues, the same trend was observed when comparing **HG-II** and **B**, where the latter was found less active but more *Z*-selective than **HG-II**. Homogeneous complex **A** proved to be very unstable under the reaction conditions, leading to big amounts of isomerization and limited metathesis production. However, it is remarkable the stabilization induced by anchoring the Ru complex onto silica in **Mat-A**. When comparing homogeneous catalysts to immobilized catalysts (**HG-II** and **B** vs **Mat-A** and **Mat-B**), the same trend was observed: the increased steric bulk around the Ru center generated by the silica surface for the supported sites leads to higher *Z*-selectivities, but a decrease in productivity (TOF = 10³ h⁻¹ vs 10² h⁻¹, after 2 h), which may be partly related to initiation problems.¹⁷ Unfortunately, these materials were not reusable and deactivated with time, probably via intramolecular pathways, as suggested in the literature.¹⁸

Finally, we studied the possibility of **HG-II** physisorption on silica during the immobilization of the Ru complex. To do so, the immobilization of **HG-II** on **Mat-PhSH** was carried out without addition of KHMDS. The resulting material was tested in the homometathesis of 1-hexene in the conditions from Table 2. After 7 hours, a poor yield (0.1% for **P2**) demonstrated that the active complexes are in fact properly anchored.

In summary, we have developed an effective methodology for the immobilization of Ru-olefin metathesis catalysts via a single anionic exchange with a silica-supported thiolate ligand. This experimental procedure gave new supported stereogenic-at-metal Ru-NHC complexes for which the molecular analogues are very challenging to prepare and isolate. Furthermore, a great enhance of stability was observed when immobilizing catalyst **A**. In the metathesis of terminal alkenes, increased Z-selectivity was observed when increasing the size of the thiolate ligand and due to possible interactions of the Ru active site with the silica surface. This new immobilization protocol opens the door to support other ruthenium alkylidene catalysts bearing thiolate ligands, as for example highly Z-selective or stereoretentive olefin metathesis catalysts, like **1**, **2** or **4**. We are currently exploring this possibility.

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Conflicts of interest

There are no conflicts to declare.

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