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Cationic rhodium(I) complex-catalyzed σ- and π-bond activation cascade: Isomerization of allyl propargyl ethers to allenic aldehydes and dienals*

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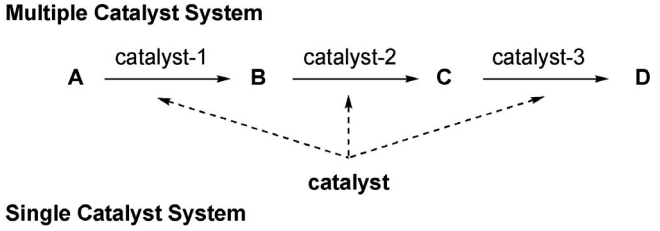
Abstract: A cationic rhodium(I)/1,1'-bis(diphenylphosphino)ferrocene (dppf) complex catalyzes isomerization of allyl propargyl ethers to allenic aldehydes in good yields at room temperature 40 °C. At 80 °C, carbonyl migration from allenic aldehydes proceeds further to give dienals in good yields. The cationic rhodium(I)/dppf complex acts as a dual catalyst for activation of σ- and π-bonds in these isomerization reactions.

Keywords: cascade reactions; C–H bond activation; isomerization; π-bond activation; rearrangement; rhodium.

INTRODUCTION

Cascade reactions can eliminate a number of reaction steps and reduce hazardous waste and solvents, therefore cascade reactions have attracted much attention in current organic synthesis [1]. If a single catalyst can catalyze multiple reaction steps without using multiple catalysts, convenient operation can be realized (Scheme 1). When a single catalyst can act as multiple roles and catalyze multiple reaction steps without loss of catalytic activity, we can realize such an attractive process. It is well known that transition-metal complexes are able to activate σ-bonds by oxidative addition or electrophilic substitution pathway [2]. π-Bonds can also be activated through the formation of a complex between an electrophilic transition metal and π-electrons of alkene or alkyne multiple bonds [3]. Sequential activation of these bonds by a single transition-metal complex would allow developing a novel cascade reaction. We anticipated that cationic rhodium(I) complexes would be promising catalysts for this purpose.



Scheme 1 Catalytic cascade reactions: Multiple catalyst system vs. single catalyst system.

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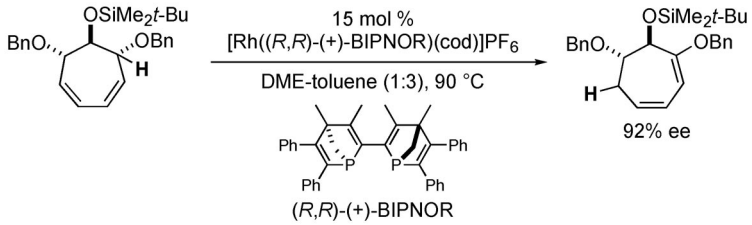
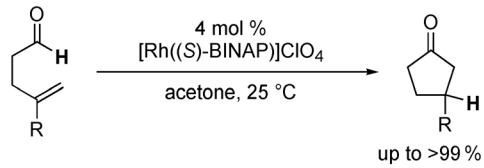
Cationic rhodium(I) complexes are able to catalyze isomerization [4] of allyl ethers to enol ethers through allylic C–H bond activation (eq. 1) [5,6], and hydroacylation of alkenes with aldehydes through aldehyde C–H bond activation (eq. 2) [7,8]. Also, this complex is able to catalyze the aromatic amino-Claisen rearrangement through alkyne triple-bond activation (eq. 3) [9].



(1)



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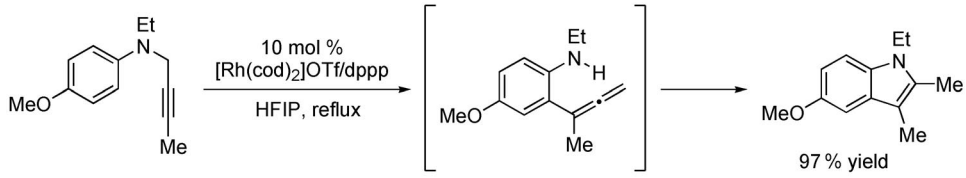
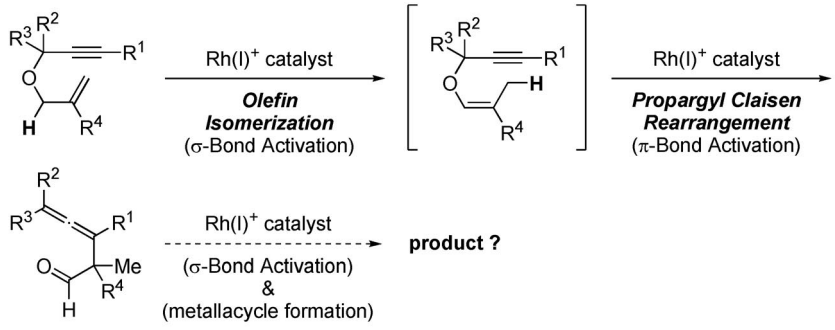


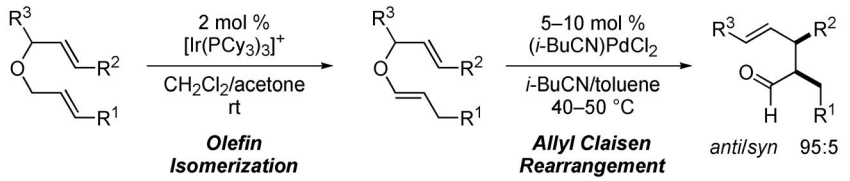
(3)

As a target for a cationic rhodium(I) complex-catalyzed cascade reaction, we focused our attention on a combination of olefin isomerization and the propargyl Claisen rearrangement, that has not been realized to date. If the isomerization of readily prepared and stable allyl propargyl ethers to propargyl vinyl ethers followed by the propargyl Claisen rearrangement can be catalyzed by a single cationic rhodium(I) complex, this would be useful from a synthetic point of view. Furthermore, the product allenic aldehyde would react with the cationic rhodium(I) complex, which might furnish another product through aldehyde C–H bond activation followed by rhodacycle formation (Scheme 2) [10].

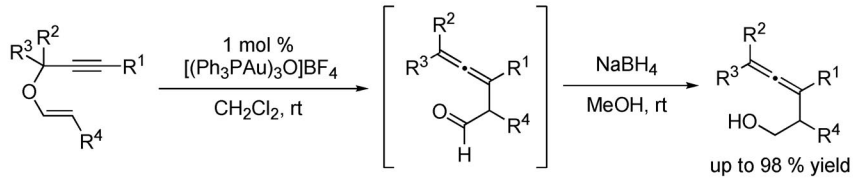


Scheme 2 Our plan for the cationic Rh(I) complex-catalyzed olefin isomerization/propargyl Claisen rearrangement cascade.

Nelson and others reported a number of sequential catalytic olefin isomerization and the thermal or metal-catalyzed allyl Claisen rearrangement (eq. 4) [11]. On the other hand, Toste reported the highly efficient gold-catalyzed propargyl Claisen rearrangement (eq. 5) [12,13]. However, the transition-metal-catalyzed olefin isomerization/propargyl Claisen rearrangement cascade has not been reported to date.



(4)

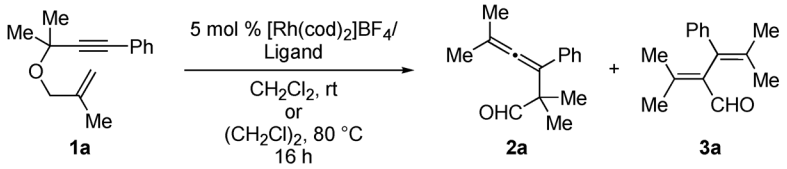


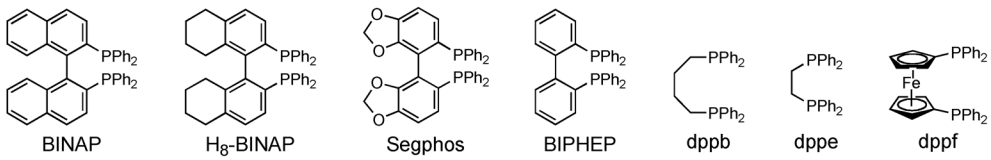
(5)

RESULTS AND DISCUSSION

We first investigated the reaction of allyl propargyl ether **1a** in the presence of a cationic rhodium(I)/BINAP complex as shown in Table 1. Pleasingly, the expected olefin isomerization/propargyl Claisen rearrangement proceeded at room temperature to give the corresponding allenic aldehyde **2a**, and carbonyl migration product **3a** was also generated (entry 1). After screening of bisphosphine

Table 1 Screening of reaction conditions for Rh-catalyzed isomerization of allyl propargyl ether **1a**.





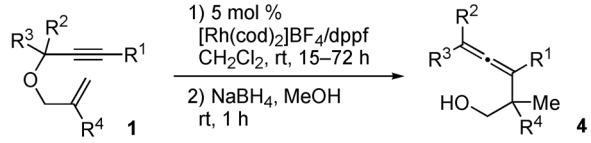
Entry	Ligand	Temp. (°C)	Convn. (%)[a]	**2a**: Yield (%)[a]	**3a**: Yield (%)[a]
1	BINAP	rt	100	39	27
2	H_8-BINAP	rt	100	67	0
3	Segphos	rt	100	70	0
4	BIPHEP	rt	100	67	0
5	dppb	rt	72	56	0
6	dppe	rt	10	0	0
7	dppf	rt	100	80	5
8	dppf	80	100	0	82

[a]Determined by ^{1}H NMR.

ligands (entries 1–7), we found that the use of 1,1'-bis(diphenylphosphino)ferrocene (dppf) furnished allenic aldehyde in the highest yield (entry 7). The selective formation of dienal could also be realized by increasing the reaction temperature to 80 °C (entry 8).

Thus, we explored the scope of the olefin isomerization/propargyl Claisen rearrangement cascade by using 5 mol % of the cationic rhodium(I)/dppf complex as shown in Table 2. The products were isolated as the corresponding reduced alcohols **4** due to the instability of allenic aldehydes **2**. Electronically diverse aryl and sterically diverse alkyl groups could be incorporated at the alkyne terminus (entries 1–5). With respect to substituents at the propargylic position, not only methyl- but also cycloalkyl-, and *i*-propyl-substituted tertiary propargyl ethers could participate in this reaction to yield the corresponding tetrasubstituted allenes in good yields (entries 1–7). Phenyl instead of methyl substitution of the alkene moiety is tolerable, although prolonged reaction time was required (entry 8).

Table 2 Cationic rhodium(I)/dppf complex-catalyzed isomerization of allyl propargyl ethers **1** to homoallenic alcohols **4**.

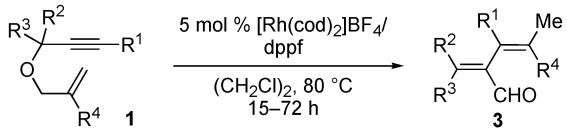


Entry	**1**	R^1	R^2, R^3	R^4	Time (h)	**4**	Yield (%)[a]
1	**1a**	Ph	Me, Me	Me	23	**4a**	74
2	**1b**	4-$MeOC_6H_4$	Me, Me	Me	19	**4b**	72
3	**1c**	4-ClC_6H_4	Me, Me	Me	44	**4c**	71
4	**1d**	*n*-Bu	Me, Me	Me	17	**4d**	69
5[b]	**1e**	Cy	Me, Me	Me	30	**4e**	49
6	**1f**	Ph	$(CH_2)_5$	Me	23	**4f**	70
7	**1g**	Ph	*i*-Pr, Me	Me	15	**4g**	81
8[b]	**1h**	Ph	Me, Me	Ph	72	**4h**	45

[a]Isolated yield.
[b]At 40 °C.

The scope of the olefin isomerization/propargyl Claisen rearrangement/carbonyl migration cascade was also examined by using the same substrates and the same rhodium catalyst as shown in Table 3. In all entries 1–8, the desired isomerization proceeded at 80 °C to yield the corresponding hexasubsitituted dienals in good yields.

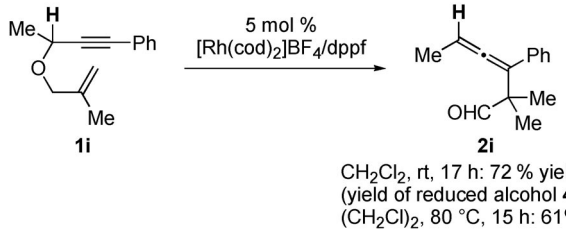
Table 3 Cationic rhodium(I)/dppf complex-catalyzed isomerization of allyl propargyl ethers **1** to dienals **3**.



Entry	**1**	R^1	R^2, R^3	R^4	Time (h)	**3**	Yield (*E*/*Z*)[a]
1	**1a**	Ph	Me, Me	Me	16	**3a**	82
2	**1b**	4-$MeOC_6H_4$	Me, Me	Me	16	**3b**	76
3	**1c**	4-ClC_6H_4	Me, Me	Me	16	**3c**	76
4	**1d**	*n*-Bu	Me, Me	Me	16	**3d**	72
5	**1e**	Cy	Me, Me	Me	72	**3e**	43[b]
6	**1f**	Ph	$(CH_2)_5$	Me	16	**3f**	77
7	**1g**	Ph	*i*-Pr, Me	Me	16	**3g**	67 (4:1)
8	**1h**	Ph	Me, Me	Ph	40	**3h**	80 (2:1)

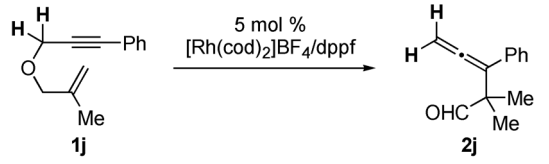
[a]Isolated yield.
[b]The corresponding allenic aldehyde **2e** was remained in ~32 % yield.

Not only tetrasubstituted allenes but also tri- and disubstituted allenes **2i** and **2j** could be obtained in good yields at room temperature (eqs. 6 and 7). Interestingly, the isomerizations to dienals did not proceed at elevated temperature (80 °C), and the isomerizations were terminated at the stage of the allenic aldehydes **2i** and **2j** (eqs. 6 and 7).



CH_2Cl_2, rt, 17 h: 72 % yield
(yield of reduced alcohol **4i**)
$(CH_2Cl)_2$, 80 °C, 15 h: 61% yield

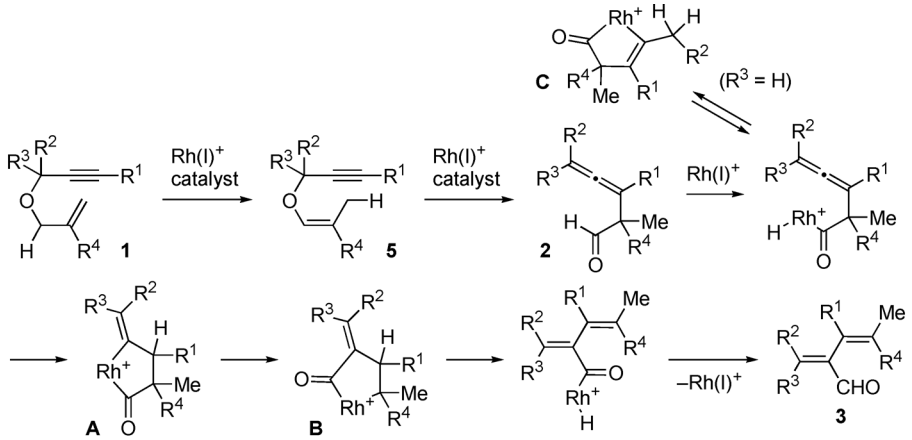
(6)



CH_2Cl_2, rt, 72 h: 65 % yield
$(CH_2Cl)_2$, 80 °C, 16 h: 35 % yield

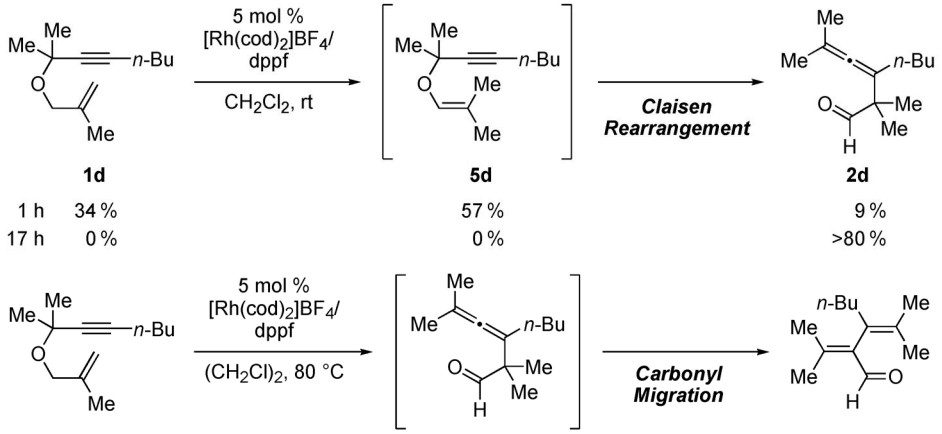
(7)

A possible mechanism for the present isomerization is shown in Scheme 3. In the first step, the olefin isomerization of allyl ether **1** proceeds to give enol ether **5**. Next, the propargyl Claisen rearrangement proceeds through activation of the alkyne triple bond, giving allenic aldehyde **2**. At elevated temperature, activation of the aldehyde C–H bond followed by hydrorhodation of the pendant allene furnishes rhodacycle **A**. Carbonyl migration undergoes to produce conjugated rhodacycle **B**. β-Hydride elimination followed by reductive elimination generates dienal **3**. When R^3 is hydrogen, allenic aldehyde **2**, not dienal **3**, is generated presumably due to reversible hydrorhodation/β-hydride elimination through rhodacycle **C**. Fu and Rovis already reported the similar rhodium-catalyzed carbonyl migration reactions [14].



Scheme 3 A possible mechanism for the isomerization of allyl propargyl ether **1** to allenic aldehyde **2** and dienal **3**.

Consistent with this pathway, enol ether **5d** and allenic aldehyde **2d** were observed by ^{1}H NMR at room temperature for 1 h. After 17 h, allenic aldehyde **2d** was observed as a sole product (eq. 8). Furthermore, allenic aldehyde **2d** and dienal **3d** were observed by ^{1}H NMR at 80 °C for 1 h. After 16 h, dienal **3d** was observed as a sole product (eq. 9).



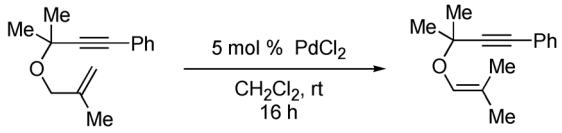
	1d	**5d**	**2d**
1 h	34 %	57 %	9 %
17 h	0 %	0 %	>80 %

(8)

	1d	**2d**	**3d**
1 h	0 %	69 %	31 %
16 h	0 %	0 %	>80 %

(9)

Four additional experiments further provide useful mechanistic information. Electrophilic $PdCl_2$, which is known to be a very effective catalyst for isomerization of allyl ethers to enol ethers through electrophilic double-bond activation [15], did not catalyze isomerization of **1a** to **5a**, which suggests that the electrophilic double-bond activation by the cationic rhodium(I) complex might not be involved in this olefin isomerization (eq. 10). The thermal propargyl Claisen rearrangement of **5d** to **2d** did not proceed (eq. 11), while chiral induction was observed in the reaction of **1h** to **4h** by using a chiral rhodium(I) complex (eq. 12). These results clearly indicate that the cationic rhodium(I) complex indeed catalyzes the propargyl Claisen rearrangement. Furthermore, isolated allenic aldehyde **2a** was indeed transformed to the corresponding dienal **3a** at 80 °C (eq. 13).



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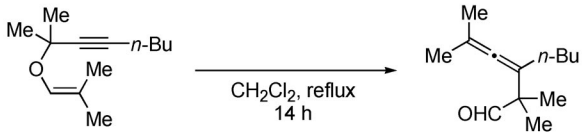
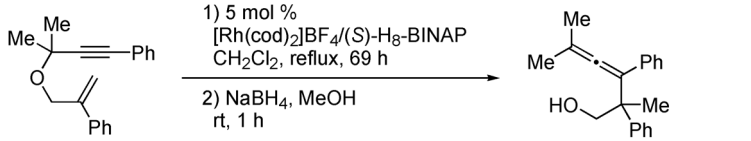
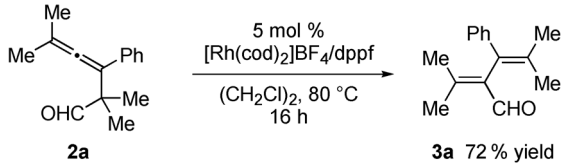


(11)



(12)



(13)

CONCLUSION

In conclusion, we have developed the cationic rhodium(I)/dppf complex-catalyzed isomerizations of allyl propargyl ethers to allenic aldehydes and dienals [16]. The cationic rhodium(I)/dppf complex acts multiple roles and effectively catalyzes multiple reaction steps without loss of catalytic activity. Various cascade reactions catalyzed by the cationic rhodium(I) complex are currently pursued in our laboratory.

ACKNOWLEDGMENTS

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