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Rhodium-catalyzed cycloisomerization of allenenes via metalacycle intermediates

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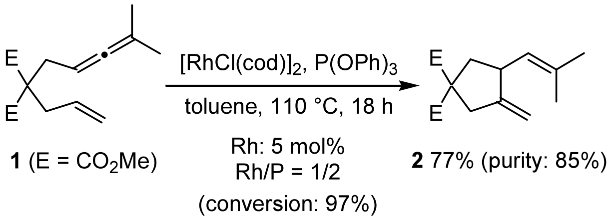
Abstract—In the presence of a catalytic amount of the rhodium complex, allenenes undergo cycloisomerization reactions to result in the selective formation of five and seven membered *exo*-alkylidenecarbocycles and heterocycles via novel *exo*-alkylidenerhodacyclopentane intermediates.

Transition metal-catalyzed carbocyclizations of alkenes and alkynes are powerful protocols for the construction of a wide range of carbocycles and heterocycles with high efficiency and selectivity.[1] Above all, transition metal-catalyzed cycloisomerization reactions are atom economical and environmentally benign synthetic methods[2] because there is no requirement of additional reactants excepting catalysts.[3] In this context, numerous cyclo-isomerizations of 1,n-enynes[4] and 1,n-dienes[5] have been eagerly investigated with various transition metal catalysts. On the other hand, allenes have received much less attention as a component of such cycloisomerizations compared to the alkenes and alkynes.[6,7] To the best of our knowledge, there have been only three reports on the transition metal-catalyzed cycloisomerization reactions of allenenes. Trost et al. reported the pioneering studies with Ni–Cr[8a] and Pd[8b] catalysts. Recently, Kang's group has found that the Ru-catalyzed cycloisomerizations of allenenes afforded cyclic 1,3-dienes or 1,4-dienes.[8c] Many issues, however, still remain to be solved for the cycloisomerization of allenenes. It is particularly important to find highly effective and selective metal-ligand combinations for the cyclo-isomerization catalysts and to uncover the role of central metals and their ligand in regioselectivity at the allenic moiety. Herein, we wish to report the first example of the rhodium-catalyzed cycloisomerization of allenenes with the participation of the internal allenic π-bond to generate cyclic 1,4-dienes with high efficiency and selectivity.

The treatment of the allenene **1** with a catalytic amount of $[RhCl(cod)]_2$ (5 mol% based on Rh) and $P(OPh)_3$ (Rh/P = 1/2) in toluene at 110°C gave us an encouraging result, that is, the *exo*-methylenecyclopentane **2**[9] was isolated in 77% yield with 85% purity as the cycloisomerization product (Eq. (1)).[10]



1 ($E = CO_2Me$)

2 77% (purity: 85%)

(1)

The results for the various allenenes under optimized conditions are summarized in Table 1. The reaction of **1** using the more bulky phosphite ligand $P(O\text{-}o\text{-}tol)_3$ (entry 1) furnished **2** with a higher purity than in the case of $P(OPh)_3$.[11] The reaction of **3** derived from the tosylamide proceeded smoothly to afford a pyrrolidine derivative (entry 2), whereas the benzylamine derivative **5**, which contains the more electron-rich nitrogen atom, resulted in a significant decrease in the yield of the desired product **6** (entry 3). Similarly, the O-tethered allenene **7** gave a poor result (entry 4). In the both reactions, unidentified oligomers mainly formed.[12] The electron-rich hetero atoms of **5** and **6** in the tethers may be strongly coordinated to result in the same improper orientation of the substrates for cyclization. The phenyl- or trimethylsilyl-substituted (*E*)-ene-allenes **9** and **11** gave only the corresponding (*E*)-1,4-dienes **10** and **12**, respectively (entries 5 and 6).[13] The reaction of **13** with only one alkyl substituent at the allenic termi-

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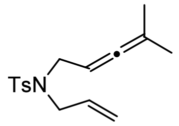
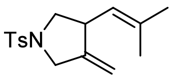
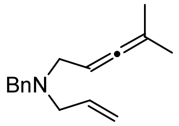
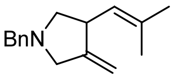
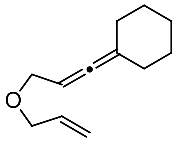
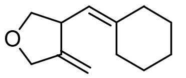
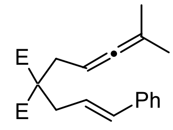
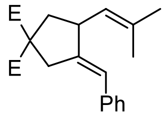
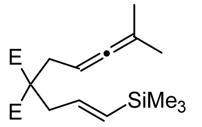
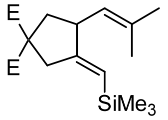
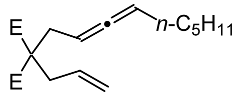
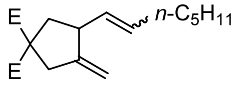
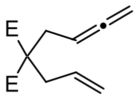
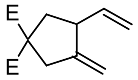
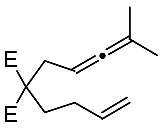
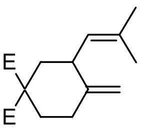
Table 1. Rh(I)-catalyzed cycloisomerization of various allenenes[a]

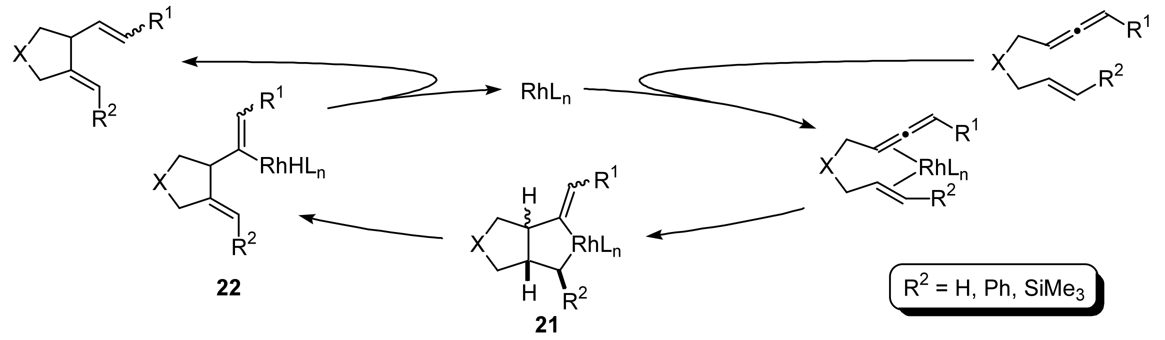
entry	allenene[b]	product	cat. amount	time	conv.[c]	yield[d] (purity[c,e])
1	**1**	**2**	5 mol%	18 h	>99%	92% (99%)
2	 **3**	 **4**	5 mol%	3 h	99%	93% (86%)
3	 **5**	 **6**	10 mol%	24 h	>99%	28% (97%)
4	 **7**	 **8**	10 mol%	24 h	>99%	32% (84%)
5	 **9**	 **10**	10 mol%	24 h	98%	97% (96%)
6	 **11**	 **12**	10 mol%	24 h	97%	94% (92%)
7	 **13**	 **14**	5 mol%	24 h	>99%	78% (>99%) (*E*/*Z* = 2.6/1)
8	 **15**	 **16**	5 mol%	3 h	>99%	41% (92%)
9	 **17**	 **18**	20 mol%	24 h	98%	83% (93%)

[a] All reactions were carried out using $[RhCl(cod)]_2$ and $P(O\text{-}o\text{-}tol)_3$ (Rh/P = 1/2) in 1,4-dioxane at 110 °C (bath temp.) under Ar atmosphere.

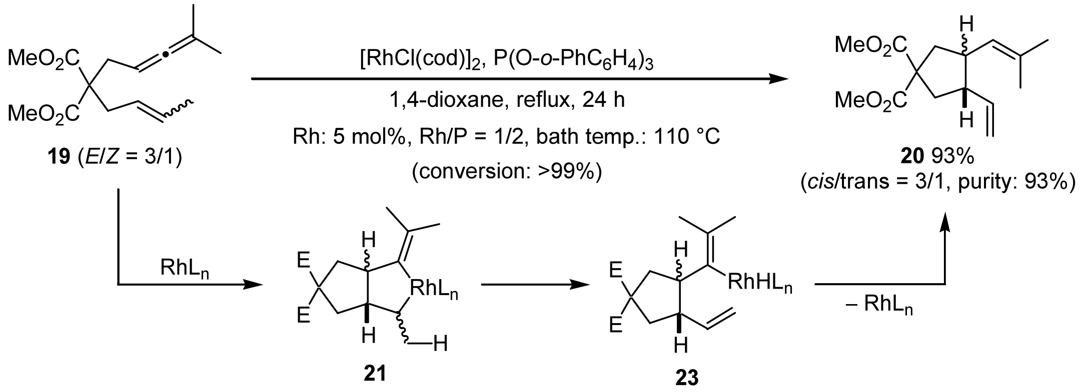
[b] E = CO_2Me. [c] Determined by GC analyses. [d] Isolated yield. [e] The recovered allenenes were included in the impurity.

nus resulted in the formation of the 1,4-diene **14** as an *E*/*Z* mixture (entry 7). Even the allenene **15** possessing the parent allenyl moiety underwent cycloisomerization despite in the low yield of **16** (entry 8). The cycloisomerization of one carbon homologated allenene such as **17** selectively provided the *exo*-methylenecyclohexane **18** without the undesirable isomerization of the C–C double bonds, although high loading of the catalyst was required (entry 9).

A plausible mechanism for the rhodium-catalyzed cycloisomerization of allenenes is depicted in Scheme 1. The absence of hydride sources in the system implies that the cycloisomerization proceeds via a metalacycle intermediates. The initial step is the coordination of the allenene to the rhodium(I) complex at the internal allenic π-bond.[14] Subsequently, the oxidative cyclization gave the *exo*-alkylidenerhodacyclopentane **21**, which undergoes the selective elimination of the β-hydrogen



Scheme 1.

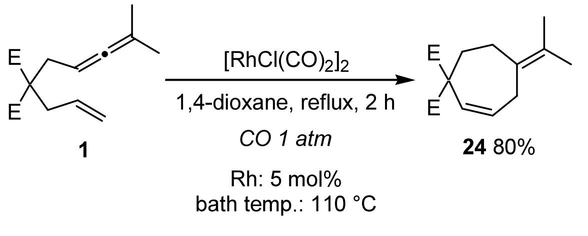


Scheme 2.

atom at the vinylic moiety to give the hydride vinyl complex **22**, which immediately induces the reductive elimination to furnish the 1,4-diene product. Presumably, the elimination of the β-hydrogen derived from the allenic hydrogen would be disfavored due to the existence of the sp^2 carbon at the α position of the metalacycle intermediate **21**, because the Rh–C–C–H moiety cannot take a coplanar conformation required for such a β-hydrogen elimination.

The allenenes **19**, which has a methyl group at the external carbon of the alkene moiety, underwent the cycloisomerization to generate the 1,5-diene. The treatment of **19** ($E/Z=3/1$) with 5 mol% $[RhCl(cod)]_2$ and 10 mol% of $P(O\text{-}o\text{-}PhC_6H_4)_3$ gave the cyclic 1,5-diene **20** in 93% yield and 93% purity as a diastereomeric mixture (*cis*/*trans* = 3/1; Scheme 2).[15] In the case of **19**, the elimination of a β-hydrogen from the pendant methyl group in **21** exclusively occurs to afford **20** by way of the hydride vinyl complex **23**.

Alternatively, in the presence of $[RhCl(CO)_2]_2$ (5 mol% based on Rh) *under a CO atmosphere* the allenene **1** furnished the unexpected *exo*-alkylidenecycloheptene **24**[16] in 80% yield (Eq. (2)).[17]



(2)

It is noteworthy that the analogous reaction of the 1,6-diene such as dimethyl diallylmalonate resulted in recovery of the starting material. This result apparently indicates that the allene moiety plays a key role in the cycloisomerization reaction.[18]

In summary, we have found that allenenes smoothly cycloisomerized in the presence of a catalytic amount of the rhodium complex to allow the selective formation of carbocycles and heterocycles. Further studies on these effective transformations are now in progress.

Acknowledgements

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635–662; (c) Negishi, E.; Copéret, C.; Ma, S.; Liou, S.-Y.; Liu, F. *Chem. Rev.* **1996**, *96*, 365–393; (d) Trost, B. M.; Toste, D. F.; Pinkerton, A. B. *Chem. Rev.* **2002**, *101*, 2067–2096.

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8. (a) Trost, B. M.; Tour, J. M. *J. Am. Chem. Soc.* **1988**, *110*, 5231–5233; (b) Trost, B. M.; Matsuda, K. *J. Am. Chem. Soc.* **1988**, *110*, 5233–5235; (c) Kang, S.-K.; Ko, B.-S.; Lee, D.-M. *Tetrahedron Lett.* **2002**, *43*, 6693–6696.
9. Analytical data for **2**: colorless oil; IR (neat) ν 889 (m), 1072 (m), 1173 (m), 1199 (m), 1269 (s), 1376 (w), 1435 (m), 1657 (w), 1737 (vs), 2954 (m) cm^{-1}.; ^{1}H NMR (500 MHz, CDCl$_3$) δ 1.64 (d, J=1.5 Hz, 3H), 1.73 (d, J=1.5 Hz, 3H), 1.86 (dd, J=11.5, 13.0 Hz, 1H), 2.54 (ddd, J=1.3, 7.5, 13.0 Hz, 1H), 2.95 (ddt, J=2.3, 2.3, 17.0 Hz, 1H), 3.08 (bd, J=17.0 Hz, 1H), 3.32–3.37 (m, 1H), 3.72 (s, 3H), 3.75 (s, 3H), 4.72–4.74 (m, 1H), 4.88–4.89 (m, 1H), 4.95–4.97 (m, 1H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$) δ 18.07, 25.63, 40.04, 40.82, 42.37, 52.68, 52.75, 58.26, 106.92, 125.62, 133.59, 151.26, 172.11, 172.37 ppm. MS (FAB) m/z (rel. intensity, %) 193 (79), 253 (MH$^+$, 100). HRMS (FAB) calcd for $C_{14}H_{20}O_4$: 252.1362. Found: 252.1329.
10. The purity was determined by GC analysis of the isolated product **2**. The recovered allenene **1** was included in the impurity.
11. Typical procedure for rhodium(I)-catalyzed cycloisomerizations of allenenes: to an oven-dried Schlenk flask containing [RhCl(cod)]$_2$ (3.1 mg, 0.013 mmol) was added a solution of P(O-*o*-tol)$_3$ (9.4 mg, 0.027 mmol) in degassed dry 1,4-dioxane (1 ml). Then a solution of dimethyl 2-(4-methyl-2,3-pentadienyl)-2-(2-propenyl)malonate (**1**) (62.1 mg, 0.25 mmol) in degassed dry 1,4-dioxane (1.5 ml) was added to the reaction vessel. The mixture was stirred at 110°C for 18 h under an Ar atmosphere. After cooling to room temperature, the volatile materials were removed in vacuo. The residue was subjected to silica gel flash column chromatography (eluent; *n*-hexane/ethyl acetate = 20/1) to afford dimethyl 3-methylene-4-(2-methyl-1-propenyl)cyclopentane-1,1-dicarboxylate (**2**) (56.9 mg, 92%) as colorless oil. The gas chromatographic analysis of the isolated product revealed that **2** was contained in 99% purity.
12. In the case of **7**, the structure of side products are not determined at present.
13. The stereochemistry of **10** and **12** were determined by NOE experiments.
14. In the case of the cycloisomerization of allenynes, the allene moiety coordinates to the rhodium(I) center at the external allenic π-bond to form the rhodacyclopentene. See Ref. 6.
15. The use of P(O-*o*-tol)$_3$ slightly lowered both yield and purity of **20** (90% yield and 87% purity).
16. The structure of **24** was assigned based on the ^{1}H, ^{13}C, COSY, HETCOR and HMBC spectra. Analytical data for **24**: colorless oil; IR (neat) ν 807 (m), 1066 (s), 1229 (vs), 1373 (m), 1434 (s), 1737 (vs), 2952 (s) cm^{-1}.; ^{1}H NMR (500 MHz, CDCl$_3$) δ 1.57 (s, 3H), 1.60 (s, 3H), 2.39 (bs, 4H), 2.85 (bd, J=6.3 Hz, 2H), 3.70 (s, 6H), 5.64 (dt, J=1.5, 10.8 Hz, 1H), 5.95 (dt, J=6.3, 10.8 Hz, 1H) ppm. ^{13}C NMR (125 MHz, CDCl$_3$) δ 20.03, 20.32, 27.92, 30.30, 30.63, 52.67, 60.21, 124.80, 126.37, 128.45, 131.83, 171.35 ppm. MS (FAB) m/z (rel intensity, %) 192 (83), 253 (MH$^+$, 100). Anal. calcd for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99. Found: C, 66.51; H, 8.01.
17. Recently, Trost et al. reported the formation of *exo*-alkylidenecycloheptenes by the ruthenium-catalyzed cyclo-isomerization of 1,6-enynes, see: (a) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **1999**, *121*, 9728; (b) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2002**, *124*, 5025. Similar mechanism is considered to also be operative in the present case.
18. Similar results were obtained in the transition metal-catalyzed carbonylative [4+1] cycloaddition of vinylallenes and [5+1] cycloaddition of allenylcyclopropanes, see: (a) Murakami, M.; Itami, K.; Ito, Y. *Organometallics* **1999**, *18*, 1326–1336; (b) Murakami, M.; Itami, K.; Ito, Y. *J. Org. Chem.* **1998**, *63*, 4–5.