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Novel Rhodium(I)-Catalyzed Cycloisomerization of 1,3-Diene with Alkene in a Tether: Competitive Reaction with [4 + 2] Cycloaddition

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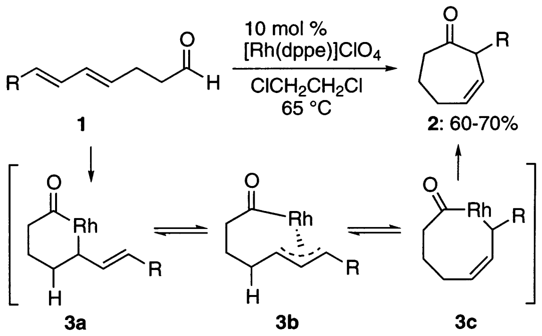
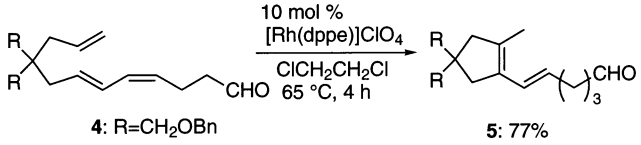
Summary: Rh(I)-catalyzed cycloisomerization of 1,3-dienes with alkenes in a tether proceeded smoothly, giving cyclopentene derivatives in good yields. It was interesting that the existence of a heteroatom between a 1,3-diene moiety and alkene in the tether affected the reaction course and that only a [4 + 2] cycloaddition product was produced.

Transition-metal-catalyzed cyclization is one of the most promising strategies for the construction of various cyclic compounds.[1] We have recently reported a Rh(I)-catalyzed intramolecular hydroacylation of 4,6-dienals by which various cycloheptenones were obtained in good yields via reductive elimination from rhodacyclooctene **3c** (Scheme 1).[2] During our ongoing investigation of this hydroacylation, we found that the reaction of 4,6-dienal **4**, having an olefin in the tether, gave cyclopentene **5** in 77% yield *via cycloisomerization of the 1,3-diene moiety and the tethered olefin* (Scheme 2). Although several Rh(I)-catalyzed [4 + 2] cycloadditions of 1,3-dienes with alkenes or alkynes have been reported,[3] no report on the Rh(I)-catalyzed cycloisomerization of 1,3-dienes with alkenes has appeared in the literature to date.[4,5] Herein we report the results of further investigation of this novel cycloisomerization.

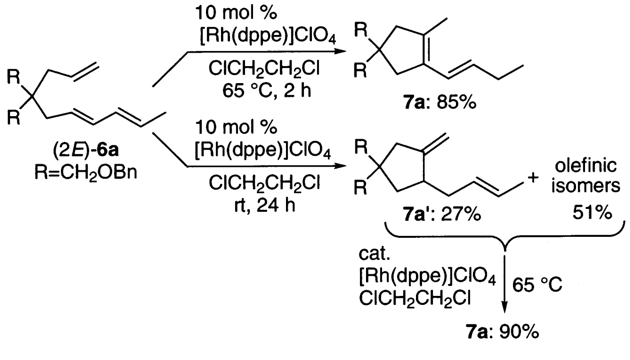
Scheme 1



Scheme 2



Scheme 3



Initially, the reaction of (2*E*)-**6a**, having no aldehyde moiety, was carried out in order to investigate the effect of an aldehyde group in the substrate **4** on this reaction. Treatment of (2*E*)-**6a** with 10 mol % of [Rh(dppe)]ClO$_4$ in dichloroethane at 65 °C for 2 h gave cycloisomerization product **7a** in 85% yield (Scheme 3). This result indicates that an aldehyde group in the substrate is not necessary for this cycloisomerization. Since [4 + 2] cycloadditions of 1,3-dienes with alkenes or alkynes under similar conditions (catalyst [Rh(dppe)]SbF$_6$, CH$_2$Cl$_2$, 25 °C) have already been reported,[3e,f] the reaction of (2*E*)-**6a** was carried out at room temperature using [Rh(dppe)]ClO$_4$ as a catalyst in dichloroethane. As a

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[1] For reviews, see: (a) Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635 and references therein. (b) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49 and references therein. (c) Trost, B. M. *Science* **1991**, *254*, 1471 and references therein. (d) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 259 and references therein.

[2] Sato, Y.; Oonishi, Y.; Mori, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 1218.

[3] (a) Jolly, R. S.; Luedtke, G.; Sheehan, D.; Livinghouse, T. *J. Am. Chem. Soc.* **1990**, *112*, 4965. (b) McKinstry, L.; Livinghouse, T. *Tetrahedron* **1994**, *50*, 6145. (c) O'Mahony, D. J. R.; Belanger, D. B.; Livinghouse, T. *Synlett* **1998**, 443. (d) Heath, H.; Wolfe, B.; Livinghouse, T. Bae, S. K. *Synthesis* **2001**, 2341. (e) Gilbertson, S. R.; Hoge, G. S. *Tetrahedron Lett.* **1998**, *39*, 2075. (f) Gilbertson, S. R.; Hoge, G. S.; Genov, D. G. *J. Org. Chem.* **1998**, *63*, 10077. (g) Wang, B.; Cao, P.; Zhang, X. *Tetrahedron Lett.* **2000**, *41*, 8041.

[4] For a review of transition-metal-catalyzed cycloisomerizations, see: (a) Trost, B. M.; Krische, M. J. *Synlett* **1998**, 1. For Rh-catalyzed cycloisomerizations of α,ω-dienes, see: (b) Bright, A.; Malone, J. F.; Nicholson, J. K.; Powell, J.; Shaw, B. L. *J. Chem. Soc., Chem. Commun.* **1971**, 712. (c) Schmitz, E.; Urban, R.; Heuck, U.; Zimmermann, G.; Gründemann, E. *J. Prakt. Chem.* **1976**, *318*, 185. (d) Schmitz, E.; Heuck, U.; Habisch, D. *J. Prakt. Chem.* **1976**, *318*, 471. (e) Grigg, R.; Mitchell, T. R. B.; Ramasubbu, A. *J. Chem. Soc., Chem. Commun.* **1980**, 27. (f) Grigg, R.; Malone, J. F.; Mitchell, T. R. B.; Ramasubbu, A.; Scott, R. M. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1745. For Rh-catalyzed cycloisomerizations of enynes, see: (g) Cao, P.; Wang, B.; Zhang, X. *J. Am. Chem. Soc.* **2000**, *122*, 6490. (h) Cao, P.; Zhang, X. *Angew. Chem., Int. Ed.* **2000**, *39*, 4104.

[5] For cycloisomerizations of 1,3-dienes with alkenes, only the iron-catalyzed reactions have been reported so far by Takacs; see: (a) Takacs, J. M.; Anderson, L. G. *J. Am. Chem. Soc.* **1987**, *109*, 2200. (b) Takacs, J. M.; Anderson, L. G.; Creswell, M. W.; Takacs, B. E. *Tetrahedron Lett.* **1987**, *28*, 5627. (c) Takacs, J. M.; Newsome, P. W.; Kuehn, C. *Tetrahedron* **1990**, *46*, 5507. (d) Takacs, B. E.; Takacs, J. M. *Tetrahedron Lett.* **1990**, *31*, 2865. (e) Takacs, J. M.; Myoung, Y. C. *Tetrahedron Lett.* **1992**, *33*, 317.

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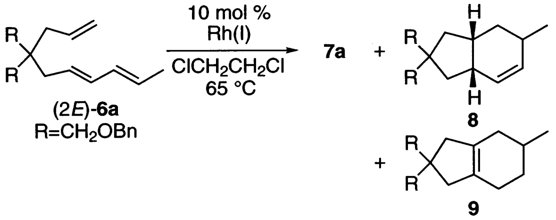
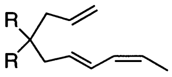
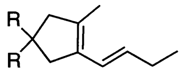
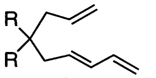
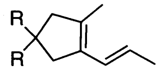
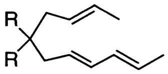
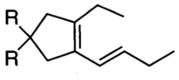
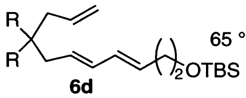
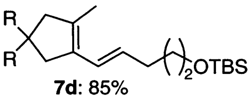
Table 1. Reactions of (2*E*)-6a Using Various Rh(I) Complexes



run	cat.	time (h)	yield (%)		
			7a	**8**	**9**
1	[Rh(dppe)]ClO$_4$	2	85	–	–
2	[Rh(dppp)]ClO$_4$	6	34	–	41
3	[Rh(dppb)]ClO$_4$	12	trace	–	70
4	RhCl(PPh$_3$)$_3$	30	–	81	–

Table 2. Reactions of Various Trienes with [Rh(dppe)]ClO$_4$

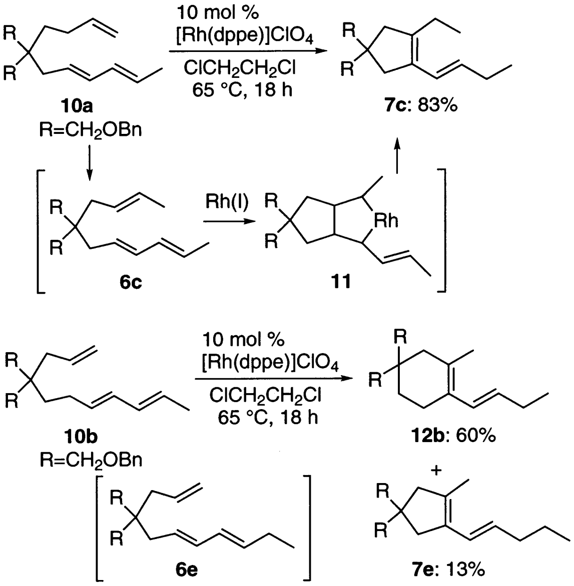
run	substrate[a]	condition[b]	product
1	 (2*Z*)-**6a**	65 °C, 14 h	 **7a**: 80%
2	 **6b**	65 °C, 12 h	 **7b**: 59%
3	 **6c**	65 °C, 18 h	 **7c**: 77%
4	 **6d**	65 °C, 4 h	 **7d**: 85%

[a] R = CH$_2$OBn. [b] All reactions were carried out in ClCH$_2$CH$_2$Cl using 10 mol % [Rh(dppe)]ClO$_4$ complex generated in situ from [Rh(nbd)(dppe)]ClO$_4$ under an atmosphere of hydrogen.

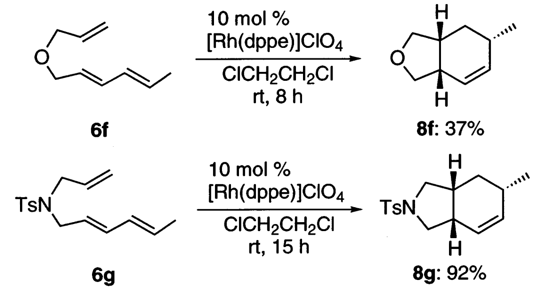
result, **7a′** was obtained in 27% yield along with an inseparable mixture of the products (51% yield) (Scheme 3). When the mixture was treated again with a catalytic amount of [Rh(dppe)]ClO$_4$ in dichloroethane at 65 °C, **7a** was obtained in 90% yield as a single isomer. This result indicates that this cycloisomerization proceeds even at room temperature and that [4 + 2] cycloaddition does not occur under our conditions.

Next, we turned our attention to the use of various Rh(I) complexes in the reaction of (2*E*)-**6a**. The use of [Rh(dppe)]Cl, generated in situ from [Rh(cyclooctene)$_2$Cl]$_2$ (5 mol %) and dppe (10 mol %), gave no product, and the starting material (2*E*)-**6a** was recovered in 78% yield. On the basis of this result, our investigation was focused on the cationic Rh(I) complexes, and the results are summarized in Table 1. The reaction of (2*E*)-**6a** with [Rh(dppp)]ClO$_4$ gave the cycloisomerization product **7a** in 34% yield along with the [4 + 2] cycloaddition product **9** in 41% yield. The use of [Rh(dppb)]ClO$_4$ or RhCl(PPh$_3$)$_3$ promoted [4 + 2] cycloaddition, and **9** or **8** was obtained in 70% or 81% yield, respectively. These results suggested that the reaction course of this cycloisomerization is strongly affected by the nature of ligands, and [Rh(dppe)]ClO$_4$ is the best catalyst for this cycloisomerization.

Scheme 4



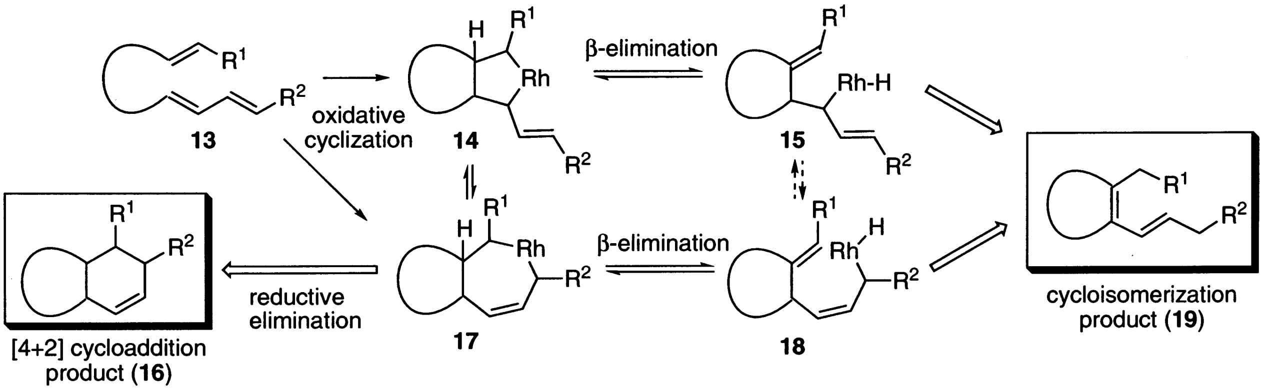
Scheme 5



Encouraged by these results, cycloisomerization of various trienes using [Rh(dppe)]ClO$_4$ was investigated (Table 2). The reaction of (2*Z*)-**6a**, an olefinic isomer of (2*E*)-**6a** with respect to the C2 carbon, gave **7a** in 80% yield (run 1), indicating that the difference in geometry at the 1,3-diene moiety does not affect the reaction course. In the reaction of the terminal diene **6b**, the corresponding cyclized product **7b** was produced in 59% yield (run 2). The reaction of **6c**, having an internal diene and disubstituted olefin in a tether, also proceeded smoothly to afford **7c** in 77% yield (run 3). The existence of a silyloxy group in the side chain is tolerated in this cycloisomerization, and the reaction of **6d** gave cyclopentene **7d** in 85% yield (run 4).

When **10a**, whose reaction was expected to give a six-membered-ring product, was treated with 10 mol % of [Rh(dppe)]ClO$_4$ in dichloroethane at 65 °C for 18 h, the five-membered-ring product **7c** was obtained in 83% yield (Scheme 4). It was thought that the olefin isomerization of **10a** occurred under the conditions, giving **6c**, and that **7c** was produced via rhodacycle **11** generated from **6c** and the rhodium catalyst. On the other hand, the reaction of **10b** under the same conditions gave the six-membered-ring product **12b** in 60% yield along with the five-membered-ring product **7e** in 13% yield. Interestingly, we found that only a [4 + 2] cycloaddition reaction proceeded in the case of **6f** or **6g**, having a heteroatom between a 1,3-diene moiety and alkene in the tether, to give **8f** or **8g** in 37% or 92% yield, respectively (Scheme 5).[6]

Scheme 6. Mechanism of Cycloisomerization and [4 + 2] Cycloaddition



A plausible reaction course of the cycloisomerization and [4 + 2] cycloaddition is shown in Scheme 6. The rhodacyclopentane **14** or **17** would be initially formed via oxidative cycloaddition of **13** to a Rh(I) complex. The rhodacyclopentane **14** would be in equilibration with rhodacycloheptene **17**, and β-elimination of **14** or **17** would give the rhodium hydride complex **15** or **18**. The cycloisomerization product **19** would be produced through reductive elimination from **15** or **18** followed by an olefin isomerization reaction. On the other hand, the [4 + 2] cycloaddition product **16** would be obtained via reductive elimination from **17**. At present, the diverging point in the cycloisomerization vs the [4 + 2] cycloaddition is still unclear, although the results for the reaction of **6e** and **6f**, in which only a [4 + 2] cycloaddition product was produced, suggest the existence of a diverging point. Further studies to determine the scope, limitations, and the mechanism of this cycloisomerization are in progress.

Supporting Information Available: Text giving the typical procedure for cycloisomerization and spectral data of the substrates (**4**, (2*E*)-**6a**, (2*Z*)-**6a**, **6b**, **6c**, **6d**, **10a**, and **10b**) and cyclized products (**5**, **7a**, **7a′**, **7b**, **7c**, **7d**, **7e**, **8**, **9**, and **12b**). This material is available free of charge via the Internet at http://pubs.acs.org.

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(6) The [4 + 2] cycloaddition of **6f** or **6g** had been independently reported by Livinghouse (**6f** and **6g**) and Gilbertson (**6f**),[3] in which the same [4 + 2] adduct **8f** or **8g** was obtained. The spectral data of **8f** and **8g** obtained by us were completely identical with those.