## [5+2] Cycloaddition

## **Rhodium(I)-Catalyzed Intramolecular [5+2] Cycloaddition Reactions** of Alkynes and Allenylcyclopropanes: Construction of Bicyclo-[5.4.0]undecatrienes and Bicyclo[5.5.0]dodecatrienes\*\*

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Highly strained cyclopropane derivatives have served as useful and powerful  $C_3$  building blocks<sup>[1]</sup> for the construction of various ring systems, and the metal-catalyzed cleavage of the activated carbon-carbon  $\sigma$  bond of the cyclopropane ring<sup>[2,3]</sup> must be one of the most attractive methods from a synthetic point of view. Of particular interest is the Rh<sup>I</sup>catalyzed [5+2] cycloaddition of vinylcyclopropanes<sup>[3-5]</sup> with carbon–carbon  $\pi$ -components for the efficient formation of seven-membered compounds. In 1995, Wender et al. reported the first example<sup>[3a]</sup> of the Rh<sup>I</sup>-catalyzed [5+2] cycloaddition reaction of vinylcyclopropanes with alkynes to provide bicyclo[5.3.0]decadienes.<sup>[3c,g,j]</sup> This method<sup>[3,4]</sup> was successfully applied to the [5+2] cycloaddition reactions of allenes<sup>[3e,f,h]</sup> as well as alkenes<sup>[3b,d,g,j,4a]</sup> as an alternative carbon-carbon  $\pi$ -counterpart. In sharp contrast to the extensive investigation of vinylcyclopropanes,<sup>[2b,c,e,3-5]</sup> very few examples<sup>[6]</sup> of the ringclosing reaction of allenvlcyclopropane, which is regarded as an alkylidene homologue of vinylcyclopropane, have been reported. Two representative examples are shown in Scheme 1; one involves the Rh<sup>I</sup>-catalyzed cycloisomeriza-



**Scheme 1.** Metal-catalyzed ring-closing reaction of allenylcyclopropanes.

tion<sup>[6b]</sup> of allenylcyclopropanes into  $\alpha$ -alkylidenecyclopentenes, and the other is the formation of the  $\alpha$ -alkylidene-3cyclohexen-1-one frameworks by the Ir<sup>I</sup>-catalyzed carbonylative [5+1] ring-closing reaction<sup>[6c]</sup> of allenylcyclopropanes.

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[**]	This work was supported by a Grant-in-Aid for Scientific Research

from the Ministry of Education, Culture, Sports, Science, and Technology (Japan), for which we are thankful.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.200906994.



Table 1: Rhodium(I)-catalyzed [5+2] cycloaddition reaction of 1.<sup>[a]</sup>

PhO<sub>2</sub>S

 $\wedge$ 

	10	10 mol% Rh <sup>I</sup> catalyst			
		30 °C or RT, N <sub>2</sub>	2	TsN	
	1			2	
Entry	Rh <sup>I</sup> catalyst	Solvent	T [°C]	<i>t</i> [h]	Yield [%] <sup>[b]</sup>
1	$[{RhCl(CO)_2}_2]$	toluene	80	2	66
2	$[{RhCl(CO)_2}_2]$	toluene	RT	24	57
3	[{RhCl(CO)dppp} <sub>2</sub> ]	toluene	80	0.2	90
4	[{RhCl(CO)dppp} <sub>2</sub> ]	toluene	RT	1	88
5	$[{RhCl(CO)_2}_2]$	dioxane	80	0.3	64
6	$[{RhCl(CO)_2}_2]$	dioxane	RT	1.5	55
7	$[{RhCl(CO)_2}_2]$	DCE	80	1	80
8	$[{RhCl(CO)_2}_2]$	DCE	RT	30	66
9	[{RhCl(CO)dppp} <sub>2</sub> ]	dioxane	80	1	72
10	[{RhCl(CO)dppp} <sub>2</sub> ]	dioxane	RT	11	n.r. <sup>[c]</sup>
11	[{RhCl(CO)dppp} <sub>2</sub> ]	DCE	80	0.5	69
12	[{RhCl(CO)dppp} <sub>2</sub> ]	DCE	RT	3	79

[a] Reaction conditions: 0.1 M solution of alkyne-allenylcyclopropane 1 was treated with the Rh<sup>I</sup> catalyst (10 mol%) under a nitrogen atmosphere. [b] Yield of isolated product. [c] n.r. = no reaction. DCE = dichloroethane, dppp=1,3-bis(diphenylphosphino)propane, Ts=4-tol-uenesulfonyl.



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SO2Ph

addition product was formed when a terminal alkyne was employed.<sup>[9]</sup> Other catalysts were tested, such as  $[RhCl(PPh_3)_3],$ [RhCl(CO)- $[{RhCl(cod)}_2],$  $(PPh_3)_2],$  $[{RhCl(CO)dppp}_2],$ [Rh- $(C_{10}H_8)cod]^+BF_4^-$ , and [Rh(CO)- $(dppp)_2$ ]<sup>+</sup>Cl<sup>-</sup>, with or without a silver salt; however, much lower yields or no reaction at all was observed in all cases, apart from  $[{RhCl(CO)dppp}_2]$ . Indeed, the addition of compound 1 to  $10 \mod \%$  [{RhCl(CO)dppp}<sub>2</sub>] in toluene at 80 °C for 10 min afforded 2 in a higher yield (90%; Table 1, entry 3). Similarly, a satisfactory yield was obtained when the reaction was performed at room temperature for 1 h (Table 1, entry 4). Therefore,  $[{RhCl(CO)_2}_2]$  and [{RhCl(CO)dppp}<sub>2</sub>] were found to be suitable catalysts for our purpose. Next, we examined two solvents, dioxane and dichloroethane, both of which are frequently employed in rhodium-catalyzed reactions.<sup>[3]</sup> Dichloroethane furnished higher yields in the [{RhCl(CO)<sub>2</sub>}<sub>2</sub>]-catalyzed reaction (Table 1, entries 7 and 8), although [{RhCl(CO)dppp}<sub>2</sub>]/toluene (Table 1, entries 3 and 4) was superior to both dioxane and dichloroethane (Table 1, entries 9-12).

1

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The [5+2] cycloaddition of several substrates that contain a terminal triple bond was examined using the complementary and interchangeable use of two sets of conditions: [{RhCl(CO)<sub>2</sub>]<sub>2</sub>]/dichloroethane and [{RhCl(CO)dppp}<sub>2</sub>]/toluene (Table 2). Treatment of 3a with  $[{RhCl(CO)_2}_2]$  afforded the corresponding ring-closed product 4a in satisfactory yields at both 80°C and at room temperature (Table 2, entry 1). Bis(phenylsulfonyl) derivative **3b** and dimethyl acetal derivative 3c showed similar behavior to **3a** under the





[a] Reaction conditions: 0.1 M solution of alkyne-allenylcyclopropane 3 was treated with 10 mol% of [{RhCl(CO)<sub>2</sub>}<sub>2</sub>] in dichloroethane or with 10 mol% of [{RhCl(CO)dppp}<sub>2</sub>] in toluene under a nitrogen atmosphere. [b] Yield of isolated product. [c] Compound 3d was recovered in 35% yield. [d] Reaction was performed in 0.05 M solution of toluene in the presence of 20 mol% of  $[{RhCl(CO)_2}_2]$ . [e] Reaction was carried out in 0.05 M solution.

 $[{RhCl(CO)_2}_2]$  conditions to furnish **4b** and **4c** in high yields (Table 2, entries 2 and 3). In the case of malononitrile derivative 3d, the [5+2] product 4d was formed in moderate yield (53%) with the formation of a cyclopentene derivative by-product **5d** <sup>[10]</sup> when exposed to [{RhCl(CO)dppp}<sub>2</sub>] (Table 2, entry 4). Compound 3e, which contained a simple methylene tether between two reaction centers, provided the corresponding [5+2] product **4e** in 65% or 51% yields for the

two reaction conditions (Table 2, entry 5). A slightly lower yield of 4e (compared with those of 4a-c) might be largely due to a loss of the bis(substituent) effect.<sup>[11]</sup> Oxygen analogue 4 f was obtained in moderate yields with [{RhCl(CO)dppp}<sub>2</sub>] (Table 2, entry 6). Therefore, the results in Tables 1 and 2 may be summarized as follows: 1) judicial choice of two catalysts consistently and complementarily afforded the corresponding [5+2] products 4 (and 2) in moderate to high yields; and

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2) [{RhCl(CO)<sub>2</sub>}<sub>2</sub>] usually produced better results than those with [{RhCl(CO)dppp}<sub>2</sub>], although this depends on the substrate.

There are two plausible mechanisms for the production of the [5+2] product **4**, based on the previously proposed mechanism for the metal-catalyzed [5+2] cycloaddition of vinylcyclopropanes containing  $\pi$ - $\pi$  multiple bonds (Scheme 2).<sup>[3,4]</sup> Path a involves the initial production of a



 $\it Scheme \ 2.$  A plausible mechanism for the formation of 4, 5, and 6 from 3.

rhodacyclohexene intermediate I from the Rh<sup>I</sup>-catalyzed cycloisomerization reaction between a cyclopropane ring and the distal double bond of an allenyl moiety.[6b,c] The insertion reaction of the  $C_{sp^2}$ -Rh<sup>III</sup> bond into the triple bond of I would lead to rhodabicyclo[6.4.0]dodecatriene intermediate II. Reductive elimination of Rh<sup>III</sup> from intermediate II should then provide 4. Isolation of cyclopentene derivative  $5^{[6b]}$  would strongly rationalize the intermediacy of I (path a). Reductive elimination, instead of the insertion reaction of I. would result in the formation of 5. The other possible reaction pathway is indicated by path b. The oxidative addition reaction of the Rh<sup>I</sup> catalyst to an alkyne group and the distal double bond of the allenyl moiety would initially form the rhodabicyclo[4.3.0]nonadiene intermediate III, which might be susceptible to a ring expansion assisted by the release of the ring strain in the cyclopropane ring to generate the eight-membered intermediate II. Path b, via intermediate III, might be indirectly supported by the fact that a carbonylative [2+2+1] product 6 was obtained as a byproduct together with 2, when 1 was reacted under a carbon monoxide atmosphere instead of nitrogen.<sup>[12]</sup> Thus, it seems that both reaction pathways are feasible for this [5+2] ringclosing reaction, depending on the reaction conditions.

Next, we examined the Rh<sup>I</sup>-catalyzed [5+2] cycloaddition reaction between an allenylcyclopropane and internal alkyne groups (Table 3). Treatment of *N*-Ts derivative **7a** and malonate derivative **7c**, both of which contain a 2-heptynyl residue, with a catalytic amount of [{RhCl(CO)<sub>2</sub>}<sub>2</sub>] provided

Table 3: Rhodium(I)-catalyzed [5+2] cycloaddition reaction of 7.<sup>[a]</sup>



[a] Reaction conditions: 0.1 M solution of alkyne-allenylcyclopropane **7** was treated with 10 mol% of [{RhCl(CO)<sub>2</sub>}<sub>2</sub>] in dichloroethane under a nitrogen atmosphere. [b] Yield of isolated product. TMS = trimethylsilyl.

bicyclo[5.4.0] derivatives **8a** and **8c** in satisfactory yields (Table 3, entries 1 and 3). The terminal TMS compounds **7b** and **7d** furnished their corresponding [5+2] cycloaddition products **8b** and **8d**, respectively, in lower yields compared to those of **8a** and **8c** (Table 3, entries 2 and 4). In the case of **7d**, the formation of cyclopentene derivative **9d**, which is structurally similar to **5d** and **5f** (Table 2), was observed (Table 3, entry 4). The alternative [[RhCl(CO)dppp]<sub>2</sub>] catalyst was not as effective in the transformation of **7** into **8**.

Our next objective was the application of the alkyneallenylcyclopropane ring-closing reaction to the construction of the larger-sized bicyclo[5.5.0]dodecatriene to preliminarily confirm the scope of this procedure (Scheme 3). Exposure of one-carbon homologated substrate 10 to a catalytic amount of  $[{RhCl(CO)_2}_2]$  under the standard condition provided the desired bicyclo[5.5.0]derivative **11** in low yields (22–32%). Changing the catalyst from  $[{RhCl(CO)_2}_2]$ to [{RhCl(CO)dppp}<sub>2</sub>] produced a significant improvement to furnish 11 in 63 % yield along with the formation of 12(17%). [{RhCl(CO)dppp}2] was also effective for nitrogen-atomcontaining substrate 13. Indeed, 14 was obtained in 74% yield together with 15 (4%) when heated in toluene for two hours.

Finally, it was shown that having a phenylsulfonyl substituent on the allenyl moiety was not essential for the efficient [5+2] ring-closing reactions of the alkyne-allenylcyclopropane derivatives. Furthermore, treatment of **16** with



Scheme 3. Construction of a bicyclo[5.5.0]dodecatriene skeleton.

10 mol% of [{RhCl(CO)dppp}<sub>2</sub>] effected the cycloisomerization to produce the corresponding methyl derivative **17** exclusively in 86% yield. Faster consumption of **16** was observed in the presence of 10 mol% of [{RhCl(CO)<sub>2</sub>}<sub>2</sub>] at 80 °C to furnish **17** in 69% yield (Scheme 4).<sup>[13]</sup>



Scheme 4. Ring-closing reaction of methyl-substituted allene 16.

In summary, we have developed a Rh<sup>I</sup>-catalyzed intramolecular [5+2] cycloisomerization reaction between alkyne and allenylcyclopropane functionalities under mild conditions, which leads to the facile formation of the bicyclo-[5.4.0]undecatriene frameworks. Judicious choice of the Rh<sup>I</sup> catalyst, [{RhCl(CO)<sub>2</sub>]<sub>2</sub>] or [{RhCl(CO)dppp}<sub>2</sub>], consistently afforded the desired products in satisfactory yields. This method was successfully applied to the construction of larger bicyclo[5.5.0]dodecatriene skeletons. Further investigation into the scope and limitations of this method, as well as its applications in the synthesis of natural products, are now underway.

Received: December 12, 2009 Published online: February 19, 2010

**Keywords:** allenes · bicyclic compounds · cycloaddition · cyclopropanes · rhodium

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- [8] The reaction of 1 with 5 mol% of [{RhCl(CO)<sub>2</sub>}<sub>2</sub>] produced 2 in 37% yield. Thus, we used 10 mol% of Rh<sup>1</sup> catalyst for the next investigation.
- [9] A successful example of [{RhCl(CO)<sub>2</sub>]<sub>2</sub>]-catalyzed [5+2] cycloaddition between the terminal alkyne and (*E*)-2-(1-ethoxycyclopropyl)vinyl moieties was reported; see Ref. [3g].
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- [12] Compound 6 (13%) was formed along with 2 (48%) when a solution of 1 was heated in toluene at 100°C in the presence of 10 mol% of [{RhCl(CO)<sub>2</sub>}<sub>2</sub>] under 10 atm of CO for 1 h.
- [13] A small amount of a by-product was obtained, the structure of which may be assigned as 18 from its <sup>1</sup>H NMR and IR spectra. The formation of 18 could be rationalized in terms of participation of carbon monoxide derived from the [{RhCl(CO)<sub>2</sub>}<sub>2</sub>] catalyst.

