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Observation of New Cycloisomerization Pattern of 1,5-Bisallenes. Catalyst and Substituent Effects

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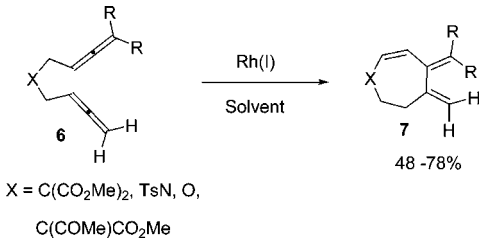
ABSTRACT



In this paper a new cycloisomerization pattern of 1,5-bisallenes based on the catalyst and substituent effects has been reported. A range of seven-membered cross-conjugated trienes 7 would be obtained efficiently via the β-H elimination and reductive elimination of the intermediates formed via cycloisomerization.

Transition-metal-catalyzed reactions have shown their beauty in organic synthesis with the privileges of mild reaction conditions, high yields, and high stereoselectivity.[1−4] In particular, cyclometalation of dienes,[5] enynes,[6] diynes,[7] allenenes,[8] and allenynes[9] have been demonstrated to be highly efficient for the synthesis of cyclic compounds. Furthermore, metal-catalyzed [5 + 2] cycloaddition reactions based on the cycloisomerizations of vinylcyclopropanes and alkynes, alkenes, or allenes offer a powerful and efficient method for the facile construction of substituted seven-membered-ring systems.[10] Recently, we have observed that the transition-metal-catalyzed bimolecular cyclization and [2 + 2]-cycloaddition of unsubstituted 1,5-bisallenes would form steroid-like tetracyclic skeletons[11] and bicyclo-[3.2.0] products[12] via the possible intermediacies of metalabicycles

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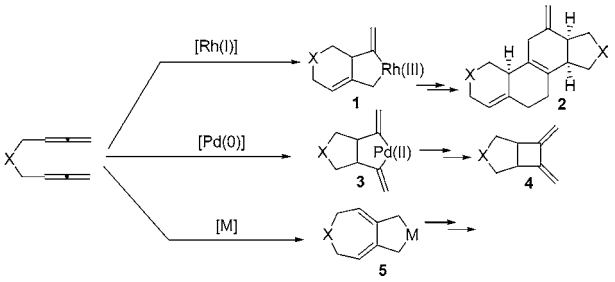
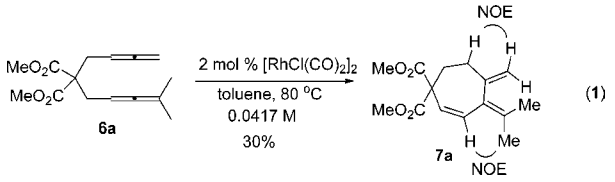
1 and **3** by applying different carbon−carbon double bonds, respectively (Scheme 1). In this paper, we would like to report our recent observation that the two carbon−carbon double bonds remote from the tether "X" may possibly undergo highly selective cycloisomerization forming **5**-type intermediates to afford 3,4-bisalkylidenecycloheptenes by applying catalyst and substituent effects.

Scheme 1



On the basis of our previous study, we tried to expand the scope of this reaction to substrates with substituents at the terminal positions of 1,5-bisallenes. When bisallene **6a** was treated with 5 mol % of trans-RhCl(CO)$(PPh_3)_2$ in toluene under reflux, besides a mixture of not-yet-fully identified regioisomeric bimolecular steroid-like products,[11] we also detected a trace amount of monocyclic product **7a**. Thus, a few rhodium catalysts were screened. Fortunately, when bisallene **6a** was treated with 2 mol % of $[RhCl(CO)_2]_2$ in toluene at 80 °C, this same monocyclic product **7a** was isolated in 30% yield with the cross-conjugated structure being confirmed by NOE study (eq 1).



The formation of seven-membered triene **7a** indicated the existence of a **5**-type of intermediate, that is, the catalyst and methyl groups of the starting bisallene changed the pattern of the cyclization cleanly.

The solvent effect was then studied with typical results being summarized in Table 1. The best result was obtained when acetonitrile was used as solvent (entry 4). The reaction in dioxane or nitromethane gave inferior yield (entries 1 and 5). Notably, a moderate yield of product **7a** was achieved in DMF (entry 2). We also found that the reaction gave the product **7a** in similar yields when $[RhCl(COD)]_2$/dppp or dppe was used as catalyst in acetonitrile (entries 7 and 8). Triene **7a** was obtained in 55% yield on a reaction scale of 1.5 mmol under the catalysis of $[RhCl(COD)]_2$/dppp (entry 9). We assumed that the nitrile group in the solvent may coordinate with the catalytically active rhodium species to suppress the formation of oligomeric byproducts, which is in accordance with what we found in our study of solvent effect on the formation of steroid-like tetracyclic skeletons via the cyclometalation of 1,5-bisallenes.[11a]

Table 1. Optimization of Reaction Conditions for the Cycloisomerization of **6a**[a]

entry	solvent	time (h)	yield of **4a** (%)
1	dioxane	19	33
2	DMF[b]	19	53
3	THF	41.5	44
4	CH_3CN	17.5	62
5	CH_3NO_2	18	26
6	DMA[b]	7.5	53
7	CH_3CN[c]	20	52
8	CH_3CN[d]	45	56
9	CH_3CN[e]	24	55

[a] The reaction was carried out using **6a** (0.25 mmol, at a concentration of 0.0417 M) and 2 mol % rhodium catalyst under reflux. [b] The reaction was conducted at 100 °C. [c] $[RhCl(COD)]_2$ (5 mol %) and dppe (10 mol %) were used as the catalyst. [d] Conditions B: $[RhCl(COD)]_2$ (2.5 mol %) and dppp (5 mol %) were used as the catalyst. [e] The reaction was carried out using **6a** (1.5 mmol, at a concentration of 0.0417 M), $[RhCl(COD)]_2$ (2.5 mol %), and dppp (5 mol %) under reflux.

Further investigation for the scope of the reaction was conducted with different alkyl substitutents R and tethers "X" (Table 2). Bisallene **6b** possessing the 1, 1-pentamethylene on the distal position of the allene provided the triene **7b** in 54% yield under the catalysis of $[RhCl(COD)]_2$ and dppp (conditions B) while the reaction under the conditions A gave **7a** with a lower purity (entries 1 and 2). A higher reaction temperature was required (conditions C) when bisallenes **6c** and **6d**, in which both terminal positions of the two allene moieties were fully substituted, were used (entries 3 and 4). The reaction of **6e** gave **7e** in moderate yields indicating that the malonate moiety was not necessary (entry 5). An azepine derivative[13] could also be obtained efficiently under the conditions A from the substrates with NTs as the tether (entries 6−8). The bisallene (*S*)-(−)-**6i** underwent efficient cycloisomerization to afford the triene (*S*)-(+)-**7i** in 67% yield without obvious racemization under

(10) For [5 + 2] cycloaddition reactions of vinylcyclopropanes (VCPs) with alkynes, see: (a) Wender, P. A.; Takahashi, H.; Witulski. B. *J. Am. Chem. Soc.* **1995**, *117*, 4720. (b) Wender, P. A.; Williams, T. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 4550. For cycloaddition reactions of VCPs with alkenes, see: (c) Wender, P. A.; Husfeld, C. O.; Langkopf, E.; Love, J. A. *J. Am. Chem. Soc.* **1998**, *120*, 1940. (d) Wender, P. A.; Husfeld, C. O.; Langkopf, E.; Love, J. A.; Pleuss, N. *Tetrahedron* **1998**, *54*, 7203. For cycloaddition reactions of VCPs with allenes, see: (e) Wender, P. A.; Glorius, F.; Husfeld, C. O.; Langkopf, E.; Love, J. A. *J. Am. Chem. Soc.* **1999**, *121*, 5348. For applications in natural product synthesis, see: (f) Wender, P. A.; Fuji, M.; Husfeld, C. O.; Love, J. A. *Org. Lett.* **1999**, *1*, 137. (g) Wender, P. A.; Zhang, L. *Org. Lett.* **2000**, *2*, 2323.

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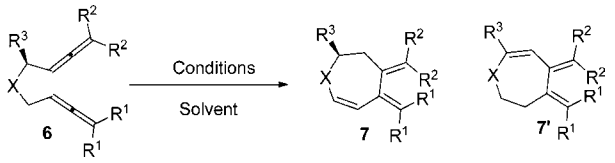
Table 2. The Rhodium-Catalyzed Cycloisomerization of 1,5-Bisallene **6**



entry	X[a]/R³	R¹, R¹	R², R²	conditions/ time (h)	yield of **7** (%)
1	CE_2/H	-$(CH_2)_5$-	H, H (**6b**)	A[b]/9.5	68 (**7b**)[c]
2	CE_2/H	-$(CH_2)_5$-	H, H (**6b**)	B[d]/22	54 (**7b**)[e]
3	CE_2/H	Me, Me (**6c**)		C[f]/5	71 (**7c**)
4	CE_2/H	-$(CH_2)_5$- (**6d**)		C/9	56 (**7d**)
5	AcCE/H	Me, Me	H, H (**6e**)	B/21	48 (**7e**)[e]
6	NTs/H	Me, Me	H, H (**6f**)	A/69	70 (**7f**)[g]
7	NTs/H	Et, Et	H, H (**6g**)	A/57	78 (**7g**)[g]
8	NTs/H	-$(CH_2)_5$-	H, H (**6h**)	A/69	65 (**7h**)[g]
9[h]	NTs/Me	-$(CH_2)_5$-	H, H (**6i**)	A/24	67 (**7i**)[e]
10	O/H	Et, Et	H, H (**6j**)	A/2	61 (**7j**)[i]

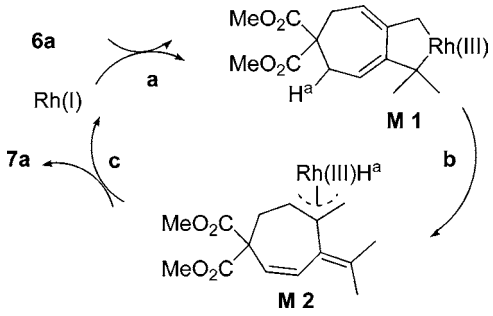
[a] *E* = CO_2Me, Ac = CH_3CO. [b] Conditions A: **6** (0.25 mmol, at a concentration of 0.0417 M) was treated with 2 mol % $[RhCl(CO)_2]_2$ in acetonitrile under reflux. [c] **7b**/**7′b** = 7.3:1. [d] Conditions B: **6** (0.25 mmol, at a concentration of 0.0417 M) was treated with 2.5 mol % $[RhCl(COD)]_2$ and 5 mol % dppp in acetonitrile under reflux. [e] The formation of **7′**-type product was not observed. [f] Conditions C: **6** (0.25 mmol, at a concentration of 0.0417 M) was treated with 2 mol % $[RhCl(CO)_2]_2$ in DMF at 110 °C. [g] The formation of **7′**-type regioisomers should be <5%, if any. [h] The ee values of (*S*)-**6i** and (*S*)-**7i** (84% ee) were determined by the chiral HPLC. [i] **7j**/**7′j** = 16:1.

the conditions A (entry 9). The bisallene **6j** with O as the tether also afforded the oxepine derivative efficiently (entry 10).

A possible mechanism was proposed for the above results (Scheme 2). Bisallene **6a** underwent cycloisomerization to afford seven-membered bisallylic rhodium intermediate **M1**, which would undergo highly regioselective β-H^a elimination affording intermeidate **M2**. Subsequent reductive elimination would afford **7a** with regeneration of the rhodium catalyst.[7,8]

In conclusion, we have reported an efficient route for the synthesis of seven-membered trienes via rhodium-catalyzed

Scheme 2. A Possible Mechanism for the Rhodium-Catalyzed Transformation of 1,5-Bisallenes[a]



[a] Mechanisms: (a) cyclometalation; (b) β-H elimination; (c) reductive elimination.

cycloisomerization of 1,5-bisallenes. It is quite interesting to observe that the catalyst and substituents switch the pathway of cyclization completely. Further studies in this area are being pursued in our group.

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Note Added after ASAP Publication. Some compound numbering in Table 2 and the Supporting Information was incorrect in the version published ASAP May 2, 2007; the corrected version was published ASAP May 7, 2007.

Supporting Information Available: Experimental procedures and characterization data of all new products. This material is available free of charge via the Internet at http://pubs.acs.org.

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