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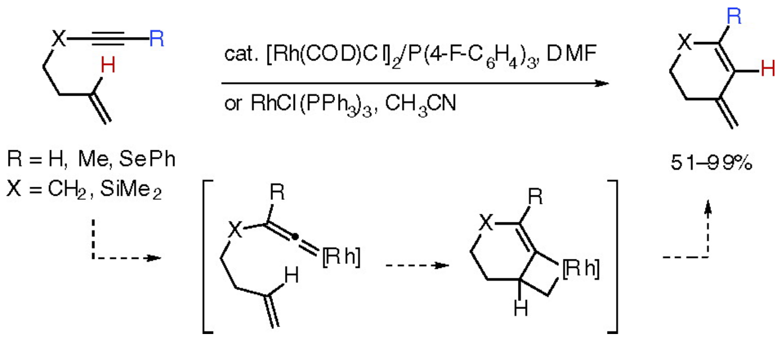

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Cycloisomerization of Enynes via Rhodium Vinylidene-Mediated Catalysis

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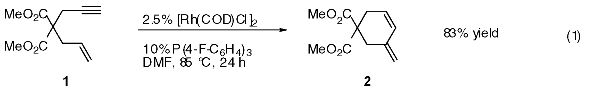
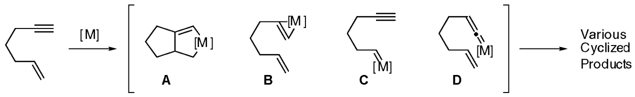
The transition metal-catalyzed cycloisomerization of enynes is a powerful method for accessing cyclic structures from acyclic precursors of substantially less molecular complexity.[1] In this inherently atom-economical process, the unsaturated substrates are mobilized to undergo cyclizations typically infeasible under thermal conditions. From a mechanistic perspective, the majority of the reported examples can be classified into a few modalities based on key intermediates, such as metallacycle (**A**),[2] metallo-η^2-alkyne (**B**),[3] and metal alkylidene (**C**)[4] species (Scheme 1). An intriguing mechanistic motif is the potential intermediacy of a metal vinylidene (**D**). This strategy is attractive since a variety of transition metals are capable of generating vinylidene complexes from alkynes under mild conditions.[5] However, the involvement of a metal vinylidene in the cycloisomerization process has been noted only in dienyne systems, particularly in the context of aromatic substrates.[6] A potentially more useful prototype with a simple unactivated alkene, such as **D**, has remained unreported. We reasoned that the archetypal reaction pathways making use of intermediates **A**−**C** could be diverted by facile formation of a metal vinylidene and its subsequent C−C bond-forming process induced by a reaction between the two remote π-systems of the C═M and C═C bonds. Described here are the verification of this proposition and consequent discovery of a new mode of enyne cycloisomerization mediated by rhodium(I) catalysis.

On the basis of the vinylidene hypothesis, our studies were started with cyclization of 1,6-enyne **1** by screening various catalyst systems known to provide a metal vinylidene (eq 1). Whereas initial attempts using ruthenium-based catalysts led mainly to formation of complex mixtures of products, the use of [RhCl(COD)]$_2$/P(4-FC$_6$H$_4$)$_3$ as the catalyst in DMF induced conversion of enyne **1** to its cyclic diene isomer **2** at 25 °C, albeit in low yield (ca. 5%).[7] When the reaction was performed at 85 °C, diene **2** was produced in 83% yield with exclusive endoselectivity (i.e., the alkyne formally became an endoalkene as a consequence of the cyclization). As this type of unusual cyclization had been observed under RhCl(PPh$_3$)$_3$ and cationic Au(I) catalyses, wherein hydridorhodium and aurocarbene intermediates were invoked, respectively,[3b,8] we set out to conduct a series of deuterium-labeling experiments in order to gain more insight into the mechanism (vide infra).

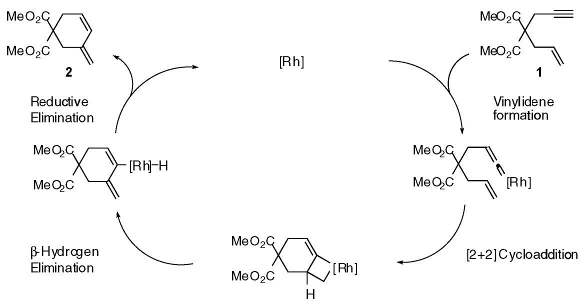


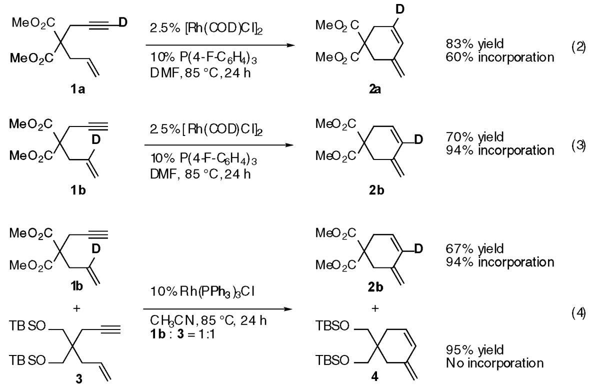
Under the same conditions as eq 1, the reaction of enyne **1a** bearing an acetylenic deuterium label brought about formation of diene **2a** through translocation of the deuterium exclusively to the adjacent carbon with 60% incorporation, suggesting the pertinence of a vinylidene mechanism (eq 2).[9] In the reaction of **1b**, almost complete migration of the vinylic deuterium to the formerly terminal acetylenic carbon was observed (eq 3). This outcome is particularly significant because it cannot be accounted for by any of the previously proposed reaction pathways. Moreover, no crossover of the deuterium took place in the reaction system employing a 1:1 mixture of the labeled and unlabeled enynes **1b** and **3** (eq 4), indicating that a rhodium hydride or free radical mechanism is unlikely. It should also be noted that these results could be reproduced using Rh(PPh$_3$)$_3$Cl as the catalyst. These observations, taken altogether, support our proposed mechanism in which the catalytic cycle consists of formation of a rhodium vinylidene followed by [2 + 2] cycloaddition with the alkene[10] and ring-opening of the rhodacyclobutane (Scheme 2).[11]

Scheme 1. Enyne Cycloisomerization Reaction Pathways



Scheme 2. Proposed Catalytic Cycle for Cycloisomerization of **1**

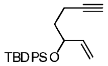
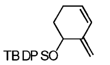
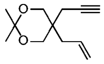
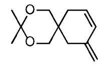
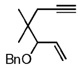
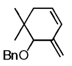
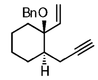
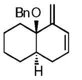
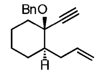
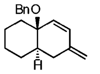
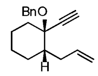
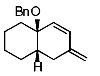
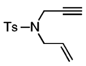
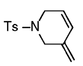
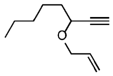
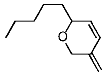
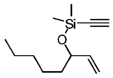
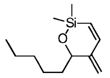
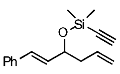
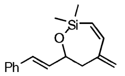




The double H-shift cycloisomerization was found to be feasible with a range of α,ω-enynes to give rise to the corresponding cyclized products with complete endoselectivity (Table 1). As observed in the labeling experiments, the two catalyst systems (conditions A and B) exhibited comparable activities. Both *trans* and *cis* decalins were easily accessed, despite the potential complications arising from the sensitivity of propargylic and allylic ether systems (entries 4−6). The reaction also tolerated heteroatoms in the tether to furnish aza-, oxa-, and siloxacycles (entries 7−10). Notably, the cyclization of dienyne **23** took place only in a 1,7-mode to yield the seven-membered ring triene **24** as the product (entry 10).

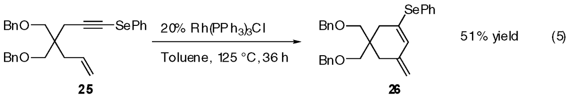
10.1021/ja052775j CCC: $30.25

Table 1. Rhodium-Catalyzed Cycloisomerization of Enynes[a]

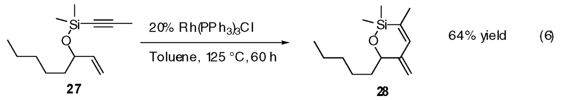
entry	reactant		product		yield[b]
1		**5**		**6**	80% (A) 77% (B)
2		**7**		**8**	90% (B)
3		**9**		**10**	90% (A) 82% (B)
4		**11**		**12**	90% (A) 90% (B)
5		**13**		**14**	99% (B)
6		**15**		**16**	67% (A)
7		**17**		**18**	54% (A)
8		**19**		**20**	58% (A) 53% (B)
9		**21**		**22**	98% (A) 95% (B)
10		**23**		**24**	77% (C)

[a] Condition A: 5 mol % of $[Rh(COD)Cl]_2$; 25 mol % of $P(4\text{-}FC_6H_4)_3$; DMF (0.1 M); 85 °C; 24 h. Condition B: 10 mol % of $Rh(PPh_3)_3Cl$; CH_3CN (0.1 M); 85 °C; 24 h. Condition C: 20 mol % of $Rh(PPh_3)_3Cl$; 20 mol % of PPh_3; slow addition 10 h; final concentration = 0.1 M in CH_3CN. [b] Isolated yields.

The new mode of cycloisomerization could also be applied to substrates possessing internal alkynes (eq 5 and 6). When the selenyl-substituted enyne **25** was subjected to 20 mol % of Wilkinson's catalyst in toluene at 125 °C, diene **26** was produced in 51% yield as a single product. Similarly, enyne **27** was cyclized to diene **28** in 64% yield with apparent vicinal migration of a methyl group. While detailed understanding awaits further studies, these processes are believed to proceed through selenyl[12] and silyl[13] rather than alkyl migrations.



25 **26**



27 **28**

The present study demonstrates the feasibility of transition metal vinylidene-mediated catalysis as a means of new enyne cycloisomerization. The reaction proceeds through a distinct pathway involving formation of a rhodium vinylidene, [2 + 2] cycloaddition, and ring-opening of a rhodacyclobutane. This mechanism allows for rapid access to diverse cyclic structures from a variety of enynes with exclusive endoselectivity via a dual group-transfer cyclization process. On the basis of the findings described herein, we envision many new opportunities for C−C bond formation by transition metal vinylidene-mediated catalysis. Investigations in this direction are currently underway.

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Supporting Information Available: Experimental procedures and spectral data for all new compounds. This material is available free of change via the Internet at http://pubs.acs.org.

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