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Research Article

Imposing Latency in Ruthenium Sulfoxide-Chelated Benzylidenes: Expanding Opportunities for Thermal and Photoactivation in Olefin Metathesis

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Cite This: *ACS Catal.* 2020, 10, 4827−4834

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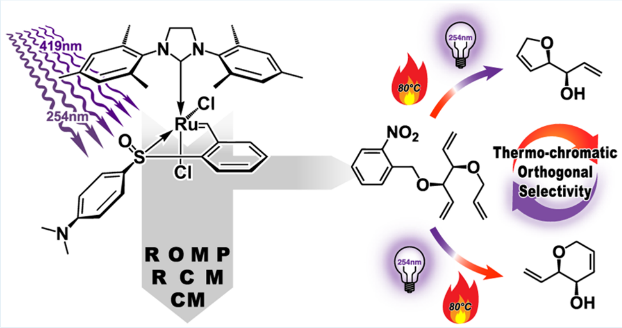
ABSTRACT: Herein we show the design and synthesis of an electron-rich, sulfoxide-chelated, ruthenium benzylidene. In contrast to previously reported sulfoxide-chelated ruthenium benzylidenes, this complex is more stable in a *cis*-dichloro conformation and is thus latent in typical olefin metathesis reactions. The complex was characterized by NMR, UV−vis, and X-ray spectroscopy, alongside density functional theory computations. The latent precatalyst could be activated thermally and, depending on the solvent, by UV−C or visible light. In addition, an original "thermo-chromatic" orthogonal sequence was developed, further improved by the use of a thioether chelated complex, where a divergent two-step synthesis can lead to a dihydrofuran or a dihydropyran depending only on the order by which the different stimuli, heat or light, are applied.



KEYWORDS: *olefin metathesis, ruthenium, sulfoxide, photoinduced, sulfur-chelated*

■ INTRODUCTION

Olefin metathesis is a powerful synthetic tool in organic chemistry that allows for the straightforward formation of carbon−carbon double bonds. The importance of this reaction has driven an enormous growth in the design and synthesis of well-defined catalysts, which in turn have given organic chemists the opportunity for further enrichment and fine-tuning of selected reaction parameters and synthetic strategies.[1] Most recent efforts in the field of catalyst diversification are focused on the design and modification of the ligand shell around the metal center, resulting in the improvement of selectivity,[2] activity,[3] or other properties.[4] For example, a judicious choice of ligands can inhibit the initiation step, facilitating the design, synthesis, and study of latent precatalysts that can be activated by external stimuli, such as heat, acid, ultrasound, or light (Figure 1).[5]

While many different strategies have been used to achieve latency,[6] a convenient approach is the use of sulfur chelation.[7] These complexes exist mainly in a stable and inactive *cis*-dichloro configuration that can undergo isomerization to the reactive *trans*-dichloro isomer to initiate the olefin metathesis reaction.[8] A related family of sulfur bound ruthenium alkylidene complexes uses sulfoxides as the chelating unit.[9] In contrast to the thioether-containing complexes, the sulfoxide chelated complexes appear only in *trans*-dichloro configurations and are consequently all active at room temperature. These complexes are more stable in the active *trans*-dichloro configuration probably because the chelating sulfoxide moiety is a weaker sigma electron donor ligand (compared to the thioether).[8b,d] It was our hypothesis that strengthening the electron donation of the sulfoxide could lead to a change in the geometry of the complex.

Herein, we report the synthesis, characterization, and catalytic properties of the first latent *cis*-dichloro sulfoxide chelated ruthenium benzylidene. This was achieved by increasing the electron density on the sulfur atom by introducing an electron donating group on the corresponding aromatic ring. The rich photochemistry of sulfoxide-ruthenium complexes[10] provided a novel entry to photoactivation of the metathesis precatalyst at wavelengths different than those used in the photoactivation of S-chelated complexes. These results inspired the development of an original thermo-chromatic orthogonal selective synthesis of five- or six-membered ring substrates, depending on the sequence of the applied stimuli.

Received: February 8, 2020
Revised: March 26, 2020
Published: March 27, 2020

ACS Publications

https://dx.doi.org/10.1021/acscatal.0c00676
ACS Catal. 2020, 10, 4827−4834

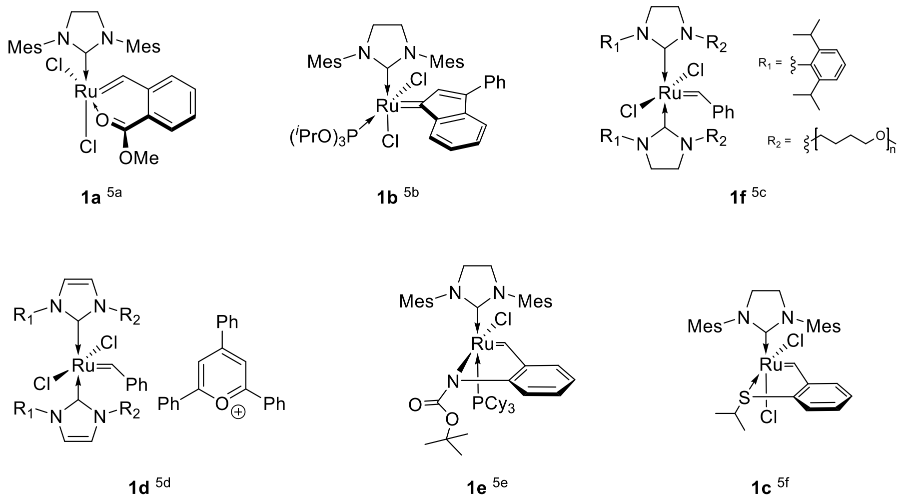
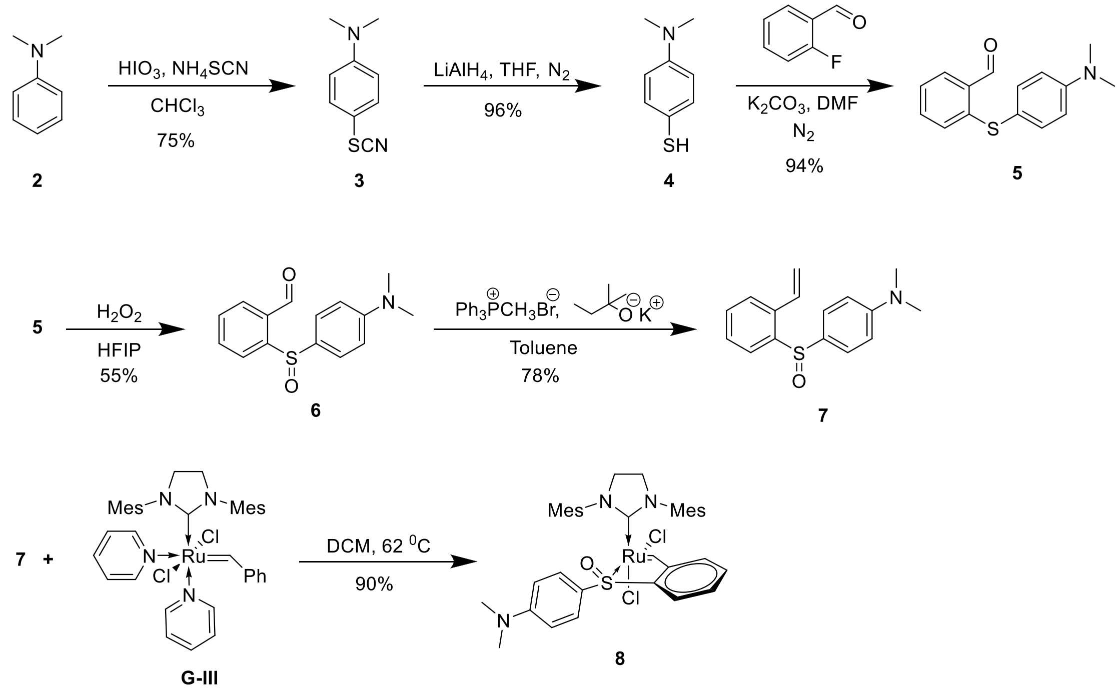


Figure 1. A few examples of latent olefin metathesis catalysts.

Scheme 1. Synthesis of Complex 8



RESULTS AND DISCUSSION

In a most influential finding, Grela et al. discovered that adding a strong electron withdrawing group (EWG), i.e., a nitro group, to the benzylidene ring in a Hoveyda−Grubbs complex can significantly enhance its catalytic activity.[11] Concomitantly, it was also shown that an electron donating group (EDG) reduced the activity of the complex.[12] As previously mentioned, sulfoxide-chelated ruthenium catalysts are not latent for typical olefin metathesis reactions at ambient conditions. Nevertheless, we hypothesized that increasing the electron density on the sulfur atom could stabilize a *cis*-dichloro configuration, leading to a new type of latent complex. To support this theory, preliminary density functional theory (DFT) calculations were conducted on a sulfoxide-chelated ruthenium benzylidene complex containing a dimethylaniline EDG, **8**. Indeed, the computational studies predicted a significant preference for the *cis*-dichloro configuration (with an energy difference of 8.1 kcal/mol); thus, a pathway was outlined for its synthesis.

The desired complex was synthesized according to Scheme 1. Thiocyanation of *N*,*N*-dimethylaniline **2**, followed by reduction of intermediate **3** with $LiAlH_4$, afforded thiophenol **4** in good overall yields. **4** was mixed with commercially available 2-fluorobenzaldehyde in dry DMF in the presence of potassium carbonate to provide the aromatic nucleophilic substitution product **5**. Then, thioether **5** was oxidized with hydrogen peroxide in hexafluoroisopropanol (HFIP), followed by a classical Wittig reaction that produced the desired styrene ligand **7**. Finally, a simple ligand exchange with **G-III** yielded complex **8** as the major product with 90% yield.

The novel ruthenium complex was fully characterized by ^{1}H- and ^{13}C NMR, HR-MS, UV−vis, and single crystal X-ray spectroscopy (Figure 2).

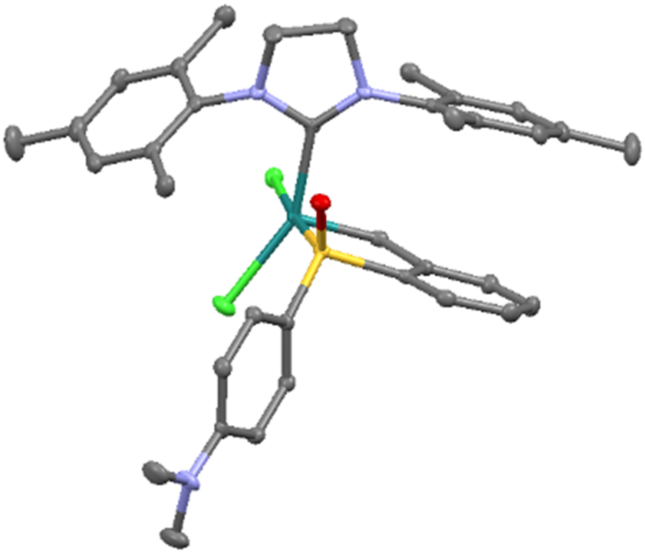


Figure 2. Single-crystal X-ray structure of **8**. Ellipsoids are shown at the 50% probability level. Hydrogen atoms and solvent molecules were omitted for clarity.

Several insights regarding the structure of **8** could be attained from its synthesis and characterization. First, the *trans*-dichloro complex was observed as the kinetic product, which quickly isomerized to the cis geometry in solution, mimicking the behavior observed for the thioether complexes (see Supporting Information). Moreover, as predicted by computations, the heteroatom that chelates the ruthenium center is the sulfur and not the oxygen (the latter being 10.6 kcal/mol higher; see Supporting Information).

Table 1 compares critical bond lengths between complex **8** and relevant examples of both *cis*-dichloro and *trans*-dichloro S-chelated complexes from the literature.[7g,10b,c] Notably, the Ru−S bond in complex **8** is significantly shorter than the Ru−S bond in *cis*-dichloro thioether complex **10** (2.258 Å vs 2.347 Å) (and also shorter than the Ru−S bond for a recently reported nonchelated DMSO complex),[13] making this the shortest Ru−S bond to date for S-chelated Ru alkylidenes. In addition, **8** also portrays the shortest $C_{benzylidene}$−Ru bond for all the complexes shown.

All DFT computations were carried out with Gaussian[14] at the MN15/def2-TZVP(DCM)//MN15/def2-SVP level,[15,16] including implicit solvent with the SMD[17] method in the single point energies and Gibbs energy corrections with the geometry optimization method. The computations indicate that compound **8** in its cis form is 8.1 kcal mol^{-1} more stable than its trans isomer, supporting the experimental findings. However, the DFT results for **9** are conflicting, as it also suggested a cis conformation for this complex (8.2 kcal mol^{-1} lower than the trans), in stark contrast to the experimental outcome. This contradiction between theory and experiment remains an open question that we will attempt to address in the near future.

To complete the characterization of **8**, its UV−vis absorption spectrum in methylene chloride (DCM) was measured and compared to that of complex **10** (Figure 3).

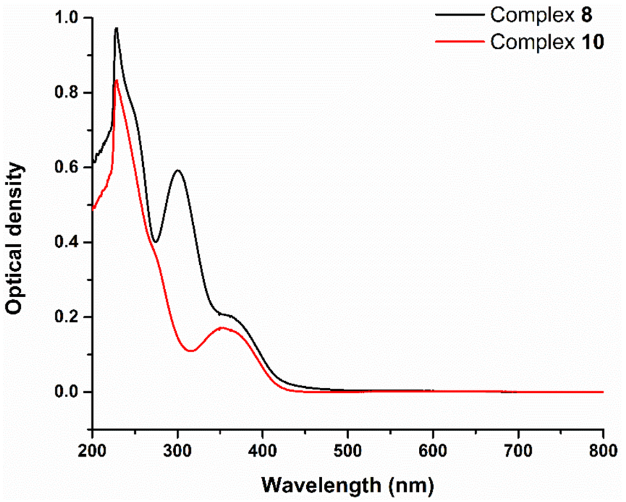
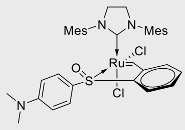
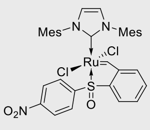
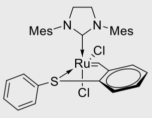
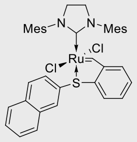


Figure 3. UV−vis absorption spectrum of complexes **8** (black) and **10** (red) in DCM.

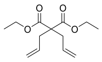
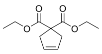
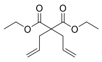
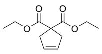
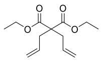
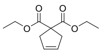
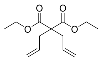
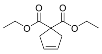
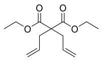
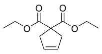
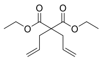
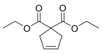
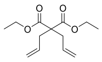
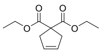
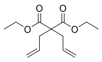
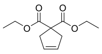
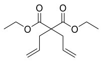
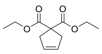
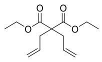
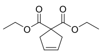
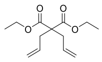
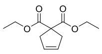
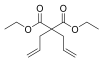
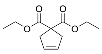
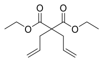
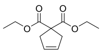
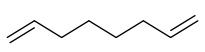
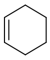
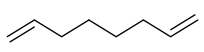
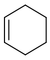
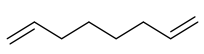
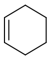
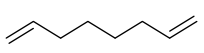
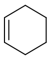
The most salient difference between the spectra is a strong absorption band for complex **8** at 303 nm. The same additional absorption appearing on **8** but not on **10** can be seen in the computed TD-DFT spectra (see Supporting Information), confirming the validity of the computational results.

Table 1. Bond Lengths of Complexes 8−11[a]

Bond	 8	 9	 10	 11
Ru-S	2.258Å (2.297Å)	2.3318Å (2.391Å)	2.347Å	2.475Å
$C1_{NHC}$-Ru	2.029Å (2.013Å)	2.102Å (2.041Å)	2.024Å	2.035Å
$C_{benzylidene}$-Ru	1.828Å (1.818Å)	1.834Å (1.824Å)	1.844Å	1.841Å

[a] In parentheses, the computed values.

Table 2. RCM Reactions Catalyzed by 8 under Different Activation Stimuli[a]

Entry	Substrate	Product	Solvent	Activation method	Time (h)	Conversion (%)
1			DCM-d_2	Thermal 30^{0}C	1 24	0 0
2			toluene-d_8	Thermal 30^{0}C	3.5 21.5	2 2
3			toluene-d_8	Thermal 80^{0}C	1 21	19 28
4			DCM-d_2	UV 254nm	1 3	0 0
5			toluene-d_8	UV 254nm	0.5 1.5	36 (1) 49 (1)
6			DCM-d_2	UV 300nm	1 22	0 0
7			toluene-d_8	UV 300nm	0.5 3	4 (0) 14 (0.5)
8			DCM-d_2	UV 350nm	3.5 24	0 (0) 10 (0)
9			toluene-d_8	UV 350nm	1 23	15 (2) 69 (4)
10			DCM-d_2	Vis 419nm	1 20	3 (0) 74 (4)
11			toluene-d_8	Vis 419nm	1 20	6.5 (0) 17 (2)
12			Benzene-d_6	Vis 419nm	1 21.5	4 (1) 21 (3)
13			TCE-d_2	Vis 419nm	1 20	3 (0) 32 (1)
14			DCM-d_2	Thermal 30^{0}C	24 96	0 5
15			toluene-d_8	Thermal 30^{0}C	96	11
16			DCM-d_2	Vis 419nm	1 69	4 (1) 94 (7)
17			tolene-d_8	UV 254nm	0.5 2	39 (2) 51 (4)

[a] Conditions: 2 mol % catalyst loading, 0.1 M substrate in 0.5 mL solvent, irradiation was performed in a Rayonet photoreactor, temperature in the reactor while running reactions was 30 °C. Conversions were monitored and determined by ^{1}H NMR (see Supporting Information) (in parentheses, dark control experiments).

■ RELATIVE REACTIVITY STUDIES

Having structurally characterized complex **8**, its activity in the benchmark ring closing metathesis reaction (RCM) of diethyl diallylmalonate (DEDAM) was studied. To our satisfaction, **8** was indeed found to be latent for RCM after 24 h at room temperature both in DCM and toluene (Table 2, entries 1 and 2). The complex was then stimulated by two methods: heating (thermal) and UV irradiation (photochemical). Heating the toluene solution to 80 °C afforded about 30% conversion after 1 day, highlighting the fact that even though thermal activation is possible, it is not an efficient way to activate **8**. We then turned our attention to activation with light. Notably, after 24 h irradiation at 350 nm in DCM, only 10% conversion to the RCM product was observed by NMR, as well as significant decomposition of the complex. Shorter wavelengths, i.e., 300 and 254 nm did not induce RCM in DCM at all due to decomposition of the complex. Thus, irradiation with a less energetic light source, 419 nm, was attempted with the expectation that this would reduce catalyst decomposition. To our great satisfaction, 74% RCM conversion could be observed in this case (Table 1, entry 10), making it the first ruthenium−sulfur chelated complex that can be efficiently photoactivated with visible light.

Irradiation with 419 nm light proved to be much less efficient in other solvents compared to DCM (Table 1, entries 11−13). However, the photochemical behavior of **8** in toluene proved to be quite surprising. The best wavelength for activation in toluene was found to be 350 nm, where about 70% conversion was achieved after 23 h of irradiation. Nonetheless, the most surprising result was that irradiation at 254 nm gave fair RCM conversions (Table 1, entry 5), making this the first example of an S-chelated complex that can be activated for metathesis by irradiation with UV-C. Because no significant difference could be observed in the computed absorption spectra of **8** in DCM and toluene, we carried out an experiment to determine whether aggregation induced emission in toluene, derived from the lower solubility of the complex in this solvent, could be the cause for the activity. Indeed, an additional emission in the UV-A region was observed when a toluene solution of **8** was irradiated with UV-C. This phenomenon was not observed when the same experiment was repeated in DCM (see Supporting Information). To further study this interesting phenomenon, the photoinduced RCM of 1,7-octadiene (OD) with UV-C in toluene and with visible light in DCM was also studied. Indeed, the results in toluene were similar for both RCM reactions. On the other hand, visible light induced RCM of OD in DCM was even more efficient than the RCM of DEDAM. Nearly full conversion to cyclohexene was observed after prolonged irradiation times, disclosing that the precatalyst can be activated even after days of continuous visible light irradiation.

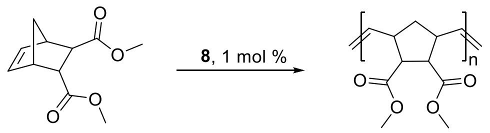
To summarize the photochemical activation of RCM, it was shown that there is a strong solvent dependency which dictates which solvent should be used depending on the color of light used. If UV-C (254 nm) is needed, then toluene should be used as a solvent, but if irradiation is in the visible range (419 nm), then DCM was shown to be the best solvent for this reaction.

A wider scope of photoinduced olefin metathesis reactions was then probed. The self-metathesis reaction of methyl oleate was first studied. Neat methyl oleate was heated at 100 °C for 24 h in the presence of 1 mol % of **8**. GC-MS analysis showed the expected self-metathesis products with some isomerization byproducts typically obtained when the reaction is run at high temperatures.[4b] In contrast, when the reaction was carried out in the visible light protocol with DCM as the solvent, self-metathesis proceeded without any double bond migration byproducts. In addition, the useful self-metathesis reaction of jojoba oil was also considered. Under thermal activation, neat jojoba oil was consumed, and the expected volatile C18 component (together with the isomerized homologues) could be readily observed by GC-MS analysis. However, contrary to the observation with the methyl oleate, the reaction did not proceed at all when carried out in DCM with visible light irradiation. The extracted jojoba oil usually possesses a yellowish tint derived from impurities present in the jojoba seeds. To our satisfaction, when the jojoba oil was purified with activated charcoal to remove the colored impurities, the visible light protocol with DCM as the solvent efficiently promoted the self-metathesis of this natural product (see Supporting Information). This example is quite revealing and clearly shows that colored impurities in the samples may hinder catalyst activation within this protocol.

Furthermore, the catalytic activity of precatalyst **8** for the difficult cross metathesis (CM) with acrylates was also studied. Under the visible light protocol, CM of 1-octene with methyl acrylate (1:3) in DCM afforded just 34% conversion. Even though conversions in this case are relatively low, to the best of our knowledge this is the first example where visible light photoinduced CM with an acrylate is successful.

One of the most widely used olefin metathesis reactions, especially when these are photoactivated, is ring-opening metathesis polymerization (ROMP). Thus, photoinduced ROMP (PROMP) of dimethyl 5-norbornene-2,3-dicarboxylate was initiated in toluene by irradiation with 254 nm light and in methylene chloride with 419 nm light (Table 3). Both these wavelengths had not been previously used for PROMP with S-chelated catalysts. Happily, the polymerization in toluene-d_8 proceeded as expected (Table 3 and Supporting Information). Unfortunately, with DCM-d_2 as the solvent and 419 nm light, the reaction was much slower and afforded only 35% conversion after 3 days of irradiation. Notwithstanding the relatively low conversions, in both cases the photochemical reactions produced well-defined metathesis polymers that could be isolated and characterized, expanding the possibilities of using different light sources for PROMP with S-chelated photolatent catalysts.

Table 3. ROMP of Dimethyl 5-Norbornene-2,3-dicarboxylate[a]



entry	solvent	activation method	time (h)	conversion (%)[b]	M_w (g/mol)[c]	PDI[c]
1	Tol-d_8	UV 254 nm	4	64	399,200	1.4
2	DCM-d_2	Vis 419 nm	72	35	580,900	2.0

[a] Conditions: 1 mol % catalyst loading, 0.5 M substrate in solvent, irradiation was performed in a Rayonet photoreactor. [b] Conversions were determined by ^{1}HNMR integration of the olefin signals. [c] Determined by triple detector GPC analysis (see Supporting Information).

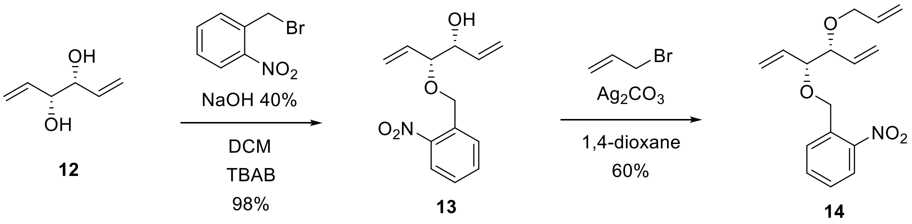
REGIOSELECTIVE THERMO-CHROMATIC ORTHOGONALITY

The fact that **8** could be activated by two different wavelengths inspired us to develop a novel chromatic orthogonal system.[18,19] Specifically, given that visible light could be used in a much more effective manner for catalyst activation, we decided to probe the use of the ubiquitous *o*-nitrobenzyl protecting group to help guide the sequence of the photoinduced reaction.

Thus, the novel substrate 1-((((3*R*,4*R*)-4-(allyloxy)hexa-1,5-dien-3-yl)oxy)methyl)-2-nitrobenzene (**14**) was prepared from (3*R*,4*R*)-3,4-dihydroxy-1,5-hexadiene (**12**)[20] (Scheme 2).

First, the conditions needed for the cleavage of the photolabile protecting group (PPG) in compound **14** were studied. Indeed, facile photocleavage was conveniently achieved both in DCM and toluene with 300 nm light. Unfortunately, irradiation of **14** at 419 nm in the presence of **8**

Scheme 2. Synthesis of Substrate 14



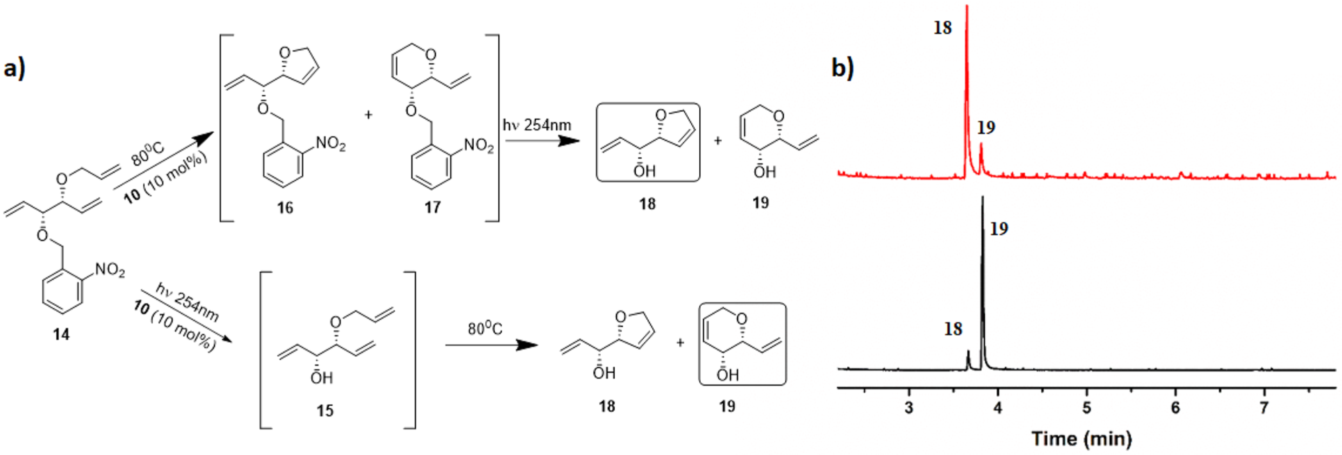


Figure 4. Thermo-chromatic orthogonal system. (a) Reaction sequence. (b) GC-MS trace of the isolated product mixture (top, heating followed by irradiation; bottom, irradiation followed by heating; see Supporting Information for experimental details).

could not induce the desired metathesis reaction. As previously observed with the jojoba self-metathesis reaction, it appears that the yellowish color of the solution of compound **14** prevented the efficient photoactivation of precatalyst **8** with visible light. Therefore, a different approach was envisioned, dubbed the "thermo-chromatic orthogonal system". In this, the guiding protecting group can be removed by using light, while the metathesis reaction can be induced by heat in an orthogonal fashion. However, when complex **8** was thermally activated under the reaction conditions, the efficiency was poor, and only about 30% RCM conversion could be obtained. Fortunately, using complex **10** resulted in a much more efficient system. Thus, either compound **18** or **19** could be selectively produced as the major product with good to excellent selectivity by just applying the different stimuli in opposite order. As shown in Figure 4, when the PPG was cleaved first by irradiation at 254 nm, followed by heat induced metathesis, a 9:1 selectivity in favor of the dihydropyran was obtained. This selectivity is due to the lessened steric hindrance for the formation of the six-membered ring after the PPG is removed. Notably, when the order was reversed and heat preceded the light stimulus, the dihydrofuran compound was obtained as the major product with 4:1 selectivity. Both pathways afforded conversions of about 85%. The GC-MS traces in the figure nicely highlight the divergent selectivity that could be achieved by this simple methodology.

CONCLUSIONS

A profound understanding of the factors that are required to produce latent *cis*-dichloro ruthenium benzylidenes in S-chelated systems led to the synthesis of the first olefin metathesis latent *cis*-dichloro sulfoxide chelated ruthenium benzylidene, **8**. The new complex was fully characterized by several experimental techniques, such as NMR, UV–vis, and single crystal X-ray spectroscopy, and computational DFT analyses. Its olefin metathesis thermal and photochemical induced activity was studied for several RCM, CM, and ROMP reactions; showing that **8** can induce olefin metathesis in DCM when irradiated with visible light and also in toluene when UV-C is used. Moreover, a novel orthogonal "thermo-chromatic" system was developed, where either a five-membered ring or a six-membered ring can be selectively synthesized depending on the order of the stimuli applied. The novel interplay of light activation and thermal activation can lead to important advances in the field of photochemistry, and we are currently further developing this original methodology.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acscatal.0c00676.

Synthetic procedures and characterization (^{1}H-, ^{13}C NMR, and HRMS), crystallographic data summary for **8**, DFT computational details, NMR spectra of thermal and photoactivated metathesis and GC-MS analyses (PDF)

(CIF)

(TXT1, TXT2, TXT3, TXT4, TXT5, TXT6)

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https://pubs.acs.org/10.1021/acscatal.0c00676

Funding

The Israel Science Foundation is gratefully acknowledged for financial support.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

Dr. Ravindra Phatake is gratefully acknowledged for technical assistance in the orthogonal thermo-chromatic and fluorescence experiments.

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