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Allenyl esters as quenching agents for ruthenium olefin metathesis catalysts

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ABSTRACT

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Keywords: Metathesis quenching Metathesis poison Allenyl esters **Abstract**— In the attempt to synthesize substituted allenyl esters through a metathesis coupling of unsubstituted allenyl esters and alkenes using a variety of ruthenium catalysts, it was discovered that allenyl esters themselves cleanly arrested the activity of the catalysts. Further studies suggests possible utility of allene esters as general quenching agents for metathesis reactions. To explore this idea, several representative olefin metathesis reactions, including ring closing, were successfully terminated by the addition of simple allenyl esters for more convenient purification.

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Our recent work in the area of allenyl carbonyl chemistry has focused on the development of synthetic methods for their construction¹ and utilization in the synthesis of densely functionalized bridged bicycles.² Recently, we investigated the reactivity of simple allenyl esters in cross metathesis reactions with alkenes to form more substituted allenyl esters using catalysts 1 - 4 developed by Grubbs and Hoveyda (Figure 1). Although the use of ruthenium catalysts for olefin metathesis, ring-closing metathesis, and enyne metathesis are well documented in the literature, their use with carbonyl-conjugated allenes is unknown.³ In the present work, we describe our attempts to form γ -substituted allenyl esters using a metathesis approach. As will be discussed, ruthenium based catalysts failed to afford the desired cross-coupling (or even homo-coupling) products. Instead, we found that allenyl esters acted as effective catalyst quenching agents.



Figure 1. Catalysts used in this study (Grubbs and Grubbs – Hoveyda).

We began our studies with commercially available allenyl ester ethyl 2,3-butadienoate (5). Attempts to react allene 5 with 4pentenyl acetate (6) utilizing olefin metathesis catalysts 1 - 4 in refluxing CDCl₃ failed to yield the desired cross metathesis product 7 (Scheme 1).

*Corresponding author. Tel: (561) 297-0330. Fax: (561) 297-2759 E-mail address: slepore@fau.edu When catalysts 1 and 3 were used, unreacted starting materials were primarily recovered from the reaction. Additional attempts to promote the cross metathesis reaction with 1 or 3 under varying reaction conditions (solvent, temperature, and concentration) primarily resulted in allene decomposition. However, with catalysts 2 and 4, which contain heterocyclic carbene units, we observed that allenyl ester 5 was converted to an oligomeric material containing a 2-butenoate repeating unit (such as structure 8) although we have not been able to determine the exact structure.⁴



Scheme 1. Metathesis reactions with allenyl ester 5 and primary alkene 6.

Others have reported oligomerization products with aliphatic allenes.^{3a} These oligomerization reactions may proceed by a carbene catalyzed process.⁵ Interestingly, homo-metathesized allene and alkene products were also not detected in these metathesis reactions. Attempts to cross-metathesize allenyl ester **5** and alkyl allenyl **9** (Figure 2) using catalyst **4** led only to oligomeric material derived from allenyl ester **5**. We found this somewhat surprising since others have shown that hydrocarbon allenes readily undergo homo-metathesis.^{3a} Under both high-dilution and standard conditions, ring-closing metatheses (RCM) of **10** and **11** also failed (Figure 2). Based on these studies, we surmised that allenyl esters react irreversibly with the catalysts in our study to form a catalytically inactive ruthenium species.

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Figure 2. Substrates for various metathesis studies.

To test this hypothesis, we reacted catalyst **4** with allene **14** using one-to-one stoichiometry; with this allene, no oligomeric product is observed (Scheme 2). In monitoring this reaction by NMR, we noted that the characteristic Ru=C(H) carbene shifts of catalyst **4** and the allenic (sp and sp²) shifts of **14** disappeared in the ¹³C NMR. Isopropoxy styrene **15** peaks were also observed. These data suggest that allenyl ester **14** underwent a single metathesis cycle with the ruthenium catalyst possibly to give a vinylidene complex⁶ but ultimately leading to an unknown ruthenium species (see Supplementary data for NMR spectra of **16**)⁷ that was no longer active in olefin metathesis. In another experiment (not shown), catalyst **3** was first reacted with allene **5** (3 eq) followed by the addition of alkene **6**. No homo-metathesis product of **6** was observed further confirming the loss of catalytic activity upon addition of an allenyl ester.



Scheme 2. Proposed catalyst poisoning reaction.

To explore the use of allenyl esters as catalyst quenching agents we sought to inhibit the ring closing metathesis of diethyl diallyl malonate (17). This substrate was chosen as a challenging case for metathesis inhibition due to the rapidity of this intramolecular reaction to give cyclopentene 18 (< 2 h). Indeed, ring closing metathesis of 17 is completely arrested when 10 equivalents (relative to catalyst 4) of allenyl ester (5, 12 – 14) is added at the start of the reaction. Allenyl ester 14 was particularly effective in this regard (Table 1) since no oligomer byproducts were formed during catalyst arrest. Importantly, excess quenching agents are easily removed in vacuo due to their low boiling points.

Typically, metathesis reactions generate colored ruthenium byproducts, which can be difficult to remove and often require multiple chromatographic purifications. Incomplete removal of the ruthenium byproducts may lead to double bond isomerization during distillation or a decomposition of reaction products.⁸ Due to this persistent problem, a variety of approaches have been employed to remove these colored impurities. The majority of these strategies involve the use of oxidizers or chelating agents that deactivate the metal and facilitate its removal often by aqueous extraction.9 More recently, a variety of alternative approaches have also been reported such as the use of a redoxdriven processes to control the activity of Ru catalysts and facilitate their removal from reactions mixtires.¹⁰ Others have developed metathesis catalysts with an affinity for commercially available silica gel.¹¹ A complementary technique has also been reported involving unmodified catalysts that are sequestered by resins modified to contain an isocyanide ligand.¹²

To examine the potential utility of allene 14 as a non-oxidizing quenching agent¹⁴ in the context of typical metathesis reactions,

we examined several inter- and intramolecular coupling reactions (Scheme 3). We observed that the addition of allene **14** after the completion of metathesis reactions facilitated the removal of colored metathesis impurities in a single chromatographic separation. The cross-metathesis of olefin **6** with methyl acrylate using catalyst **4** led to a 61% isolated yield of **19** (after a second purification over alumina), which is a known compound.⁵ After the addition of **14** upon reaction completion, we realized an improved isolated yield of 91%. Similarly, the isolated yield of RCM reactions of **22** improved with the addition of allene **14** as a quenching agent upon reaction completion.

Table 1. Inhibition of ring closing olefin metathesis with 14added in varying amounts at the beginning of the reaction.

MeO ₂ C	7 4, CHCl ₃ , rt allene 14	MeO ₂ C CO ₂ Me
Entry	Equiv 14 ^a	% yield 18 ^b
1	0	89 (86 ^c)
2	2.0	61
3	4.0	36
4	6.0	3
5	8.0	<1
6	10	0
7^{d}	10	0

^aEquivalents based on limiting substrate **17**. Quenching agent **14** was added at the beginning of the reaction. ^bYield determined by GC with the balance being unreacted **17**. ^cIsolated yield. ^dReaction was refluxed in benzene for 12 h.

The amount of Ru impurity left after quenching with allene ester was found to be significantly lower compared to metathesis product without treating with allene ester. This is verified by measuring strong absorbance of Ru carbene complexes (at 376 nm due to MLCT to π^* of Ru=CHR) using UV-VIS spectroscopy.¹³ For example, after the metathesis reaction of compound **20** was complete, a portion of product **21**, was purified over standard flash silica gel (40-63 µm, 60Å). A UV/Vis analysis of this product revealed a strong absorption at 376 nm, which indicated that the colored byproducts were likely derived from the Ru catalyst (Scheme 4).¹³



Scheme 3. Comparison of metathesis reactions with and without **14** added at the end of the reaction as a quenching agent.

A second portion of product **21** was treated with allene **14** after the metathesis reaction was complete and stirred at room temperature for an hour before purifying using the same flash chromatography conditions.¹⁵ A UV/Vis analysis suggests that quenching with allene ester removed the majority of Ruthenium impurities (Scheme 4, Ru absorbance at 376 nm was not observed).

In summary, our studies suggest that allenyl esters do not undergo olefin metathesis with traditional ruthenium catalysts. Instead, these allenes esters completely inhibit metathesis activity. The organometallic complex that forms between ruthenium catalyst and allenyl esters is conveniently removed using standard silica chromatography. This use of simple allenyl esters offers a useful alternative to traditional quenching agents for the removal of Ru impurities.



Scheme 4. (a) Various purification schemes for product 21; (b) Comparison of Ru content by UV/Vis spectra (in toluene); (I) Catalyst 4, (II) product 21 after simple silica gel flash chromatography and (III) 21 was treated with allene 14 followed by flash chromatography.

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Supplementary data

Supplementary data (general experimental details, characterization data of all products, ¹H and ¹³C NMR spectra of representative products) associated with this article can be found, in the online version, at...

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metathesis active species. This was stirred at room temperature for one hour. The solvent was then removed by evaporation and the resulting Accepted MANUSCAR crude product was directly transferred to a silica column for purification.

Highlights

- Allenyl esters cleanly arrested the activity of the ruthenium metathesis catalysts.
- These allenes are effective as mild catalyst quenching agents.
- The allenes also facilitated catalyst removal during purification.

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