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# Stability and activity of cis-dichloro ruthenium olefin metathesis precatalysts bearing chelating sulfur alkylidenes



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## ABSTRACT

S-Chelated Grubbs type complexes are usually found in their stable *cis*-dichloro conformation. These precatalysts are usually latent and necessitate external stimuli to promote olefin metathesis reactions. Herein we report the synthesis of new S-chelated ruthenium complexes, by a simple exchange of the benzylidene to an alkylidene chelating ligand. The structure of the complexes was studied by NMR spectroscopy, single crystal X-ray diffraction and DFT calculations. The new complexes were tested in a series of olefin metathesis reactions and were found to be the first *cis*-dichloro ruthenium precatalysts that are active at room temperature. The observed differences in reactivity and structure between the alkylidene complexes and their benzylidene counterparts highlight the important influence aromaticity may have on the stability and activity of chelated Grubbs type complexes. The findings may also have implications to develop alternative strategies to stabilize, or destabilize, other organometallic complexes bearing relevant chelating ligands.

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## Introduction

Olefin metathesis [1] has greatly influenced many areas of organic synthesis, among them, the production of polymers [1f,2], natural products [1f,3], drugs [4] and chemical commodities from renewable resources [5]. Much of this progress has been due to the constant development of more reactive and stable catalysts, a very active field of research that has certainly afforded impressive achievements [1e,g,6]. For example, in applications related to the preparation of thermosets, intimate control over the reaction initiation and kinetics is essential in order to obtain homogenous materials featuring the desired mechanical properties [7]. With this in mind, we recently developed a series of sulfur chelated ruthenium olefin metathesis precatalysts which display dormant behavior [8]. The sulfur–Ru bond is remarkably strong, thus allowing for exquisite control over precatalyst initiation [8b,c]. Unexpectedly, these complexes disclosed a cis-dichloro configuration, opposed to the trans-dichloro conformation typically observed for commercial catalysts (Fig. 1). Even though different cis-dihalo

http://dx.doi.org/10.1016/j.jorganchem.2014.06.027 0022-328X/© 2014 Elsevier B.V. All rights reserved. oxygen [9], halogen [10] and nitrogen [11] chelated complexes, which are active in room temperature have been reported, to date, all sulfur chelated precatalysts were found to be latent in several olefin metathesis applications at room temperature and could be activated by the use of heat [8a-c,e] or light [8d].

In order to control the initiation and performance of S-chelated precatalysts both steric and electronic effects may be harnessed. For example, the addition of a bulky group made compounds 2 and 3c to be the most active within their series (Fig. 2) [8b,d]. These studies led to the conclusion that only the *trans-dichloro* isomer is active, while the cis-dichloro isomers are latent. In addition, electronic effects were also used in order to tune the S-Ru bond dissociation and affect catalyst efficiency. Thus, addition of a strongly electron withdrawing trifluoromethyl group to the sulfur atom formed cisdichloro complex 4 (Fig. 2), which turned out to be the fastest Schelated catalyst after isomerization (either by light or heat); competing in reaction rates with the popular O-chelated catalysts [8e]. Interestingly, when using a chelating sulfoxide instead of a thioether, the trans-dichloro complex was obtained as the most stable isomer in CH<sub>2</sub>Cl<sub>2</sub> solution (5, Fig. 2), which was expectedly active towards ring-closing metathesis (RCM) and enyne metathesis reactions at ambient temperatures [12].



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Fig. 1. cis-Dichloro ruthenium sulfur complexes 1.

Recently, Grela and coworkers studied the effect of the aromaticity of the 5-membered metallacycle ring in several oxygenchelated naphthalene-based analogs of Hoveyda type catalysts [13]. Their results indicated that a stronger metallacyclic aromatic character increased chelate stability and inhibited precatalyst initiation. Therefore, in an attempt to further explore the role of aromaticity in chelated ruthenium catalysts, we decided to reduce metallacycle aromaticity by the simple approach of using an alkylidene instead of a benzylidene ligand. A literature survey reveals that alkylidene chelated complexes have been prepared in the past; for example, the 6-membered nitrogen chelated alkylidene complexes studied by Van der Schaaf and Grubbs [14], but the oxygen chelated alkylidene (5 and 6-membered) analogs were not stable enough to be isolated [15]. We expected that the stronger sulfur-ruthenium bond would still allow the formation of this binding form, albeit the reduced stability due to lack of aromaticity.

## **Results and discussion**

#### Synthesis of ruthenium complexes

The synthesis of thioethers **7a** and **7b** are described in Scheme 1. 4-Bromobutene was added to a mixture of thiol **6**, potassium carbonate and 18-crown-6 in acetone and refluxed overnight to afford



Fig. 2. Steric and electronic effects in sulfur chelated ruthenium complexes.

Synthesis of ruthenium complexes



Scheme 1. Synthesis of thioethers 7a and 7b.

the desired products **7** in quantitative yields after isolation. Consecutively, alkylidene complexes **8a** and **8b** were obtained by treatment of Grubbs 3rd generation catalyst (**Gru3**) [16] with **7a** and **7b** respectively in CH<sub>2</sub>Cl<sub>2</sub> (Scheme 2).

### Structural characterization of the prepared complexes

Complexes **8a** and **8b** were fully characterized by NMR spectroscopy and HRMS (ESI) (see Supporting information) analyses. The solid-state structure of complex **8a** was also studied using single crystal X-ray diffraction (Fig. 3).

The NMR spectra obtained were analyzed to understand the structure of ruthenium complexes **8a** and **8b** in solution. As typically observed for the *cis-dichloro* configuration, every proton and methyl group in the molecule was clearly resolved. When comparing the spectra of **8a** and **8b** to their benzylidene analogs **1d** and **1e** [8b,d], a significant difference in the chemical shift of the corresponding aromatic mesitylene protons can be observed. The most upfield mesitylene proton appears at 6.06 ppm for both **1d** and **1e** compared to 6.70 ppm (for **8a**) and 6.65 ppm (for **8b**). This change is associated with a diminished anisotropic effect in **8a** and **8b** due to the absence of the aromatic moiety in the chelated sulfur ligand. Moreover, a minor deshielding of the carbene proton can be observed in **8a** and **8b**. The proton appears at lower field (17.45 and 17.51 ppm) when compared to **1d** and **1e** (17.21 and 17.14 ppm) respectively.

Table 1 presents a comparison between selected bond lengths and angles of **8a** and its analog **1d** [8b]. Notably, despite the fact that complex **8a** is active at room temperature (*vide infra*), it exhibits a shorter sulfur—ruthenium bond compared to latent **1d**. This reduced bond length can be explained by the lack of aromaticity in the chelated ring — double bonds in aromatic rings being longer than standard double bonds [17]. Another important deviation in the structure between **1d** and **8a** can be found in the conformation of the five membered metallacycle. While in **1d** all the atoms comprising the cycle are found in the same plane, **8a** shows a



Scheme 2. Synthesis of precatalysts 8a and 8b.



Fig. 3. X-ray structure of complex 8a (ellipsoids drawn at 50% probability, hydrogen atoms and solvent molecules omitted for clarity).

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Solid state structure	comparison	of <b>1d</b> a	nd <b>8a</b> .

•		
	1d <sub>cis</sub>	8a <sub>cis</sub>
Bond		
C <sub>1</sub> -Ru <sub>1</sub>	2.024	2.030
S <sub>1</sub> -Ru <sub>1</sub>	2.347	2.334
Cl <sub>1</sub> -Ru <sub>1</sub>	2.360	2.396
Cl <sub>2</sub> -Ru <sub>1</sub>	2.394	2.397
S <sub>1</sub> -C <sub>25</sub>	1.788	1.793
S <sub>1</sub> -C <sub>24</sub>	1.797	1.821
C <sub>24</sub> -C <sub>23</sub>	1.405	1.517
C <sub>23</sub> -C <sub>22</sub>	1.447	1.500
C <sub>22</sub> -Ru <sub>1</sub>	1.844	1.823
Angle		
$Cl_1 - Ru_1 - Cl_2$	88.21	88.97
$Ru_1 - S_1 - C_{25}$	114.59	120.58
$C_{24} - S_1 - C_{25}$	100.11	101.98
$C_1 - Ru_1 - S_1$	93.88	90.75
Torsion angle		
Ru <sub>1</sub> -S <sub>1</sub> -C <sub>25</sub> -C <sub>26</sub>	118.22	21.45
$Ru_1 - S_1 - C_{25} - C_{30}$	-59.51	-165.63

typical puckered half-chair conformation (Fig. 4). This difference reduces the distance between the sulfur atom in **8a** to the mesitylene substituent on the NHC ( $C_{NHC}$ -Ru–S angle is 90.75°) compared to the structure observed for **1d** ( $C_{NHC}$ -Ru–S angle is 93.88°). Additionally, a significant structural difference between **1d** and **8a** is the orientation of the aromatic phenyl ring bonded to the sulfur atom (Fig. 4). Whereas the phenyl ring bound to the sulfur atom in **1d** is perpendicular to the mesitylene, the ring in **8a** is parallel to the mesitylene. Preliminary DFT calculations were carried out to further our understanding of the geometrical arrangements in these molecules.

### DFT calculations

In order to understand if the orientation of the S-substituent is a crystal packing effect or an electronic consequence of the nonaromaticity of the metallacycle, complexes 1a, 1d, 8a and 8b were studied by DFT calculations. Minimization and energy calculations were carried out using the same method previously developed by us [18], which provided good predictions for configurations of several chelated Ru complexes. The structures were optimized using gradient corrected (BP86) DFT calculations [19], at the LACVP\* level of theory [20]. The energies were then determined using LACV3P\*\*++ for higher level calculations with additional solvation energy, which was calculated using the Poisson-Boltzmann (PBF) continuum approximation, with  $CH_2Cl_2$  as a solvent [21]. Mimicking the experimental results, in the cis-dichloro configuration, the optimized structures for complexes 8a and 8b presented the phenyl/naphthyl rings parallel to the mesitylene ring, while 1d and 1e always converged to a structure with a perpendicular aromatic system. This calculation supports the observations from the solid state study, suggesting that the  $\pi$ -system of the aromatic substituent prefers to be perpendicular to an aromatic metallacycle, yet it may interact with the sulfur atom's available lone-pair when the metallacycle is not stabilized by aromaticity.

### Reactivity studies

To explore the reactivity profiles of the precatalysts, various olefin substrates were allowed to react in the presence of complexes **8a** and **8b**. Table 2 summarizes the results for benchmark RCM, cross-metathesis (CM) and ring-opening metathesis polymerization (ROMP) reactions. Surprisingly, good conversions were obtained for simple RCM reactions after only 4 h at room temperature (without UV irradiation). However, **8a** and **8b** were not efficient at catalyzing reactions with more challenging tetra-substituted products (entry 5, Table 2).

Even though possessing the unique *cis-dichloro* configuration, room temperature activity was observed for **8a** and **8b**, in stark contradiction to their benzylidene analogs **1d** and **1e** [8b,d]. This behavior suggests that the Ru–sulfur bond in precatalysts **8** can readily dissociate at room temperature (at r.t. only the *cis* isomer is observed in NMR spectroscopy. For a preliminary study on the *cis* to *trans* isomerization of precatalysts **8** under UV irradiation, see the Supporting information). This phenomenon may seem counterintuitive at first glance, because it conflicts with the simplistic view that the non-bonding electrons of sulfur would be more available for coordination as they do not participate in the resonance of the benzylidene. On the other hand, two effects dictate a more stable



Fig. 4. Comparison of solid state structures of 1d [8b] and 8a. The C<sub>1</sub>-Ru<sub>1</sub>-S<sub>1</sub> angles are presented. The different orientation of the phenyl ring is circled.

Table 2		
Formation of RCM, CM and ROMP n	products promoted by 8a	and <b>8b</b> .

Entry	Substrate	Product	Cat.	Conv. [%]
1	Ts N		8a 8b	75(33) <sup>a</sup> 86(36) <sup>a</sup>
2	Ts N	Ts N	8a 8b	81 <sup>b</sup> 95 <sup>b</sup>
3	EtO <sub>2</sub> C CO <sub>2</sub> Et	EtO <sub>2</sub> C CO <sub>2</sub> Et	8a 8b	76(26) <sup>a</sup> 97(34) <sup>a</sup>
4	OH	OH	8a 8b	66 <sup>a</sup> 68 <sup>a</sup>
5	EtO <sub>2</sub> C CO <sub>2</sub> Et	EtO <sub>2</sub> C CO <sub>2</sub> Et	8a 8b	0 <sup>a</sup> 0 <sup>a</sup>
6			8a 8b	4 <sup>b</sup> 35 <sup>b,c</sup>
7		PolyCOE	8a 8b	57 <sup>b,d,e</sup> 77 <sup>b,d,e</sup>

Reactions were conducted inside a nitrogen glove box. [Substrate] =  $0.1 \text{ M in CD}_2 \text{Cl}_2$ , [catalyst] = 5 mol%, 4 h,  $T = 25 \circ C$ . In brackets are yields under air.

Determined by <sup>1</sup>H NMR. b

Determined by GC-MS.

Additional products, such as (E) and (Z)-prop-1-ene-1,3-divldibenzene, were observed due to isomerization of the substrate's double bond.

With mesitylene as internal standard.

Oligomers were observed.

chelating effect for compounds 1. First, in accordance with Grela's finding [13], the aromaticity of the ruthenacycle in **1** can actually strengthen the chelate bond and inhibit precatalyst initiation. Secondly, as shown by our DFT calculations in the case of the alkylidenes 8a and 8b, the sulfur atom lone-pair electrons are strongly conjugated with the exocyclic aromatic ring, making the Ru-S bond more labile and ultimately leading to a significant increase in precatalyst initiation. As a consequence of this, also the stability of these new complexes is reduced, as clearly observed by comparing reaction conversion under air versus nitrogen (entries 1 and 3, Table 2). Precatalyst 8b, with the naphthalene moiety, exhibited even better activity compared to 8a. A possible explanation could be weakening of the Ru-S bond by a greater steric interference of the naphthalene moiety and an increased participation of the sulfur atom lone-pair electrons on the naphthyl  $\pi$ electron system.

Once again we turned to DFT energy calculations to test the hypothesis of increased activity at room temperature for 8. In addition to the cis structures of 1d and 8a described above, the dissociation transition state and dissociated structures, as well as the trans isomers, were studied at the LACVP\*/BP86 level of theory. For more precise energy results, single point energy at the



Fig. 5. Energy profiles of Ru-S bond dissociation.

LACV3P\*\*++/BP86 were calculated. As shown in Fig. 5, the aromatic complex 1d is calculated to require 146.1 kJ/mol for dissociation, compared to 96.2 kJ/mol for the non-aromatic complex 8a. This result indicates that in 8a, dissociation of the Ru–S bond (i.e. the initiation step for catalyst activation or isomerization to the trans isomer [8d]), occurs at significantly lower energies, supporting the experimental observation of room temperature activities with 8a and 8b as catalysts. The calculations also indicate that 8a is 15.2 kJ/mol more stable than  $8a_{trans}$  indicating that even though they are in equilibrium, the amounts of the trans isomer in solution is very small (for comparison, 1d is 30.3 kJ/mol more stable than 1d<sub>trans</sub>).

#### Conclusions

We have synthesized model chelating sulfur alkylidene ruthenium complexes 8a and 8b bearing a *cis-dichloro* configuration. In contrast with their benzylidene analogs, 1a and 1d, these complexes were active at room temperature. This is the first example of *cis-dichloro* sulfur chelated ruthenium precatalysts that exhibit reasonable metathesis activity at room temperature (without UV irradiation). DFT studies point to a lower transition state for the Ru-S dissociation, which allows for room temperature isomerization to the active trans form or even direct activation. On the other hand, the stability of the new complexes was hampered by the removal of aromatic stabilization of the chelating ring. The observed differences between the alkylidene complexes 8a and 8b and their benzylidene counterparts brings to light the important influence aromaticity may have on the stability and activity of chelated Grubbs type complexes. The findings may also have implications to develop strategies to stabilize, or destabilize, relevant organometallic complexes bearing chelating ligands.

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## Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jorganchem.2014.06.027.

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