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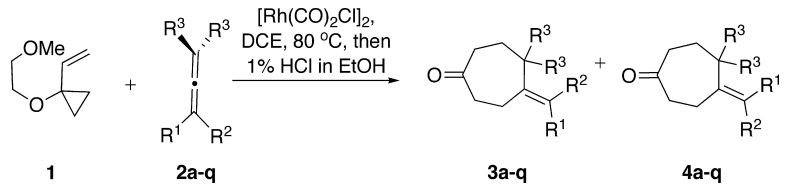

1 **2a-q** **3a-q** **4a-q**

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Transition Metal-Catalyzed Intermolecular [5+2] and [5+2+1] Cycloadditions of Allenes and Vinylcyclopropanes

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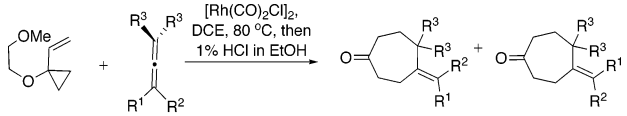
The transition metal-catalyzed [5+2] cycloaddition of vinylcyclopropanes (VCPs) and π-systems is a new and practical reaction for the formation of seven-membered rings.[1] First reported in 1995,[2] this reaction has been shown to work intramolecularly with alkynes, alkenes,[3] and allenes[4] and to provide the conceptual basis for new three-component [5+2+*n*] cycloadditions.[5] New catalysts for these reactions have been introduced by us[6] and by others,[7,8] adding further to their scope and utility. Among these, $[Rh(CO)_2Cl]_2$ has proven to be uniquely versatile, catalyzing both intra- and intermolecular cycloadditions.[9] Thus far, however, the intermolecular reaction has been limited to the cycloaddition of VCPs and alkynes. Alkenes and allenes have not worked as substrates. We report herein the first examples of the intermolecular [5+2] cycloaddition of allenes and VCPs.

Allenes are known to form stable rhodium complexes,[10] some of which undergo ligand exchange with, for example, CO, suggesting that they might be suitable substrates in the intermolecular [5+2] cycloaddition.[11] However, simple allenes, while effective in the intramolecular [5+2] reaction, possibly due to a high formal concentration effect and bidentate coordination, are unreactive in the intermolecular process. We have now found that allenes substituted with an additional coordinating group are superb C_2 components in the intermolecular reaction. Thus when alkynylallene **2a** is treated with VCP **1** in 1,2-dichloroethane (DCE) for 1 h in the presence of 5 mol % $[Rh(CO)_2Cl]_2$ and the products are submitted to hydrolytic workup, the chromatographically separable *E*- and *Z*-cycloadducts, **3a** and **4a**, are obtained in a combined yield of 95%. Significantly, the cycloaddition occurs exclusively at the distal double bond, leading to the creation of a quaternary center. In addition to being the first example of an intermolecular allenyl [5+2] cycloaddition, this is also a unique example in which addition to an alkynyl group is not preferred. The mixture of alkylidene isomers is kinetically controlled, favoring the less stable isomer.

Various rhodium catalysts differing electronically and sterically were screened for effectiveness in the above transformation. Yields and diastereomeric ratios were determined by GC. Bisacetonitrile(cyclooctadiene)rhodium hexafluoroantimonate catalyzed the formation of cycloadducts **3a**/**4a** but with lower efficiency (20%) and longer times (42 h) than did $[Rh(CO)_2Cl]_2$, albeit with the same diastereomeric ratio of 1:2. Wilkinson's catalyst in the presence of $AgSbF_6$ did give some product (15%, 2 days) with a preference for isomer **4a** (1:8). Interestingly, carbonylbis(triphenylphosphine)rhodium chloride, also in the presence of $AgSbF_6$, gave **4a** as a single diastereomer,[12] although in only 29% yield after 42 h. Given the superior performance of $[Rh(CO)_2Cl]_2$, it was selected for further reaction optimization.

Scheme 1. For Details See Tables 1 and 2



1 **2a-q** **3a-q** **4a-q**

Table 1. Cycloadditions of VCP **1** with Various Alkynyl-Substituted Allenes

Entry	R^1	R^2	R^3	T/h	Yield(%)[c] (**3a-k**:**4a-k**)
1	—TMS	H	Me	1	95 (1:1.8)
2	—Ph	H	Me	1	83 (1:1.6)
3	—Ph	CH_2CO_2Et	Me	1	92 (1:2)
4	—Ph	C_4H_9	Me	3	80 (2:3)[b]
5	—TMS	C_4H_9	Me	1	80 (2:5)
6	—CH_2CH_2OH	C_4H_9	Me	1	65 (1:1.2)
7	—CH_2OMe	H	Me	5	45 (1:1.3)
8	—CH_2NBn_2	C_4H_9	Me	1	22 (1:2.2)
9	—H	CH_2CO_2Et	Me	24	n. r.[a]
10	—H	C_4H_9	Me	36	n. r.[a]
11	—Ph	H	H	36	n. r.[a]

[a] n.r. = no reaction. [b] Diastereomers could not be separated by column chromatography. [c] Isolated yields.

A catalyst loading of as low as 1 mol % can be used without a decrease in yield. Below 1 mol % catalyst, reaction times increased significantly; at 0.5 mol % $[Rh(CO)_2Cl]_2$, the reaction required 20 h instead of 1 h, although the product was still obtained in high yield (96%). The reaction proceeds even at room temperature to give **3a** and **4a** in the same ratio, although conversion is lower (25% after 5.5 h, starting material recovered). When conducted on a 2 mmol scale and at higher reactant concentrations (2 M instead of 0.2 M), the cycloadducts were obtained in lower yield (71%) and in a ratio of 1:1. On the basis of these results, a set of optimized conditions (1 mol % $[Rh(CO)_2Cl]_2$, 0.2 M **1**, and 1.2 equiv of **2a** in DCE, 80 °C) was used to examine the generality of the reaction with a range of different alkynylallenes (Scheme 1, Table 1).

Alkynes with various terminal substituents, including trimethylsilyl, phenyl, and even a free hydroxyethyl group, reacted to give cycloheptanones in good to excellent yields (Table 1, entries 1−6). Dibenzylaminomethyl and methoxymethyl substitution caused the yields to drop (entries 7 and 8), while no reaction was observed with terminal alkynes or with a terminally unsubstituted allene (entries 9−11).

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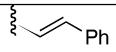
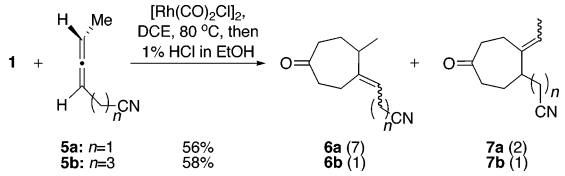
Table 2. Cycloadditions of VCP **1** with Other Functionally Substituted Allenes **2**

entry	R^1	R^2	R^3, R^3	t/h	yield (%)[c] (**3l-q**:**4l-q**)
1		H	Me	1	69 (2:1)[b]
2	CO_2Et	Me	Me	36	n. r.[a]
3	CN	H	Me	1	99 (2:3)
4	CN	H	H	36	n. r.[a]
5	CN	H		1	99 (5:2)
6	CN	H	H/Me	1	52 (1:2)[b]

[a] n.r. = no reaction. [b] Diastereomers could not be separated by column chromatography. [c] Isolated yields.

Scheme 2. [5+2] Cycloadditions of Nonconjugated Allenylnitriles

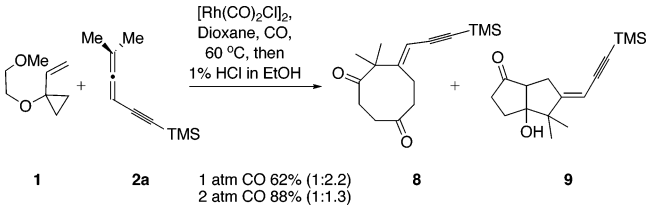


Allenes substituted with alkenyl, ethoxycarbonyl, and cyano groups were examined for a similar promoting effect (Table 2). While the styryl- and especially cyano-substituted *gem*-dimethylallenes work well, ethyl 2,4,4-trimethylallenecarboxylate did not react, and the unsubstituted cyanoallene did not yield any isolable product (entries 2 and 4). However, 1-cyano-3-methylallene did yield the expected seven-membered ring product (Table 2, entry 6). Even the sterically more encumbered cyanocyclohexylideneethene gave the cycloaddition product in 99% yield (entry 5).

To further examine the role of allenyl substituents on the course of this reaction, cyanoallenes with one and three methylene groups between the allene and the nitrile moiety were examined. Each reacted with **1** to yield seven-membered ring products (Scheme 2). While the conjugated cyanomethylallene (Table 2, entry 6) underwent cycloaddition exclusively at its distal double bond (with respect to the cyano group), the nonconjugated (cyanoalkyl)allenes reacted to give increasing amounts of addition to the proximal double bond (20% for $n = 1$ to 50% for $n = 3$ by ^{1}H NMR), suggestive of a coordinative delivery mechanism.

We have previously reported that the [5+2] cycloaddition of VCPs and alkynes can be diverted to a three-component [5+2+1] reaction when conducted under an atmosphere of CO.[5] To determine whether this process would apply to allenes, **2a** and VCP **1** were subjected to standard conditions (1 mol % $[Rh(CO)_2Cl]_2$, DCE (0.2 M), 80 °C) under an atmosphere of CO. However, only the usual seven-membered ring products **3a** and **4a** were observed. In contrast, with dioxane as solvent (1 mol % $[Rh(CO)_2Cl]_2$, 0.2 M, 60 °C), cyclooctanedione **8** and its transannular aldol product hydroxybicyclo[3.3.0]octanone **9** (ratio 1:2.2) were obtained in 88% yield (GC, isolated 62%) in only 1 h. Increasing the CO pressure to 2 atm improved the yield to 94% (GC, isolated 88%), but required a longer reaction time (15 h) and modestly changed the product ratio (**8**:**9** = 1:1.3). Both products were obtained as single *E*-isomers. It is noteworthy that, unlike [5+2+1] cycloadditions of VCP **1** with

Scheme 3. [5+2+1] Cycloadditions of Allenes, VCPs, and CO



alkynylcarbonyl compounds and CO[5], allenes without carbonyl substitution work well.

In summary, this study provides the first examples of rhodium-catalyzed *inter*molecular [5+2] and [5+2+1] cycloadditions of allenes incorporating alkynyl, alkenyl, cyano, and cyanoalkyl substituents. These reactions proceed often in good to excellent yields, even at high concentrations, and low catalyst loading. This procedure provides a new strategy for the assembly of seven- and eight-membered rings and the basis for new types of C_2 components for metal-catalyzed processes. Further studies of substrate, catalysts, ligands, conditions, and synthetic applications are in progress.

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Supporting Information Available: Procedures and spectroscopic data for representative products (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) Resubmission of each of the isomeric nonhydrolyzed cycloadducts to the reaction conditions resulted in no isomerization. The distribution of cycloadducts is therefore most likely kinetically controlled.

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