A Thermally Switchable Latent Ruthenium Olefin Metathesis Catalyst

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Summary: The synthesis and characterization of a cis-dichloro sulfur chelated olefin metathesis catalyst is presented. The catalyst was extremely stable at room temperature in solution under ambient conditions and was shown to exhibit a thermo-switchable behavior for ring-closing olefin metathesis of diethyl diallylmalonate, being active at 80 °C and inactive at room temperature.

One of the principal goals to be met in olefin metathesis chemistry is the development of a catalyst that "lives" forever.[1] In view of this, thermally activated olefin metathesis catalysts are an important target, due to the useful properties these catalysts may show, such as prolonged stability at room temperature and the ability to cope with extreme reaction conditions. Several olefin metathesis initiators show activity at elevated temperatures. Some examples are as follows: complexes with η^6-arene ligands, Fischer type carbenes, "dangling" ligand compounds, and chelating alkylidenes (parts a–e of Figure 1).

The strategy in all these cases is to protect the ruthenium catalytic center by stabilizing the ligand shell around it, either by mostly electronic[2] (Figure 1a,b) or by chelating effects[3,4] (Figure 1c–e). Recently, success has been reached in developing thermally activated ring-opening metathesis polymerization (ROMP) catalysts.[3a–f] For example, Grela's quinoline and quinoxaline initiators[3a] were latent at room temperature in ROMP type reactions, but on the other hand they showed activity for ring-closing metathesis (RCM) reactions. Also, switchable behavior has been observed by changing the chemical environment of the olefin metathesis reaction; for instance, by
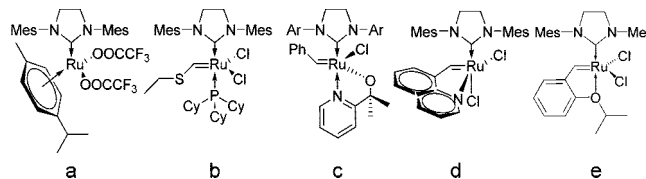

Figure 1. High-temperature olefin metathesis catalysts.

adding acid to a dormant species the catalyst's structure could be altered and consequently activated.[5]

Notwithstanding the vast literature on olefin metathesis catalysis, there are no examples for RCM catalysts that exhibit thermoswitchable behavior at room and moderate temperatures. We envisioned that a stronger ligation of the ruthenium metal by a sulfur atom instead of the typically used oxygen or nitrogen chelates would allow us to prepare an extremely stable initiator active only when heated. The use of a sulfur thioether ligand was recently explored by Grubbs in a three-point chelate catalyst[3f] and was shown to afford lower initiator rates, although no data were provided for the catalyst activity at room temperature. Thus, we set out to explore the effect of exchanging the oxygen in the well-known Hoveyda–Grubbs olefin metathesis catalyst (Figure 1e)[4] for a sulfur atom.

The styrene isopropyl thioether derivative **3** was readily synthesized by aromatic nucleophilic substitution of **1**[6] followed by Wittig olefination of **2**. Reaction of the second-generation Grubbs catalyst **4** with **3** in the presence of cuprous chloride afforded the new catalyst **5** as the major product in 64% yield (Scheme 1).[7]

The asymmetry of the NMR spectrum of **5** discloses the *cis*-dichloro arrangement (Figure 2b) of the compound. Remarkably, every single proton or methyl group in the molecule at ambient temperature was clearly resolved and characterized. As expected, at higher temperatures we were able to observe the coalescence of the NHC proton pairs (Figure 2a), indicating a fast rotation around the NHC carbon–ruthenium bond, not present at room temperature. We calculated the energy barrier for this rotation to be 18.9 kcal/mol (see the Supporting Information). To the best of our knowledge, this is the first time such a barrier has

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† Achva Academic College.
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(1) Grubbs, R. H. *Chem. Sci.* **2007**, Aug 20.
(2) (a) Louie, J.; Grubbs, R. H. *Organometallics* **2002**, *21*, 2153–2164. (b) Zhang, Y.; Wang, D.; Lönnecke, P.; Scherzer, T.; Buchmeiser, M. R. *Macromol. Symp.* **2006**, *236*, 30–37. (c) Delaude, L.; Delfosse, S.; Richel, A.; Demonceau, A.; Noels, A. F. *Chem. Commun.* **2003**, 1526–1527. (d) van der Schaaf, P. A.; Kolly, R.; Kirner, H.; Rime, F.; Mühlebach, A.; Hafner, A. *J. Organomet. Chem.* **2000**, *606*, 65–74.
(3) (a) Gstrein, X.; Burtscher, D.; Szadkowska, A.; Brabasiewicz, M.; Stelzer, F.; Grela, K.; Slugovc, C. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 3494–3500. (b) Slugovc, C.; Perner, B.; Stelzer, F.; Mereiter, K. *Organometallics* **2004**, *23*, 3622–3626. (c) Denk, K.; Fridgen, J.; Herrmann, W. A. *Adv. Synth. Catal.* **2002**, *344*, 666–670. (d) See also ref 2d. (e) Barbasiewicz, M.; Szadkowska, A.; Bujok, R.; Grela, K. *Organometallics* **2006**, *25*, 3599–3604. (f) Hejl, A.; Day, M. W.; Grubbs, R. H. *Organometallics* **2006**, *25*, 6149–6154. (g) Chang, S.; Jones, L., II; Wang, C.; Henling, L. M.; Grubbs, R. H. *Organometallics* **1998**, *17*, 3460–3465.
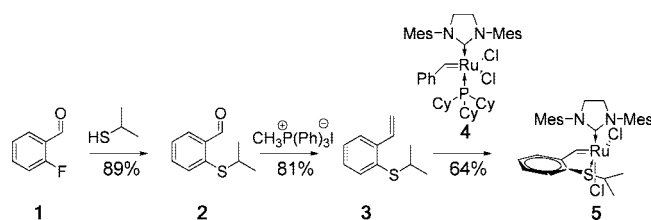(4) (a) Gessler, S.; Randl, S.; Blechert, S. *Tetrahedron Lett.* **2000**, *41*, 9973–9976. (b) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168–8179.

(5) (a) Gawin, R.; Makal, A.; Wozniak, K.; Mauduit, M.; Grela, K. *Angew. Chem., Int. Ed.* **2007**, *46*, 7206–7209. (b) See also: P'Pool, S. J.; Schanz, H.-J. *J. Am. Chem. Soc.* **2007**, *129*, 14200–14212.
(6) Zhang, H. Q.; Xia, Z.; Kolasa, T.; Dinges, J. *Tetrahedron Lett.* **2003**, *44*, 8661–8663.
(7) Under certain conditions, namely shorter reaction periods, two other byproducts could be detected. ^{1}H NMR suggests that one of the byproducts is the *trans*-dichloro derivative, while the other byproduct is a six-coordinated compound which still contains the tricyclohexylphosphine ligand. These two byproducts were shown to convert to **5** upon standing at room temperature, making their full characterization more complicated but raising the yield of **5** from 55% to 64% (see the Supporting Information).

Scheme 1

been measured in olefin metathesis catalysts.[8] Interestingly, whereas NOESY analysis revealed an exchange process for the corresponding mesitylene hydrogens and methyl groups (interchanged by 180° rotation of the Ru−NHC carbon bond); the isopropyl methyls did not undergo coalescence and no exchange could be detected even at high temperatures, suggesting that the catalyst's asymmetric structure remains stable under these conditions and probably there is no disruption of the Ru−S bond. At the highest temperature reached (145 °C), we only observed a coalescence process for the pairs of hydrogens that are exchanged by the NHC rotation around the carbon−ruthenium bond (see the Supporting Information). An additional rotation of the aromatic groups around the carbon−nitrogen bond would force coalescence of the mesitylene signals and afford just two methyl peaks and one aromatic peak, as seen in the *trans*-dichloro compound isolated (see the Supporting information). Since this is not observed, we conclude that the *cis*-dichloro arrangement prevents rotation of the mesitylene groups around the nitrogen−carbon bond. We are currently studying the implications of these rotation barriers on the increased lethargy of the *cis*-dichloro compounds.[3e]

Single-crystal X-ray analysis further corroborated the structural properties of **5** (Figure 3).[9] The sulfur−ruthenium bond length was 2.35 Å, in line with reported L-type ligand sulfur−ruthenium bonds in the Cambridge Crystallographic Database.[3f] The mesitylene groups exhibit a large-amplitude "wagging" motion/partial orientational disorder. The crystal structure shows one of the mesitylene groups overlapping the chelating phenyl ring (with a mean interplanar distance of 3.3 Å between the aryl fragments), while the other one "blocks" the sixth empty coordination site of the ruthenium. NMR also provides evidence of the aromatic ring overlap, one of the mesitylene protons being almost 1 ppm more upfield (5.9 ppm) than the other three, but on heating this overlap can easily be destroyed, as observed in the coalescence of the mesitylene signals at high-temperature NMR. The adjacent methyl protons are also affected, being 0.5 ppm more upfield (1.6 ppm) than the next methyl group.

To assess the stability of **5**, we analyzed its NMR spectrum after 20 days in deuterated 1,1,2,2-tetrachloroethane. No major differences in the spectra could be detected, signifying that the catalyst is stable in solution for long periods of time at room temperature (Figure 4). However, when both catalyst **5** and the Hoveyda−Grubbs catalyst[4] were separately heated to 90 °C in air, we observed total decomposition of both catalysts after 3 days, although **5** did not decompose by the typical aldehyde[10]

Figure 2. ¹H NMR spectrum ($C_2Cl_4D_2$) of **5** (a) at 145 °C and (b) at 20 °C with alkylidene protons shown in the insets. See the Supporting Information for full assignment and intermediate temperatures.

Figure 3. Solid-state structure of **5** with thermal ellipsoids drawn at the 50% probability level. Solvent molecules are removed for clarity.

Figure 4. ¹H NMR spectra of **5** (a) before and (b) after standing at room temperature over 20 days in $C_2Cl_4D_2$ (open to air).

byproduct pathway found for the Grubbs catalyst and many of its derivatives (see the Supporting Information).

Finally, we probed the reactivity of **5** by reacting it with diethyl diallylmalonate (**6**), a benchmark RCM reaction.[11] We observed that even after 1 week at room temperature absolutely no RCM product could be detected, while catalyst **5** remained unscathed. On the basis of our NMR studies, which showed the beginning of coalescence close to 80 °C, we heated the reaction mixture in toluene at this temperature. We could quickly

(8) For examples of other metal−NHC rotation barriers, see: (a) Dible, B. R.; Sigman, M. S. *Inorg. Chem.* **2006**, *45*, 8430–8431. (b) Chianese, A. R.; Li, X.; Janzen, M. C.; Faller, J. W.; Crabtree, R. H. *Organometallics* **2003**, *22*, 1663–1667.

(9) Crystal data: $C_{31}H_{38}Cl_2N_2RuS \cdot 2CH_2Cl_2$, MW 812.53, orthorhombic, space group *Fdd*2, $a = 48.6971(12)$ Å, $b = 21.1349(6)$ Å, $c = 15.3763(5)$ Å, $V = 15825.4(8)$ Å³, $Z = 16$, $T = 110$ K, $D_{exptl} = 1.364$ g/cm³, R1 = 0.066 for 6395 reflections with $I > 2\sigma(I)$.

(10) Kim, M.; Eum, M.; Jin, M. Y.; Jun, K.; Lee, C. W.; Kuen, K. A.; Kim, C. H.; Chin, C. S. *J. Organomet. Chem.* **2004**, *689*, 3535–3540.
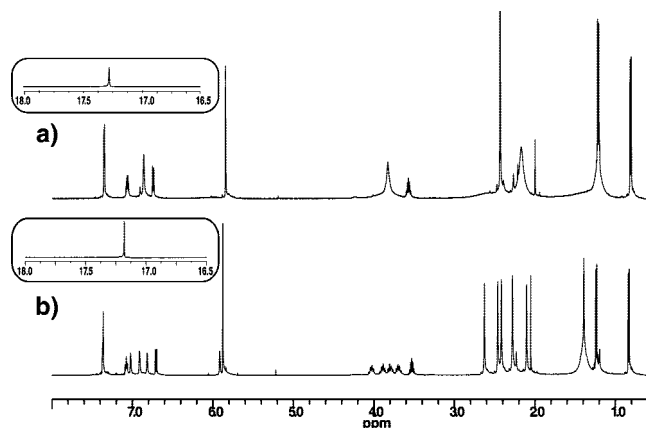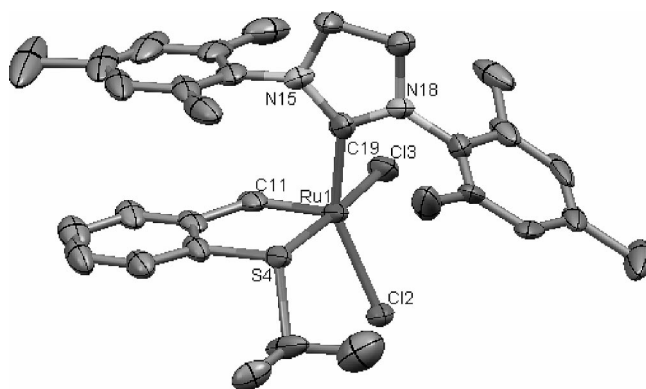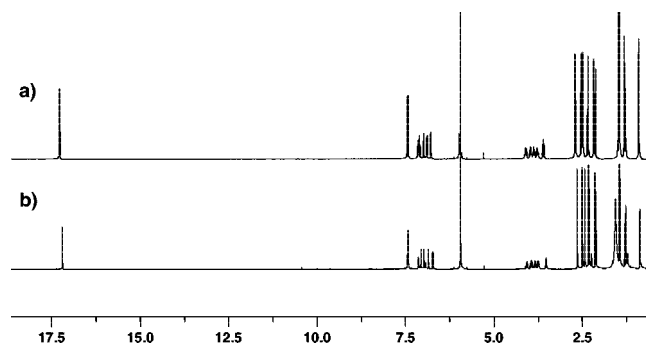
(11) Ritter, T.; Hejl, A.; Wenzel, A. G.; Funk, T. W.; Grubbs, R. H. *Organometallics* **2006**, *25*, 5740–5745.
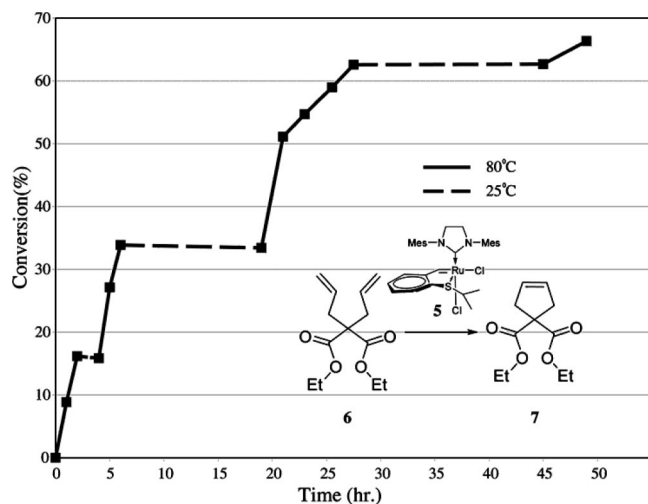
Figure 5. RCM reaction profile of 0.1 M **6** in toluene with 1 mol % of catalyst **5** at alternating temperatures (conversion measured by GC-MS).
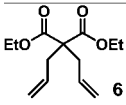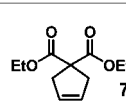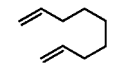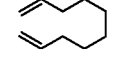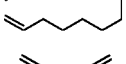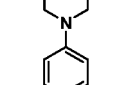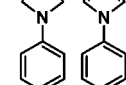
and clearly observe the formation of the anticipated cyclopentene product **7**. To check whether we could switch the catalysis on and off, we carried out a reaction with intermittent periods of heating to 80 °C and cooling to 25 °C in toluene under a nitrogen atmosphere. As shown in Figure 5, the catalyst demonstrated a completely thermo-switchable behavior even after more than 2 days.

To further check the reactivity of the catalyst, various dienes were reacted with catalyst **5**. Table 1 summarizes the results for these additional olefin metathesis reactions. Even at very low loadings of 0.1 mol %, catalyst **5** was shown to convert more than 50% of 0.1 M **6** to the ring-closed product **7** in the presence of air.

In conclusion, we have shown that by a single atom exchange of oxygen by sulfur we created a very stable olefin metathesis catalyst which is completely inert to RCM reactions at room temperature and is only active at high temperatures. Remarkably, this behavior was shown to be totally reversible, possibly bringing us closer to the goal of enhanced recyclability[12] and longevity in olefin metathesis catalysts and presenting attractive applications: e.g., in self-healing alkene-containing polymers.

(12) Clavier, H.; Grela, K.; Kirschning, A.; Mauduit, M.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 6786–6801.

Table 1

Substrate	Product/s	Conversion (%)[a]
6	**7**	84[b] 55[c]
		100
	Oligomers	86
	Oligomers	87
		42[d]

[a] Reactions were carried out at a concentration of 0.1 M, with **5** (5 mol %) in toluene (or toluene-d_8) at 90 °C for 2 days, and conversion was measured either by GC-MS or NMR. [b] With 1 mol % catalyst, in air. [c] With 0.1 mol % catalyst, in air. [d] Overall conversion for both products, identified by GC-MS NIST 2005.

Due to the exceptional characteristics of **5**, we also obtained a unique glance into the dynamics of the system, which may help us to obtain useful insights and better understand the intricacies of the metathesis mechanism in the *cis*-dichloro arrangement and its decomposition pathways. We are currently working on tuning the electronic and steric environment of the ligating sulfur atom in order to enhance and probe the properties of these types of catalysts and also trying to understand the implications of the *cis*- or *trans*-dichloro arrangement in the activity and mechanism of these catalysts.

Supporting Information Available: Text and figures giving synthetic and characterization details for **3** and **5** and full details of NMR experiments for **5** and a CIF file giving crystal data for **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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