

Rh(I)-catalyzed ring-closing reaction of allenynes: selective construction of cycloheptene, bicyclo[5.3.0]decadienone, and bicyclo[5.2.0]nonene frameworks

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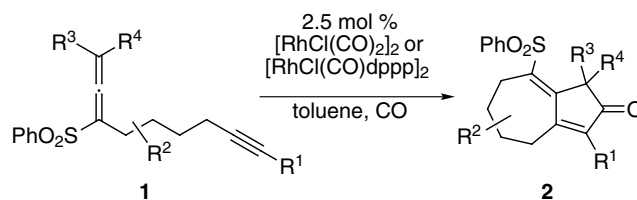
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Abstract—Highly selective formation of cycloheptene, bicyclo[5.3.0]decadienone, and bicyclo[5.2.0]nonene skeletons from tri- and tetrasubstituted allenynes has been achieved via a Rh(I)-catalyzed ring-closing reaction and proper choice of substrate and/or reaction conditions.

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The intramolecular Pauson–Khand reaction (PKR) of enynes is one of the most powerful tools available for the construction of bicyclo[3.3.0]octenones and bicyclo[4.3.0]nonenones. However, this attractive ring-closing method generally is not effective for the synthesis of bicyclo[5.3.0]decenones^{1,2} in large part due to entropic as well as enthalpic factors, which could impede the formation of larger-sized rings.³ Recent efforts from this laboratory have led to the development of a new and efficient procedure for the construction of the bicyclo[5.3.0]decadienone framework **2** ($R^3 = R^4 = H$) based on the Rh(I)-catalyzed intramolecular PKR of allenynes **1** ($R^3 = R^4 = H$).⁴ This ring-closing reaction selectively occurs between the distal double bond of the allenic moiety and the alkyne counterpart of **1** ($R^3 = R^4 = H$), resulting in the formation of the bicyclo[5.3.0]decadienones **2** ($R^3 = R^4 = H$) in moderate to high yields (Scheme 1).^{5,6}

We then applied this newly developed Rh(I)-catalyzed ring-closing reaction to tri- and tetrasubstituted allenynes. Depending on the substitution pattern of the allenic moiety of **1** (R^3 and/or $R^4 =$ substituent) and/or reaction conditions, the selective construction of (i) 3-alkylidene-2-vinylcyclohept-1-ene, (ii) bicyclo[5.3.0]deca-1,7-dien-9-one, and (iii) 2-alkylidenebicyclo[5.2.0]non-1(9)-ene



Scheme 1.

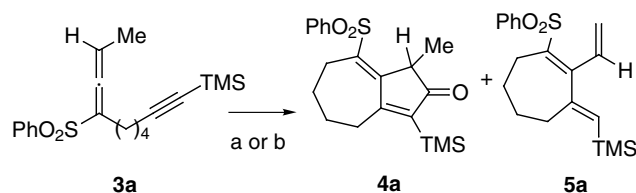
skeletons could be achieved. This letter describes our preliminary results.

According to the previously reported procedures⁴, the allene **3a**⁷ having a methyl group at the allenic terminus was treated with 2.5 mol % of $[RhCl(CO)_2]_2$ in refluxing toluene under a CO atm to give the desired bicyclic compound **4a** in 19% yield. However, the major product isolated from the reaction mixture was the seven-membered compound **5a** with the crossed-triene moiety in 68% yield.⁸ Changing the catalyst from $[RhCl(CO)_2]_2$ to $[RhCl(CO)dppp]_2$ under similar conditions produced **4a** and **5a** in 37% and 47% yields, respectively (Scheme 2).⁸

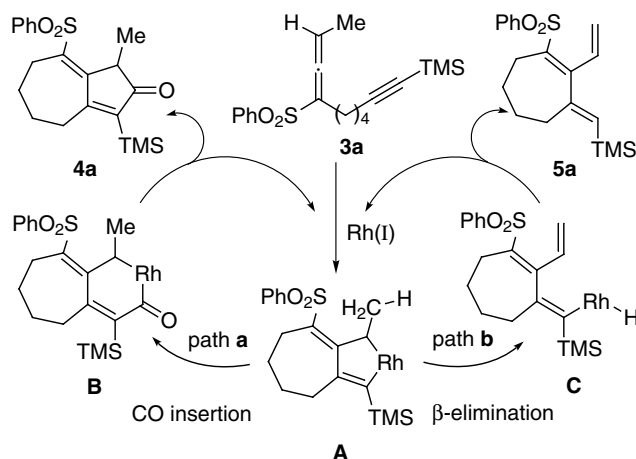
The Rh(I)-catalyzed PKR^{9,10} of allenynes would be tentatively rationalized in terms of the intermediacy of the metallacyclopentene intermediate **A**, which would collapse to the bicyclo[5.3.0] ring system via insertion of CO (path a, Scheme 3), followed by reductive elimination.⁹ Alternatively, the methyl hydrogen at the allenic terminus of the intermediate **A** would be abstracted via β -hydride elimination (path b), leading to the formation

Keywords: Pauson–Khand reaction; Cycloisomerization; Bicyclo[5.3.0]decane; Bicyclo[5.2.0]nonane; Allenyne; Electrocyclic reaction.

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Scheme 2. Reaction conditions: (a) 2.5 mol% $[\text{RhCl}(\text{CO})_2]_2$, toluene, reflux, 1 atm CO, 2.5 h, **4a** (19%), **5a** (68%); (b) 2.5 mol% $[\text{RhCl}(\text{CO})\text{dppp}]_2$, toluene, reflux, 1 atm CO, 6 h, **4a** (37%), **5a** (47%).



Scheme 3.

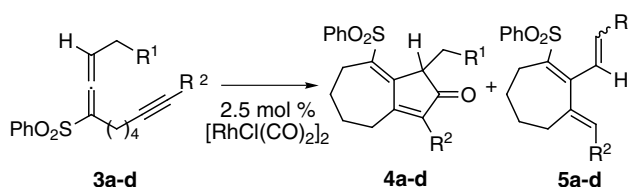
of the triene derivative (Scheme 3).^{11–13} The latter process (path b) was not observed in the case of the Rh(I)-catalyzed PKR of **1** ($\text{R}^3 = \text{R}^4 = \text{H}$), where the lack of a methyl group (or its equivalent) at the allenic terminus

eliminated path b and made path a exclusively the favored one.

With these considerations in mind, we envisioned that increasing the CO pressure in the ring-closing reaction of **3a** would facilitate the CO insertion process (path a) resulting in the preferential formation of the bicyclo[5.3.0]decadienone **4a** over β -hydride elimination (path b), whereas the ring-closing reaction under a N_2 atm (absence of external CO) must produce exclusively the triene derivative **5a**.^{14,15} Thus, the ring-closing reaction of **3a** was carried out in the presence of $[\text{RhCl}(\text{CO})_2]_2$ at 120 °C under 10 atm of CO (conditions A) to furnish the desired bicyclic compound **4a** in 79% yield along with a small amount of **5a** (8%). It should be noted that for the preparation of the 10-substituted-bicyclo[5.3.0]decadienone skeleton under conditions A, $[\text{RhCl}(\text{CO})\text{dppp}]_2$ was found to be ineffective. Several allenes having the RCH_2 functionality at the allenic terminus were submitted to conditions A. The results are summarized in Table 1, together with those obtained from the reaction under CO pressure (conditions B) as a control experiment. The ring-closing reaction of **3a–d** under conditions A consistently produced the corresponding bicyclic compounds **4a–d** in a highly selective manner in acceptable yields. However, conditions A were shown to be no longer effective for the ring-closing reaction of tetrasubstituted allenes, such as **1** ($\text{R}^3 = \text{R}^4 = \text{Me}$ in Scheme 1, e.g.), resulting in an intractable mixture, from which only a small amount of the 3-alkylidene-2-vinylcyclohept-1-ene derivative could be isolated.

We next turned our attention to the development of the selective formation of the cycloheptene derivatives from

Table 1. Rh(I)-catalyzed PKR of **3**



Conditions A: 10 atm CO, toluene, 120 °C (bath temperature)

Conditions B: 1 atm CO, toluene, reflux

a: $\text{R}^1 = \text{H}$, $\text{R}^2 = \text{TMS}$; **b:** $\text{R}^1 = \text{H}$, $\text{R}^2 = \text{Ph}$; **c:** $\text{R}^1 = n\text{Pr}$, $\text{R}^2 = \text{TMS}$; **d:** $\text{R}^1 = \text{Ph}$, $\text{R}^2 = \text{TMS}$

Entry	SM	Conditions	Bicyclo[5.3.0]		Triene		4:5
			4	Yield (%)	5	Yield (%)	
1	3a	A	4a	79	5a	8	91:9
2	3b	A	4b	80	5b	8	91:9
3 ^a	3c	A	4c	67	5c	—	100:0
4 ^a	3d	A	4d	86	5d	—	100:0
5	3a	B	4a	19	5a	68	22:78
6	3b	B	4b	14	5b	62	18:82
7 ^a	3c	B	4c	24	5c	70 ^b	26:74
8 ^a	3d	B	4d	79	5d	7 ^c	92:8

^a 5 mol% of $[\text{RhCl}(\text{CO})_2]_2$ was used.

^b *E/Z* ratio (81:19) was determined by ^1H NMR spectrum.

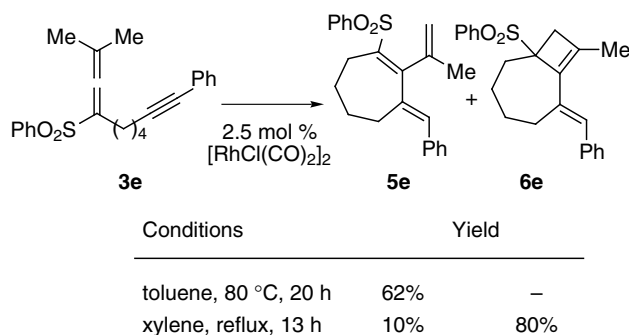
^c *E/Z* ratio (72:28) was determined by ^1H NMR spectrum.

3. The ring-closing reaction of the trisubstituted allenynes **3a–d** was carried out in refluxing toluene in the presence of $[\text{RhCl}(\text{CO})_2]_2$ under a N_2 atm (conditions C) to furnish the corresponding 3-alkylidene-2-vinylcyclohept-1-ene derivatives **5a–d** (Table 2). As expected, the bicyclo[5.3.0]decadienones **4a–c** could never be detected in the reaction mixture (entries 1–3). In the ring-closing reaction of **3d**, the corresponding CO-inserted product **4d** (12%) was detected.¹⁶ Thus, we could now develop the complementary procedure for the construction of the bicyclo[5.3.0]deca-1,7-dien-9-one and 3-alkylidene-2-vinylcyclohept-1-ene frameworks, starting from the same trisubstituted allenynes **3**, by changing the reaction conditions (conditions A and C).

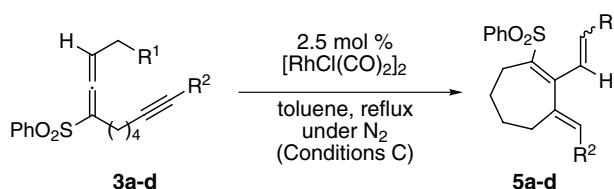
In the next phase of this investigation, which involved the ring-closing reaction of tetrasubstituted allenynes under conditions C, the tetrasubstituted allenyne **3e** having two methyl groups at the allenic terminus provided the corresponding cycloheptene **5e** in 62% yield (80 °C instead of refluxing temperature). This result was similar to those observed in the cases of the trisubstituted allenynes **3a–d**. Interestingly, and unexpectedly, the bicyclo[5.2.0]nonene derivative **6e**^{17,18} was isolated as the major product (80%), along with a small amount of **5e** (10%), when a similar ring-closing reaction was performed in refluxing xylene. The formation of **6e** could be interpreted tentatively as occurring via the reversible thermal 4π -electrocyclic reaction of **5e**. In fact, compounds **5e** and **6e** were heated separately in refluxing xylene to afford a mixture of **6e** and **5e** in a ratio of 4–5:1. In addition, transformation of **5e** to **6e** was found to be accelerated by a catalytic amount of $[\text{RhCl}(\text{CO})_2]_2$,¹⁹ although the role of $[\text{RhCl}(\text{CO})_2]_2$ in this acceleration is still uncertain. It should be noted that the triene derivatives **5a–d**, obtained from the trisubstituted allenynes **3a–d**, could never be converted into the corresponding bicyclo[5.2.0]nonene skeleton even in refluxing xylene for a prolonged period. The difference in reactivity between **5a** and **5e**, for example, would be interpreted provisionally by considering each preferred conformer.

Since the C_2 -vinyl group of **5a** could rotate freely without any serious nonbonding repulsion, the preferred conformer of **5a** is not necessarily the one depicted in Scheme 2. This is not the case for **5e**, where the nonbonding interaction between the phenylsulfonyl group and the methyl moiety on the C_2 -vinyl group would prevent free rotation of the C_2 -propylene group as well as make the conformer depicted in Scheme 4 the preferred one. Thus, **5e** could be transformed easily into **6e** via the 4π -electrocyclic reaction.

Several tetrasubstituted allenynes were then submitted to conditions C to confirm the applicability of this novel tandem cyclization. The results are summarized in Table 3. The terminal alkyne derivative **3f** afforded exclusively the bicyclo[5.2.0] derivative **6f** in refluxing toluene with a lower yield (58%) compared to **6e**, presumably due to its instability (entry 1)^{20,21}. Allenynes **3g,h** having methyl and phenyl groups at the allenic terminus provided **6g,h** in high yields (entries 2 and 3). In the case of **3i**, the triene compound **5i** was obtained as a major product (56%) along with the desired **6i** in 12% yield (entry 4). Higher reaction temperatures did not improve the chemical yield of **6i**. In addition, interconversion between **5i** and **6i** in the presence of $[\text{RhCl}(\text{CO})_2]_2$ was



Scheme 4.

Table 2. Rh(I)-catalyzed ring-closing reaction under N_2 

Entry	Allenyne 3	R^1	R^2	Triene 5	Yield (%)
1	3a	H	TMS	5a	59
2	3b	H	Ph	5b	65
3 ^a	3c	ⁿ Pr	TMS	5c	66 ^b
4 ^c	3d	Ph	TMS	5d	57 ^{d,e}

^a 5 mol% of $[\text{RhCl}(\text{CO})_2]_2$ was used.

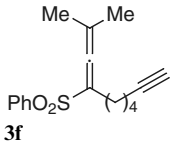
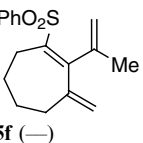
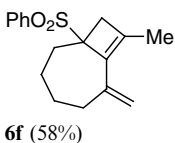
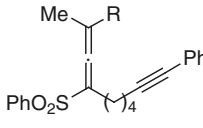
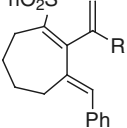
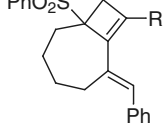
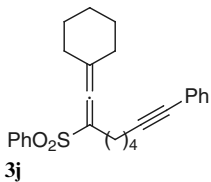
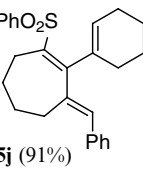
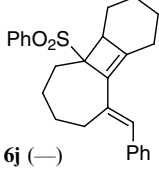
^b *E/Z* ratio (79:21) was determined by ^1H NMR spectrum.

^c 10 mol% of $[\text{RhCl}(\text{CO})_2]_2$ was used.

^d A small amount of **4d** (12%) was obtained.

^e In this case, a mixture of two stereoisomers (*E/Z* = 39:61), due to the geometry of the C_3 -TMSmethylene group of 2-(*E*-phenylethenyl)cycloheptene derivative, was obtained.

Table 3. Rh(I)-catalyzed tandem cycloisomerization–electrocyclization of **3**^a

Entry	Allenynes	Products (yield)	
1 ^b	 3f	 5f (—)	 6f (58%)
2	 3g : R = Ph	 5g (—)	 6g (88%)
3	3h : R = 4-NO ₂ C ₆ H ₄	5h (—)	6h (78%)
4	3i : R = CO ₂ Et	5i (56%)	6i (12%)
5	 3j	 5j (91%)	 6j (—)

^a Reaction was carried out in refluxing xylene under the influence of 2.5 mol % [RhCl(CO)₂]₂.

^b The reaction was carried out in refluxing toluene.

unsuccessful, presumably due to the weak coordinating ability of the α,β -unsaturated ester functionality with the rhodium catalyst. The ring-closing reaction of **3j** having a cyclohexylidene moiety provided the triene **5j**, and not **6j**, in high yield (entry 5). The exclusive formation of **5j** might reflect the steric repulsion between a cyclohexene ring and the phenylsulfonyl group, which would interfere with the transformation of **5j** into **6j**.

In summary, a reliable procedure for not only the construction of the 10-substituted-bicyclo[5.3.0]decadienone ring system, but also for the preparation of the 3-alkylidene-2-vinylcyclohept-1-ene framework has been developed by selecting appropriate reaction conditions, starting from the same trisubstituted allenynes. We have also succeeded in constructing a novel bicyclo[5.2.0]nonene framework by the Rh(I)-catalyzed consecutive cycloisomerization and electrocyclic reaction of tetrasubstituted allenynes. Application of these newly developed cyclization methods to the synthesis of natural products is now in progress.

Acknowledgement

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19. Reaction of **5e** in the presence of $[\text{RhCl}(\text{CO})_2]_2$ for 9 h provided **6e** in 60% yield, along with recovered **5e** (11%), whereas only 42% yield of **6e** and 10% of the recovered **5e** were obtained in the absence of Rh(I) catalyst for 9 h.
20. Refluxing **3f** in xylene resulted in decomposition.
21. Allenyne having TMS group at the alkyne terminus afforded the corresponding bicyclo[5.2.0]nonene derivative in 34% yield.