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Latent sulfur chelated ruthenium catalysts: Steric acceleration effects on olefin metathesis

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ABSTRACT

A series of sulfur chelated dormant ruthenium olefin metathesis catalysts is presented. The catalysts prepared were shown to possess the uncommon *cis*-dichloro arrangement and were mostly inactive at room temperature. By systematically modifying the size of the substituent groups at the chelating sulfur atom, catalyst activity at different temperatures was significantly affected; more bulky substituents fomented activity at lower temperatures. The catalysts were also shown to be stable in solution and retained their catalytic activity even after being exposed to air for two weeks.

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During the last decade well defined olefin metathesis has evolved from almost a chemical curiosity to one of the most widely used carbon–carbon bond formation reactions in synthetic organic chemistry [1]. One of the reasons for the tremendous success of this method was the introduction of ruthenium based catalysts, significantly more air and moisture stable than their predecessors [2]. The judicious tuning of the ligand shell around the metal atom spearheaded catalyst development, affording compounds with acute stability and reactivity. Two of the most significant adjustments to the environment of the ruthenium metal atom were the introduction of strong σ donating *N*-heterocyclic carbene (NHC) ligands [3] and the use of chelation to improve the stability of the complex [4] (Fig. 1).

Most efforts in the field are geared towards the development of olefin metathesis catalysts that react with a wider range of substrates (electronically and sterically challenged alkenes), display enhanced stability, and are also significantly more active. Still, pioneering examples of modified catalysts that afforded considerably lower activities at room temperature were recently put forward by Grela, Slugovc and co-workers [5]. The acquisition of catalysts with very low activity and understanding the factors that cause this, may possibly be the first step towards the generation of catalytic switches. A reversible inhibition of catalyst activity might prove beneficial not only in practical applications, but may possibly pro-

vide important insights on the catalyst mechanism. With this in mind, we envisioned that the use of a sulfur chelating atom on an analogue of Hoveyda–Grubbs catalyst **2** would strengthen the ligation to ruthenium and lower the reaction rate. Thus, we reported the synthesis, characterization and thermo-switchable olefin metathesis activity of a latent sulfur chelated ruthenium catalyst [6]. A different approach to influence reactivity of olefin metathesis catalysts is by steric effects. For example, it has been recently shown that the exchange of the isopropyl group by a methyl group in catalyst **2** leads to lower activities, probably due to a strengthening of the Ru–O chelation [7]. Herein we present a novel series of modified sulfur chelated ruthenium catalysts designed to alter initiation temperatures by systematic steric acceleration effects.

Following the synthetic pathway presented in Scheme 1, styrene ligands **5** were prepared. Compounds **5** were reacted with catalyst **1** in the presence of CuCl to obtain catalysts **6** in moderate to good yields [8].

All the sulfur chelated catalysts displayed the unusual *cis*-dichloro arrangement, even when the *tert*-butyl group was used as the substituent, as evidenced by the asymmetry of the NMR spectra (see Supplementary material). Furthermore, we were able to corroborate this geometry by obtaining single crystal X-ray structures for all new catalysts (Fig. 2) [8]. This atypical geometry has important effects on the catalyst behavior, for example, it has been shown that catalysts in the *cis*-dichloro arrangement show lower activity than their *trans*-dichloro counterparts [5c]. Grubbs et al. have also suggested the *cis*-dichloro conformation as an intermediate in asymmetric olefin metathesis reactions [9]. Interestingly, in

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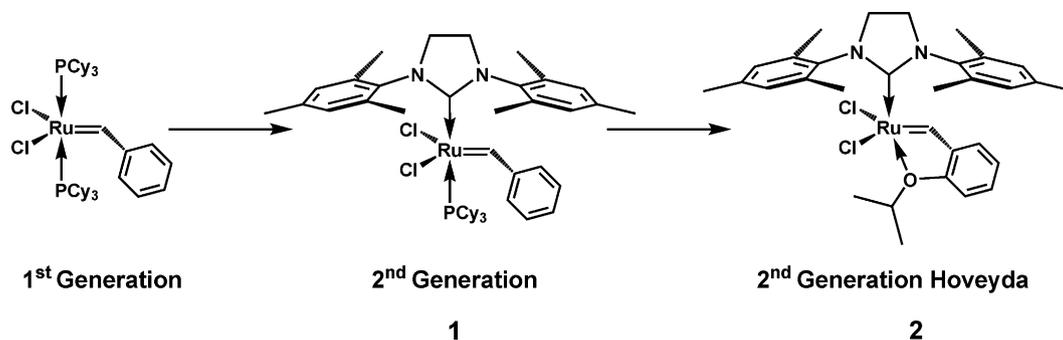
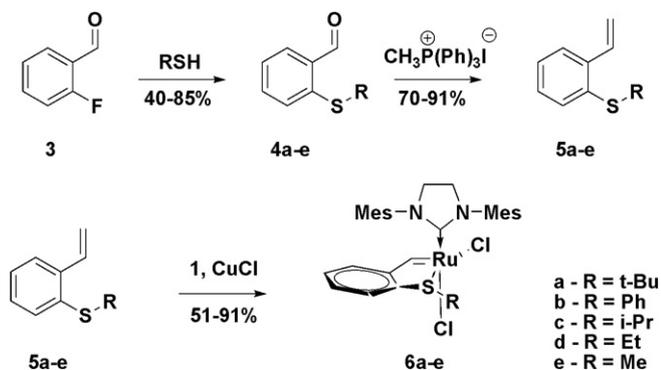


Fig. 1. Evolution of 1st generation Grubbs catalyst towards 2nd generation Grubbs catalyst **1** containing the NHC ligand and 2nd generation Hoveyda–Grubbs catalyst **2** additionally having a chelating isopropoxy group ortho to the benzylidene atom.



Scheme 1. Syntheses of catalysts **6a–e**.

Table 1
Ruthenium–sulfur bond lengths for catalysts **6** and conversion to product **9**

Catalyst	Ru–S bond length (Å)	Conversion ^a (%)
6a	2.364(1) ^c	91
6b	2.347(2)	91
6c	2.351(2)	55 ^b
6d	2.340(1)	25
6e	2.330(2) ^d	17

^a 0.1 M **8**, 0.1 mol% catalyst **6**. Reactions were carried out under air at 90 °C for 24 h.

^b See Ref. [8].

^c Average of four independent molecules.

^d Average of two independent molecules.

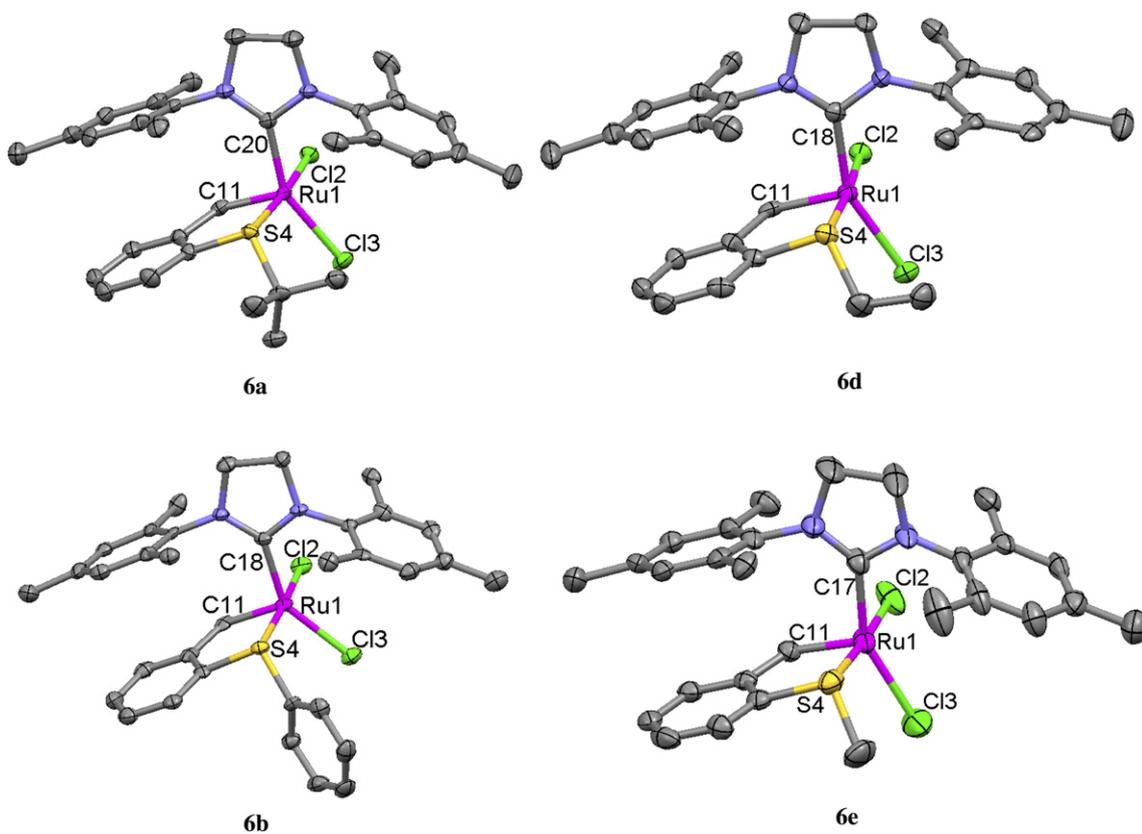


Fig. 2. Solid state structures of catalysts **6a**, **b**, **d**, **e**. Ellipsoids drawn at 50% probability, solvent molecules and hydrogens omitted for clarity.

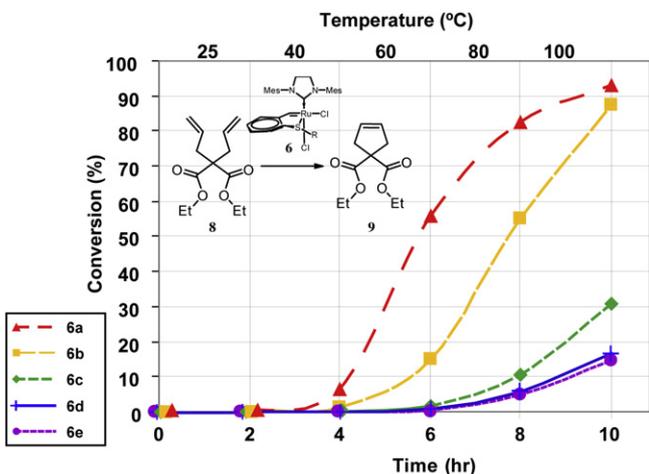


Fig. 3. RCM reaction of **8** with catalysts **6a–e** at increasing temperatures; each 2 h block was kept at constant temperature. Reactions were run at 0.1 M concentration with 1 mol% catalyst in toluene and conversion was monitored by GC–MS.

most cases observed to date, the *cis*-dichloro conformation is seen when strong chelating ligands, such as pyridyl or quinoline, are present [10].

One of the salient features extracted from the crystal structure data is the dependence of the sulfur–ruthenium bond length on the bulkiness of the sulfur substituent. As shown in Table 1, there is a small, yet significant, elongation of the Ru–S bond as the substituent on the sulfur atom becomes more bulky. Given that according to the classical metathesis mechanism the Ru–S bond must rupture for metathesis to occur, we hypothesized that the more active catalysts would possess longer Ru–S bonds.

Thermal activation behavior was tested by stepwise heating a toluene solution of the catalysts in the presence of diethyl diallylmalonate **8**. The benchmark ring closing metathesis (RCM) reaction was monitored by GC–MS while quickly raising the temperature by 20 °C every 2 h until a temperature of 100 °C was reached. The results are presented in Fig. 3.

As observed, the introduction of bulkier substituents indeed increased the reactivity of the catalyst at lower temperatures. This systematic steric acceleration effect is observed for all the alkyl substituents. The phenyl substituted catalyst **6b** shows a high activity compared to the other catalysts, and we believe that stabilizing electronic effects in the unbound state are in play here in addition to the mainly steric effects that weakened the sulfur–ruthenium bond.

Table 1 summarizes the ability of the catalysts to realize RCM reactions at low loadings of catalyst. We observed that the most

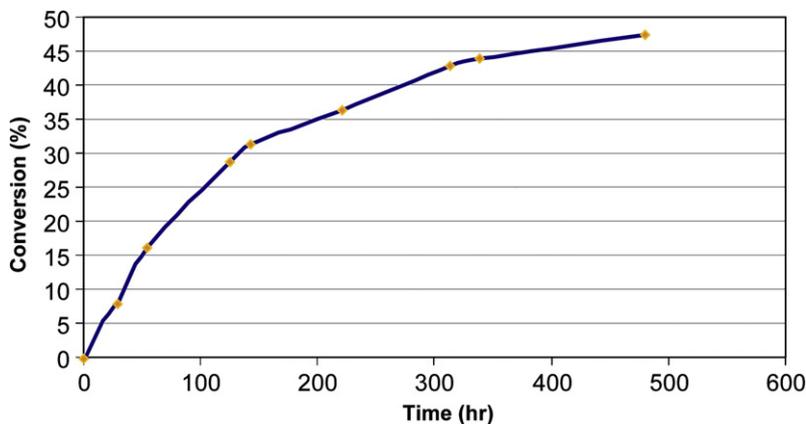


Fig. 4. RCM activity for catalyst **6a** at ambient conditions. 0.1 M **8**, 1 mol% catalyst.

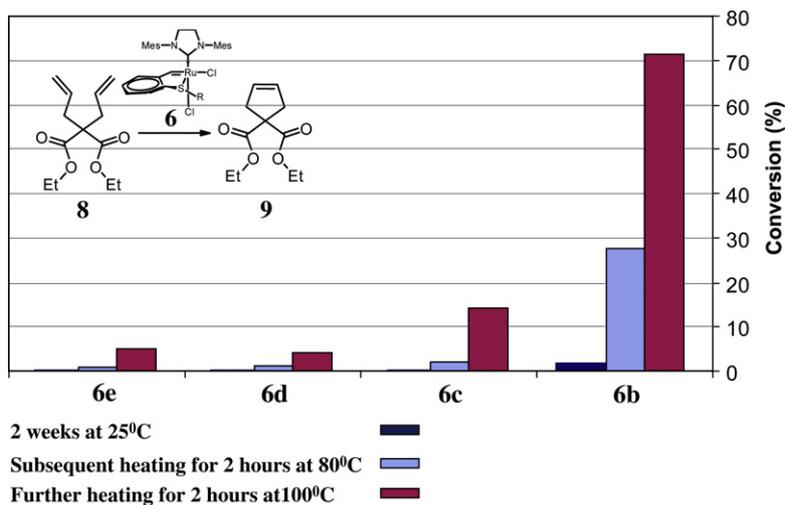


Fig. 5. RCM activity for catalysts **6b–e** in air. 0.1 M **8**, 1 mol% catalyst.

active catalysts also afforded higher turnover numbers, in line with typical available Grubbs type olefin metathesis catalysts [11].

To further probe the catalytic properties and solution stability of **6** we allowed the catalysts to stand with diethyl diallylmalonate **8** for at least two weeks at ambient conditions and monitored the conversion to the cyclic product. Out of all the series, only catalyst **6a** showed any significant catalytic activity at room temperature (Fig. 4), albeit very mild. Notably, **6a** was still active even after 20 days, reaching almost 50% conversion during this period.

In order to ascertain whether the dormant catalysts were still active after two weeks in solution under air, **6b–e** were heated first for 2 h at 80 °C and then for 2 h at 100 °C (Fig. 5). To our satisfaction, all the sulfur chelated catalysts showed noticeable RCM activity even after standing in toluene solution for two weeks under ambient conditions that include, naturally, oxygen and humidity.

In conclusion, we present a series of *cis*-dichloro sulfur chelated catalysts whose activity may be finely tuned by altering the steric interactions on the labile ligand. The most reactive catalyst, equipped with a *tert*-butyl substituent, induced an extremely slow ring closing metathesis reaction at room temperature that, remarkably, was still active after more than 20 days. All catalysts showed appreciable stability and performed ring closing metathesis reactions even after prolonged exposure to air.

We are currently investigating the effects of modulating the electronic density of the ligating atoms to modify the properties of the catalysts and their geometry.

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Appendix A. Supplementary material

Synthetic and characterization details for **3–6**; full details for RCM reaction of **8** and CIF files for **6** are available. Supplementary

data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2008.03.028.

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