

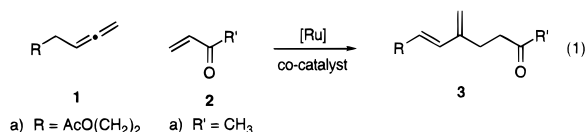
## A Ruthenium-Catalyzed Two-Component Addition To Form 1,3-Dienes

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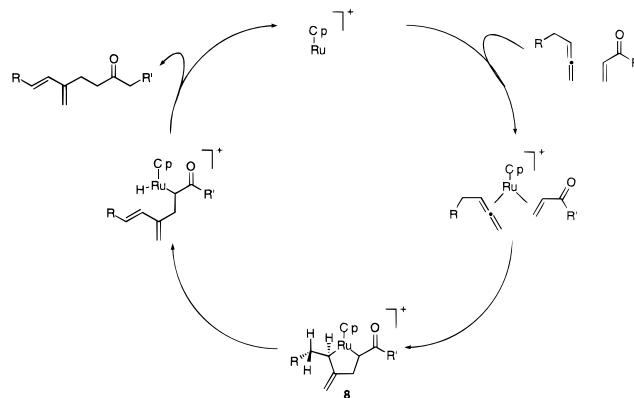
As part of our program to develop atom economical reactions,<sup>1</sup> 1,3-dienes became attractive targets since they themselves are suitable substrates for further additions.<sup>2</sup> Thus, the prospects of building complex structures by a series of simple additions increase. During the course of a study aimed at exploring ruthenium-catalyzed additions of chloride to alkynes,<sup>3</sup> we examined replacement of the alkyne by an allene to obtain a regiocomplementary process. In finding that 1,3-dienes formed in the course of this study, we optimized this process and report our preliminary observations leading to a process as depicted in eq 1.<sup>4</sup>



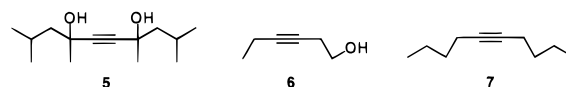
Initial studies examined the reaction of allene **1a** with MVK (**2a**). Our optimized conditions for the chloroalkylation of alkynes involved using 10% CpRu(COD)Cl (**4**) and 15% SnCl<sub>4</sub>•5H<sub>2</sub>O in the presence of ammonium chloride in 20:1 DMF:water at 100 °C. Under these conditions, the diene **3** was isolated in 14% yield. Leaving out the ammonium chloride increased the yield to 35%. Using only DMF as solvent further increased the yield to 45%. Other solvents that proved effective in some earlier ruthenium-catalyzed additions such as acetone and methanol were detrimental to ineffective. Replacing the stannic chloride hydrate by the hydrates of stannous chloride or aluminum chloride had no satisfactory effect. Neither did use of indium chloride nor triflate which has proved beneficial in many other ruthenium-catalyzed processes. On the other hand, cerium chloride appeared to be marginally better. With this latter cocatalyst, lowering the temperature from 100 to 60 °C increased the yield from 48% to 66%.

In our earlier studies of the ruthenium-catalyzed Alder ene reaction of alkenes and alkynes,<sup>5</sup> it was established that the ruthenium complex **4** was activated by the removal of COD from ruthenium by its reaction with the alkyne substrate in a [2+2+2] type cycloaddition.<sup>6</sup> Anticipating that an allene might be less

### Scheme 1. A Mechanistic Hypothesis



effective in activating the ruthenium complex **4**, an equal amount of an alkyne “activator” (**5–7**) was added. Gratifyingly, addition



of 10% **5** or **6** further increased the yield to 80–81%, whereas addition of 10% **7** had no effect. Thus, the optimized conditions became 10 mol % of **4**, 10 mol % **6**, and 15 mol % CeCl<sub>3</sub>•7H<sub>2</sub>O in DMF at 60 °C.

Adopting the above as a standard set of conditions, a range of allenes and vinyl ketones were examined as summarized in eq 1 and Table 1. As the examples in Table 1 illustrate, a wide variety of functional groups including but not limited to hydroxyl, acyloxy, carbonyl, imido, and cyano are compatible. Only the *E* isomers of the dienes, as revealed by the characteristic 16.2 ± 0.3 Hz proton couplings, were detected.

Scheme 1 outlines a working mechanistic hypothesis. The active catalyst is envisioned to be a coordinatively unsaturated cationic ruthenium complex to facilitate coordination of the two reactants. Initial bonding to the sp allenic carbon<sup>7–11</sup> sets the stage for a β-hydrogen elimination that creates the 1,3-diene. Although there are two possible ruthenacycles emanating from such an initial bonding, **8** and **9**, only **8** is competent to react further. Thus, regioisomer **9** may simply be formed reversibly. The steric interactions between the R group and the exo-methylene group of the ruthenacycle favor a conformation as depicted that forms the *E* isomer. A reductive elimination generates the product and

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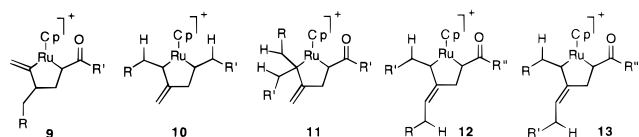
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**Table 1.** Diene Synthesis by Additions of Allenes and Vinyl Ketones

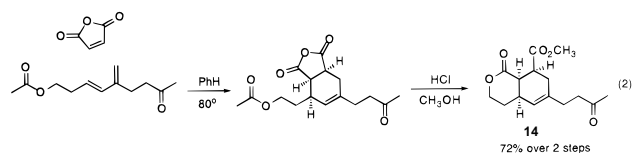
Entry	Allene 1 R	Vinyl ketone 2 R'	Product	Isolated Yield (%)
1	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub>	CH <sub>3</sub>		55%
2	HOCH <sub>2</sub>	CH <sub>3</sub>		65%
3	CH <sub>3</sub> CH(OH)	CH <sub>3</sub>		75%
4	AcO(CH <sub>2</sub> ) <sub>2</sub>	CH <sub>3</sub>		81%
5		CH <sub>3</sub>		67%
6	NC(CH <sub>2</sub> ) <sub>2</sub>	CH <sub>3</sub>		74%
7	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub>			53%
8	NC(CH <sub>2</sub> ) <sub>2</sub>			68%
9	AcO(CH <sub>2</sub> ) <sub>3</sub>			73%
10	NC(CH <sub>2</sub> ) <sub>2</sub>			62%

regenerates the active catalyst to initiate another cycle. Although this scheme nicely rationalizes the results, further experimentation is required to validate it.



The generality of the reaction, with respect to the alkene and allene partners, remains to be established. The issue in such cases is regioselectivity of the  $\beta$ -hydrogen elimination as shown in **10** from simpler alkenes and **11–13** from more substituted Allenes. For example, 1-octene does serve as a substrate, but an inseparable mixture of products results. In this first phase, we chose to avoid such complications.

The utility of this process stems, in part, from the utility of the 1,3-dienes in Diels–Alder reactions. Equation 2 illustrates an example wherein the bicyclic lactone is formed with excellent chemo- and diastereoselectivity solely by additions (with only loss of methyl acetate) from an allene, MVK, maleic anhydride,



and methanol. The success of asymmetric catalysts for the Diels–Alder reaction can convert these reactions into enantioselective ones as well. The development of such new addition reactions enhances our ability to make complex synthesis more atom economical.

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**Supporting Information Available:** General experimental procedure and procedure for preparation of **14**; characterization data for all 1,3-dienes and **14** (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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