Latent and Switchable Olefin Metathesis Catalysts

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Summary: Many latent olefin metathesis initiators have been described in the recent years. In this symposium manuscript, we present our contribution to the field, based on the use of different heteroatoms; namely sulfur, nitrogen, phosphorous and selenium; as chelators in ruthenium bidentate benzylidenes. The steric and electronic parameters were thoroughly studied and used in order to prepare not only latent pre-catalysts but also thermo- and photo-switchable systems – effectively granting control over both reaction initiation and interruption.

Keywords: latent initiators; organometallic catalysis; olefin metathesis; photochemistry; ruthenium benzylidenes

Introduction

The search for latent olefin metathesis catalysts is of special interest, principally in the context of ring-opening metathesis polymerization (ROMP) for industry.[1] Latent initiators allow mixing with the desired monomer, affording homogeneous solutions which can then be easily flowed into a mold before polymerization and/or cross-linking is induced. Also, latent initiators may prove to be safer to handle and provide longer shelf lives than more active catalysts. In a more academic setting, latency can also be explored in multi-component reactions, in the development of smart systems, and in the search for switchable catalysts, giving the tools to control when a specific reaction, among many, starts and when it ends. In ruthenium olefin metathesis, bidentate alkylidene ligands are very efficient in slowing down initiation and stabilizing the pre-catalyst by the chelate effect.[2]

Results and Discussion

The Hoveyda-Grubbs pre-catalyst **1a**,[3] being one of the most stable initiators published to date, was used as a paradigm for the development of novel latent pre-catalysts. Consequently, the exchange of the oxygen chelating atom by a sulfur atom (which typically creates stronger bonds to ruthenium atoms) should produce a less active complex by inhibiting reaction initiation, effectively providing an *off* state to the catalyst.[4]

Accordingly, a series of complexes **2a-e** with different substituents in the sulfur were prepared, and tested for olefin metathesis activity (Figure 1).[4,5] Surprisingly, the obtained complexes were observed both in *cis*-Cl_2 and *trans*-Cl_2 square pyramidal configurations; the *trans*-Cl_2 complex being only a kinetic product, which readily isomerized in solution to the *cis*-Cl_2 configuration. For the ring-closing metathesis (RCM) of diethyldiallylmalonate (DEDAM), the *cis*-Cl_2 S-chelated complexes were in all practical purposes inactive at room-temperature (25–30 °C), with the exception of complex **2e**, which presented a very sluggish reaction progress. Notably, this complex still catalyzed RCM of DEDAM in an air exposed solution after 20 days of continuous reaction![5]

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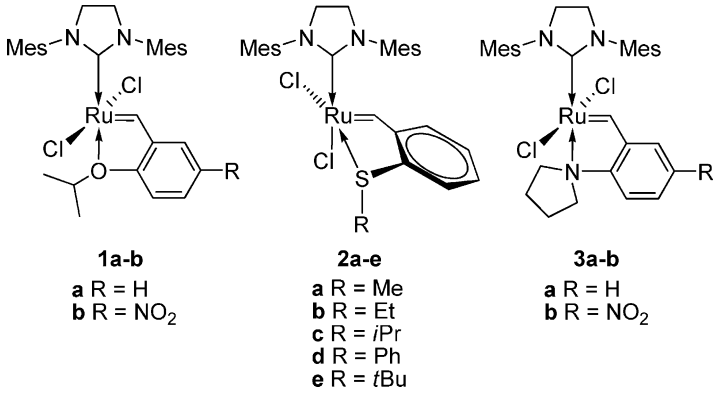


Figure 1.
Some chelated olefin metathesis catalysts.

Complexes **2a-d** could be thermally activated producing RCM products even after 2 weeks in solution with the diene, proving that the latent catalysts could be ''awakened'' after extended time periods. As expected, their activities, as well as the initiation temperatures, were clearly related to the steric hindrance caused by the sulfur substituents. Interestingly, the RCM reaction in complex **2c** could be stopped simply by cooling it to room-temperature. By alternating heating and cooling cycles, a thermally switchable system for RCM was achieved.[4]

Complex **2c** was also checked for its activity in ROMP,[6] mainly to check for latency. To our surprise, the system was also thermo-switchable with substituted norbornenes, cyclooctene and cyclooctadiene. This was unexpected, because the propagating species in ROMP does not (or should not) possess the chelating benzylidene moiety. In order to study the origin of this effect, polymer size was analyzed throughout the ROMP reaction. It was shown that from the very beginning, even at less than 5% conversion, polymers with an Mw greater than 10^6 g/mol and relatively low polydispersities (PDI ≤ 1.4) were present in solution. In addition, the sizes of the obtained polymers remained constant during the reaction and were not changed by modifying the monomer/initiator ratio. Polymer size could only be affected by changing reaction solvent and/or reaction temperature. We proposed that at high temperatures a minute amount of initiator is activated, and this propagates very quickly until decomposed. Therefore, the polymer size in this case is only a function of the turnover number (or maximum degree of polymerization) of the active species.

These satisfying results lead us to venture into other chelating atoms as ligands. In the past, Van der Schaaf,[2a] Grubbs,[2b–c] Grela[2d] and Slugovc[2e] showed how several bidentate benzylidenes with chelating sp^2 nitrogen atoms produced latent complexes. Surprisingly, no complex with a chelating sp^3 nitrogen atom had been reported. Therefore, we prepared sp^3 nitrogen containing complexes **3a-b** (Figure 1), analyzed their structures and studied their activity in olefin metathesis.[7]

Pyrrolidine complex **3a** was shown to have a thermo-switchable behavior, similar to S-chelated complexes **2**. It is worth noting that this complex showed the typical *trans*-Cl_2 configuration; nevertheless it was still latent, although its activation temperature was much lower compared to that of the sulfur complexes.

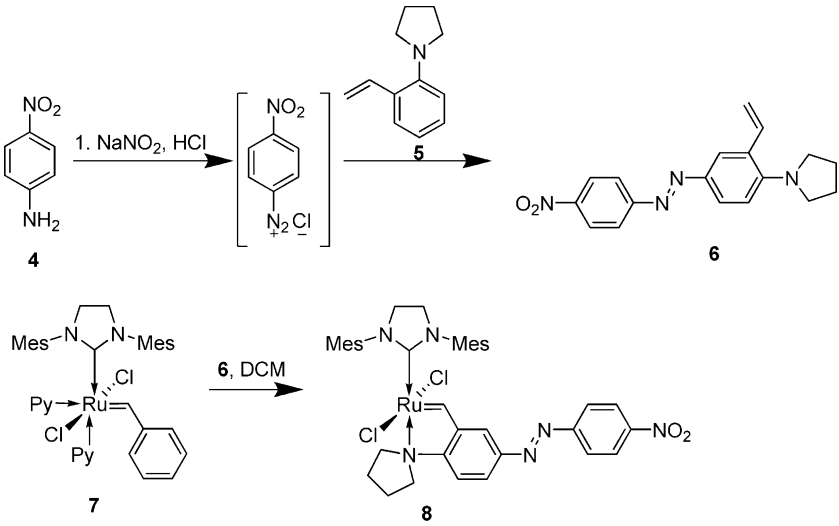
Complex **3b** proved to be fairly active at room temperature,[7] evidencing a similar effect as the Grela catalyst **1b**.[8] Taking this into account, a first attempt to prepare a light-switchable catalyst, by making use of an azobenzene *cis-trans* isomerization, was carried out.[9] The underlying concept was that if a 4'-nitroazobenzene moiety could

be attached to a bidentate N-chelating benzylidene, the electron withdrawing differences between *cis* and *trans* isomers would afford different reactivities. Thus, complex **8** was synthesized as described in Scheme 1. 4-nitroaniline **4** was converted into its azonium salt by sodium nitrite and reacted with styrene derivative **5**, prepared as described elsewhere,[7] affording the desired azostyrene derivative **6**, exclusively in the *trans* configuration. Olefin metathesis with pyridine complex **7** gave the desired compound **8** in good yields. The single crystal X-ray structure of **8** is shown in Figure 2.

Novel complex **8** and DEDAM were dissolved in methylene chloride at room temperature and, unfortunately, only sluggish reactivity was observed. When heated, olefin metathesis was more evident, as in the case of complex **3a**. However, when irradiated under UV-light, the complex quickly decomposed, and the *cis* isomer could not be observed or tested.

Using another approach, we serendipitously observed that the kinetic *trans*-Cl_2 isomer of the sulfur chelated complex **2d** could activate olefin metathesis reactions at room temperature. We were aware that previous studies had shown that $RuCl_2(DMSO)_4$ undergoes photo-dissociation and posterior isomerization from the more stable *cis*-Cl_2 configuration to the less stable *trans*-Cl_2 configuration.[10] Thus, we surmised that this photo-isomerization process may take place in the S-chelated *cis*-Cl_2 complexes as well. Indeed, UV irradiation at 365nm of *cis*-Cl_2 complexes **2c,d** and **2f,g** elicited *cis* to *trans* isomerization to about 30% conversion.[11] When substrate was added after UV irradiation, metathesis activity was observed for complexes **2d,f,g**. So, the same complexes which are completely latent to most olefin metathesis substrates could be photo-activated at room temperature, providing good conversions. Since the *cis*-Cl_2 configuration is thermodynamically more stable, heating the reaction solution at 80 °C for 5 minutes isomerizes the *trans*-Cl_2 complexes to its inactive *cis*-Cl_2 isomer, effectively stopping the reaction. At a later stage, UV light can be used to activate more complex and continue the reaction. Remarkably, a switchable system is again achieved; this time using light as the activating factor, and (somewhat counter intuitively) heat to turn the reaction off.

From these and previous results by Grubbs[2b] and Grela,[2d] it is clear that



Scheme 1.
Synthesis of catalyst **8**.

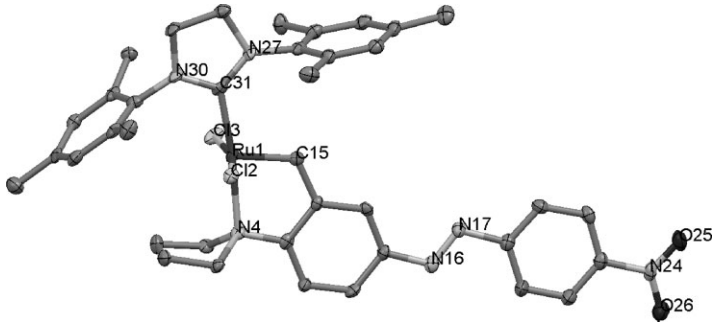
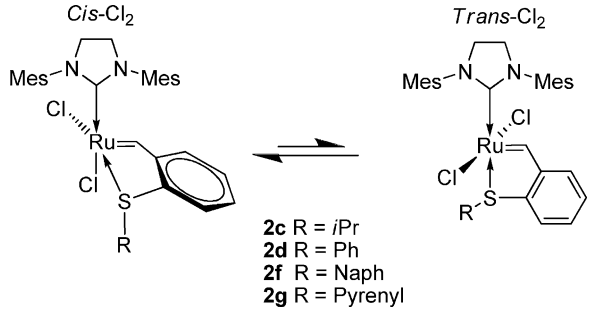


Figure 2.
ORTEP illustration of complex **8**. Ortep ellipsoids displayed at 30% probability level. Hydrogens and solvent molecules omitted for clarity.



Scheme 2.
UV *cis-trans* isomerization of sulfur chelated Ru complexes.

complexes in the *cis*-Cl_2 configuration are less active, which is a desirable property in the design of latent complexes.[12] We decided to study the influence of the heteroatom on the configuration, and as a consequence, the initiation rate of the pre-catalysts.

DFT calculations were used in order to assess the difference in the energy between *cis*-Cl_2 and *trans*-Cl_2 configurations.[13] It was clearly observed that the more electron donating heteroatoms prefer the *cis*-Cl_2 configuration, probably as a consequence of the strong *trans influence* caused by the NHC. In order to check this hypothesis we prepared complexes **9–11** (Figure 3). It was shown that, as predicted, complex **9** assumed the *trans*-Cl_2 configuration, while **10** and **11** assumed the *cis*-Cl_2 configuration in solution. This study provides significant

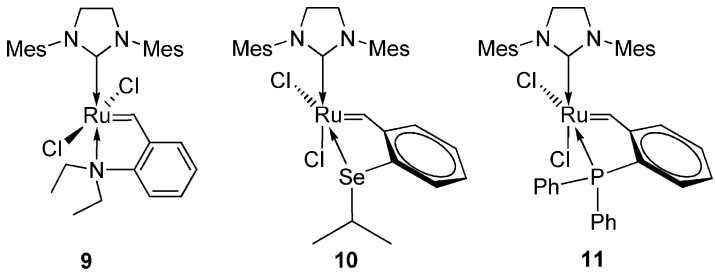


Figure 3.
N, Se, and P chelated olefin metathesis complexes.

support to the use of DFT calculations for prediction of configurational preferences in chelated ruthenium benzylidenes.

Conclusions

In order to obtain the ideal latent and switchable olefin metathesis pre-catalyst, both the *off* position – how to make the complex less active – as well as on the *on* position – high reactivity after activation – must be taken into account. Our work has shown that using complexes in the *cis*-Cl_2 configuration may prove a viable pathway towards this goal. One reason is the high barrier these complexes need to overcome in order to become active. The electronic configuration of the complex is very different between the two states – which can be exploited in order to independently alter the *off* or the *on* states. Light and/or heat can be used to interchange between the two states, and selective activation, as well as deactivation of pre-catalyst, may be judiciously achieved.

Experimental Part

General

All reagents were of reagent grade quality, purchased commercially from Sigma, Aldrich, Fluka or ABCR and used without further purification. All solvents were dried and distilled prior to use. Purification by column chromatography was performed on Davisil chromatographic silica media (40–60 μm) or Fluka 0.05–0.15 mm neutral alumina.

Mass spectrometry was obtained using an Agilent 6850 GC equipped with an Agilent 5973 MSD working under standard conditions and an Agilent HP5-MS column or with an ESI source (Thermo Fisher Scientific), where spectra were collected in the positive ion mode and analyzed by Xcalibur software (Thermo Fisher Scientific).

NMR spectra were recorded on Bruker DPX_{200} or DMX_{500} instruments; chemical shifts, given in ppm, are relative to Me_4Si as the internal standard, or to the residual protio solvent peak.

Compound **6**: A solution of **4** (1 eq, 2.89 mmol, 0.399 gr) in acetic acid (4 ml) was cooled to 10 °C. HCl (0.36 ml) was added, and the mixture was stirred for 15 min. Then, $NaNO_2$ (1.2 eq, 3.47 mmol, 0.239 gr) in H_2O (4 ml) was added dropwise, followed by **5** (1 eq, 2.89 mmol, 0.50 gr). The mixture was stirred for 1 h at room temperature. The reaction was then washed with a saturated solution of K_2CO_3 until pH = 7. The black precipitate was filtered by suction. The filtrate was then purified using neutral alumina column chromatography (petroleum ether 2: 1 DCM) and recrystallized from hexane. Purple crystals were obtained (Yield 30%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.33 (d, 2H, J = 9); 7.95 (d, 1H, J = 2.5); 7.93 (d, 2H, J = 9); 7.81 (dd, 1H, J_o = 2.5, J_m = 9); 7.05 (dd, 1H, J = 10.6, J = 17.2); 6.79 (d, 1H, J = 9), 5.61 (dd, 1H, J = 1.25, J = 17.2), 5.28 (dd, 1H, J = 1.25, J = 10.6), 3.51 (m, 4H); 1.97 (m, 4H). ^{13}C NMR (50 MHz, $CDCl_3$): 156.65, 151.55, 147.38, 144.81, 137.19, 126.59, 125.92, 124.71, 124.67, 122.64, 113.99, 51.83, 25.72. GC-MS (EI): m/z $(M\text{-}C_3H_7)^+$ calc = 279.09, found = 279.10.

Complex **8**: A solution of **7**[14] (50 mg, 0.069 mmol, 1 eq) and **6** (24.3 mg. 0.076 mmol, 1.1 eq) in 5 ml of freshly distilled DCM was refluxed for 2 h under nitrogen. Then DCM was removed under reduced pressure. The residue was washed with pentane, and then dissolved in DCM. Pentane was added for precipitation of **8** as brown crystals which were filtered and dried under high vacuum (77%). ^{1}H NMR (500 MHz, CD_2Cl_2): 16.99 (s, 1H); 8.38 (d, 2H, J = 9.3); 8.20 (dd, 1H, J_o = 8.3, J_m = 2.45); 8.01 (d, 2H, J = 9.3); 7.42 (d, 1H, J_m = 2.45), 7.36 (d, 1H, J_o = 8.3); 7.05 (bs, 4H); 4.13 (s, 4H); 3.89 (m, 2H); 2.49 (m, 20H); 1.6 (m, 2H); 1.28 (m, 2H). ^{13}C NMR (125 MHz, CD_2Cl_2): 156.14, 154.95, 152.01, 151.09, 148.52, 139.66, 138.68, 138.60, 137.90, 137.28, 133.64, 129.25, 128.53, 124.63, 123.59, 123.51, 123.08, 112.50, 58.56, 51.56, 50.85, 22.46, 20.92, 20.65, 20.31, 17.97. MS (ESI): m/z $(M\text{-}H)^+$ calc = 785.17, found = 784.72.

$C_{38}H_{42}Cl_2N_6O_2Ru$, $M = 786.75$, orthorhombic, space group $P\ bca$, $a = 8.6583(2)$, $b = 25.5194(5)$, $c = 34.9045(7)$ Å, $\beta = 90.00^\circ$, $V = 7712.3(3)$ Å^3, $Z = 8$, $T = 110(2)$ K, $\rho_{calcd} = 1.355$ gcm^{-3}, μ(Mo-Kα) $= 0.585$ mm^{-1}, 18518 reflections measured ($2\theta_{max} = 50.8^\circ$), R-Factor(%) 7.16.

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