Regio- and Stereoselective Reductive Cyclization of 1,5-Bisallenes under Hydrogenation Conditions[†]
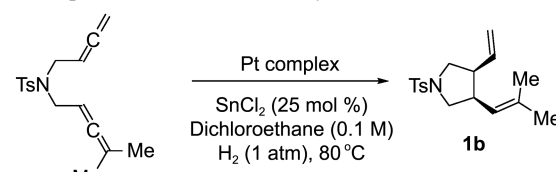
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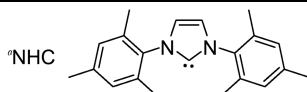*Received January 10, 2011, Accepted February 11, 2011*

The transition metal-catalyzed reaction of allenes has emerged as a useful protocol to prepare synthetically useful cyclic compounds with high levels of regio- and stereoselectivity.[1] To control the selectivity of the cumulated π-bonds of the allenes, intramolecular reactions involving allenes are often reported. In this regard, cyclizations of bisallenes have been investigated to provide attractive bicyclic products (bicyclo[3.2.0] or bicycle[3.1.1] products), organometallic reagent (silicon, stannane, and germanium)-incorporated cyclic compounds, and steroid scaffolds.[2,3,4] Although a range of transition metal-catalyzed cyclizations using bisallenes have been presented, there are no reports of reductive cyclization of 1,5-bisallenes initiated by the hydrometallation of the allene. Presumably, upon hydrometallation, the complicated regioselectivity and attenuated reactivity of the allene relative to the alkyne would result in a lack of research on the reductive cyclization of 1,5-bisallenes.

There are a few reactions initiated by hydrometallation of allenes; 1) ring expansion of allenylcyclobutanols,[5] 2) reductive aldol reaction of allenic esters,[6] and 3) reductive cyclization of allene-carbonyl compounds and allene-hydrazones.[7]

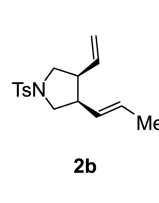**Table 1.** Optimization of reductive cyclization of 1,5-bisallene **1a**
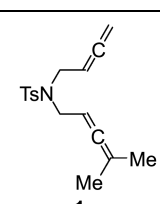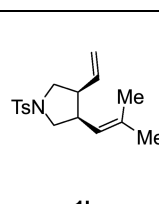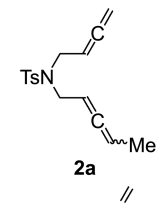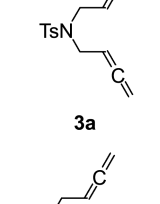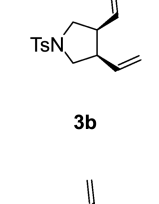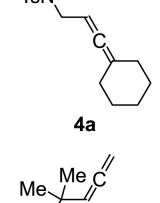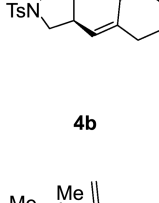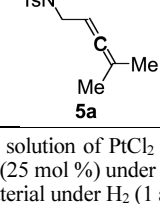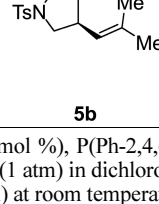
Entry	Pt(II) (5 mol %)	Ligand (mol %)	Time (h)	Yield
1	PtCl₂	P(Ph-2,4,6-OMe₃)₃ (10)	2	66%
2	PtCl₂	P(Ph-*p*OMe)₃ (10)	23	34%
3	PtCl₂	P(Ph-*o*OMe)₃ (10)	23	47%
4	PtCl₂	P(2-furyl)₃ (10)	21	36%
5	PtCl₂	P(Ph-*p*CF₃)₃ (10)	23	44%
6	PtCl₂	P(C₆F₅)₃ (10)	24	47%
7	PtCl₂	PCy₃ (10)	2	56%
8	PtCl₂	NHC (5)[a]	2	61%
9	PtCl₂(COD)	P(Ph-2,4,6-OMe₃)₃ (10)	2	36%

Table 2. The substrate scope of 1,5-bisallene cyclization

Entry	Reactant	Product	Yield
1	**1a**	**1b**	66%
2	**2a**	**2b**	39%
3	**3a**	**3b**	18%
4	**4a**	**4b**	38%
5	**5a**	**5b**	47%

To a premixed solution of PtCl₂ (5 mol %), P(Ph-2,4,6-OMe₃)₃ (10 mol %), and SnCl₂ (25 mol %) under H₂ (1 atm) in dichloroethane was added the starting material under H₂ (1 atm) at room temperature. The resulting mixture was allowed to run at 80 °C until the starting material was completely consumed.

To generate a metal-hydride complex for hydrometallation, organic acids, alcohols, pinacolborane, or hydrogen was employed along with metal complexes. As part of our efforts to develop hydrogen-mediated reductive coupling processes, platinum-catalyzed hydrogenative cyclization of 1,5-bisallenes have been studied, assuming that the platinum-hydride complexes generated under hydrogenation conditions would hydrometallate the allene to afford reductive cyclization products from 1,5-bisallenes. Remarkably, the hydrogen-mediated reductive cyclization of 1,5-bisallenes occurred with completely controlled regio- and *cis*-diastereoselectivity under hydrogenation conditions. A reaction mechanism accounting for the regio- and stereoselectivity was proposed.

Table 1 lists the optimization results of the hydrogenative cyclization of bisallene **1a**. The hydrogenative cyclization of bisallene **1a** was carried out in the presence of PtCl$_2$ (5 mol %), P(Ph-2,4,6-OMe$_3$)$_3$ (10 mol %), and SnCl$_2$ (25 mol %) in dichloroethane (DCE) under 1 atmosphere of H$_2$ at 80 °C to afford the products in 66% yield with complete *cis* diastereoselectivity (entry 1). The *cis* stereochemistry of com-

pound **1b** was determined from the NOE interactions between the protons at the ring junction. To evaluate the electronic and steric effects of the ligands, P(Ph-*p*OMe)$_3$, P(Ph-*o*OMe)$_3$, P(furyl)$_3$, P(Ph-*p*CF$_3$)$_3$, P(C$_6$F$_5$)$_3$, PCy$_3$, and N-heterocyclic carbene (NHC) ligand were screened (entries 2-8). Electron-rich and bulky ligands (P(Ph-2,4,6-OMe$_3$)$_3$, PCy$_3$, and NHC) tend to give higher yields in shorter reaction time. Other phosphine ligands including relatively electron-rich phosphines (P(Ph-*p*OMe)$_3$ and P(Ph-*o*OMe)$_3$) and electron-deficient phosphines (P(furyl)$_3$, P(Ph-*p*CF$_3$)$_3$, and P(C$_6$F$_5$)$_3$) exhibit lower yields and require much longer reaction time. PtCl$_2$(COD) catalyzed this transformation, showing decreased yield (entry 9). Under platinum-catalyzed hydrogenation conditions, the [2 + 2] cycloaddition products often observed in metal-catalyzed or thermal reactions of 1,5-bisallenes were not detected.

Table 2 illustrates the substrate scope of this reaction under the optimized conditions. The effect of the allene substituent was evaluated, as shown in compound **2b** and **3b**. The bisallene **2a** possessing a mono-methyl substituted allene participated in the reaction to produce compound **2b** in 39% yield. The bisallene **3a** was decomposed under these reaction conditions, showing only 18% yield of desired product **3b**.[8] Compound **4a** involving the cyclohexyl group at one of the allenes underwent reductive cyclization in 38% yield. Although the degree of substitution at the allene terminal is same in compounds **1a** and **4a**, the steric effect of the dimethyl group and the cyclohexyl group may be different, rendering the different yield. Compound **5b** possessing the *gem*-dimethyl group proximal to the allene was obtained in 47% yield. The oxygen-tethered substrate was decomposed due to the facile C-O bond cleavage by platinum hydride species.[7d] The carbon-tethered substrate did not participate in the reaction, implying that a heteroatom in the tether was necessary to provide the desired cyclized product.
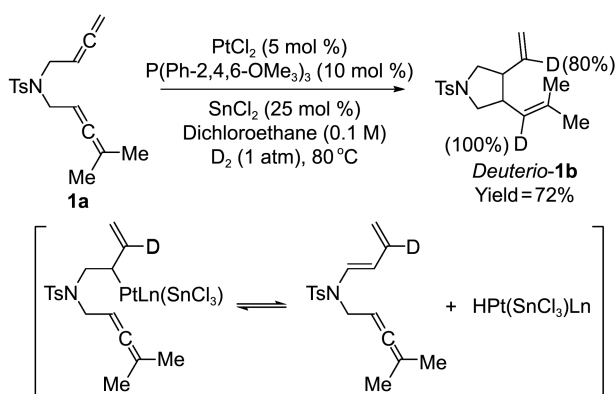
Scheme 1. Deuterium labeling study.
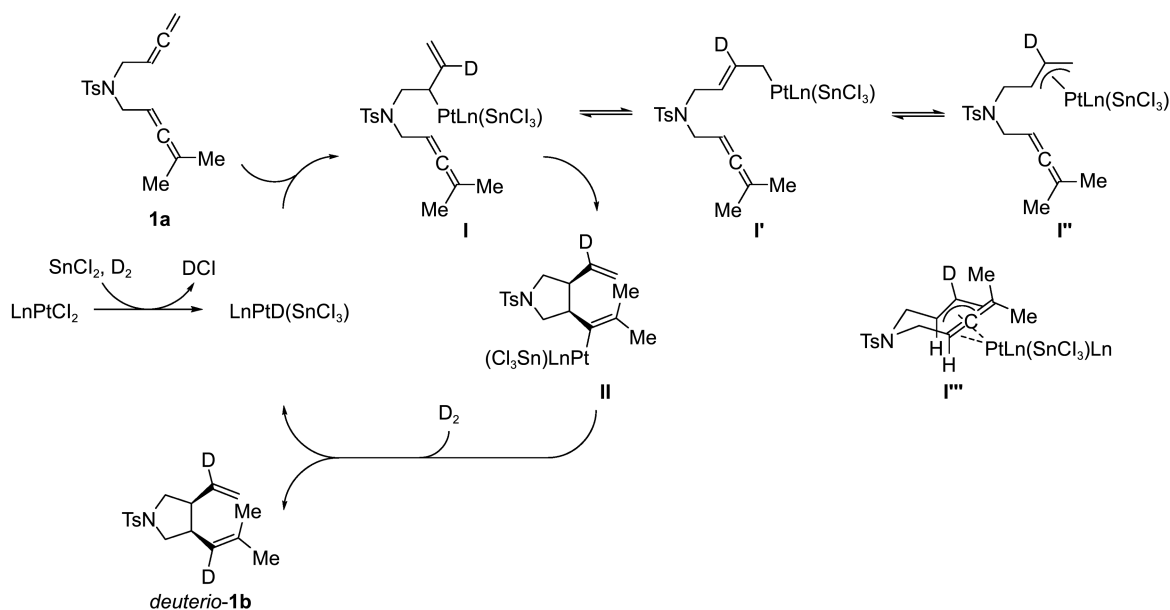
Scheme 2. A plausible catalytic cycle.

To probe the reaction mechanism, deuterium labeling experiments were carried out using bisallene **1a** (Scheme 1). Interestingly, 80% of the deuteration at the vinyl position of monosubstituted alkene of compound **1b** was observed, whereas 100% deuteration at the other alkene was detected. To account for the outcome of the partial deuteration, reversible hydrometallation of bisallene **1a** with the deuterio-platinum complex was proposed to generate a small amount of hydrido-platinum complex.

Scheme 2 presents a catalytic cycle for the hydrogenative cyclization of 1,5-bisallenes. The catalytic cycle may begin with hydrometallation of the allene by the $LnPtD(SnCl_3)$ complex. Subsequently, allylplatinum intermediate **I** reacts with the proximal allenic π-bond to afford a five-membered intermediate **II**, and the addition of D_2 promotes the product formation with the regeneration of the catalyst. The origin of high levels of *cis* diastereoselectivity in the bisallene cyclization may stem from the coordination between the allene and allylplatinum group, as depicted in intermediate **I'''**.[2a]

In summary, 1,5-bisallenes were cyclized under hydrogenation conditions to form five-membered heterocycles with excellent levels of regio- and diastereoselectivity. A tentative mechanism involving hydrometallation of the allene by the hydrido-platinum complex was proposed based on deuterium labeling studies and the stereochemical outcome.

Experimental

Representative Experimental Procedure for Platinum-Catalyzed Reductive Cyclization of 1,5-Bisallenes. To a premixed solution of $PtCl_2$ (5 mol %), phosphine (10 mol %), and $SnCl_2$ (25 mol %) under H_2 (1 atm) in dichloroethane (0.1 M) was added the bisallene under H_2 (1 atm) at room temperature. The resulting mixture was allowed to run at 80 °C until the starting material was completely consumed. The solvent was removed with a rotary evaporator to produce a residue which was purified by column chromatography on a silica gel eluting with hexane and ethyl acetate (hexane:ethyl acetate = 95:5).

References

1. Review articles regarding the cyclizaiton of allenes: (a) Hashimi, A. S. K. *Angew. Chem. Int. Ed.* **2000**, *39*, 3590. (b) Ma, S. *Acc. Chem. Res.* **2003**, *36*, 701. (b) Ma, S. *Chem. Rev.* **2005**, *105*, 2829. (c) Ma, S. *Pure Appl. Chem.* **2006**, *78*, 197. (d) Ma, S. *Aldrichimica Acta* **2007**, *40*, 91. (e) Kim, H.; Williams, L. J. *Curr. Opin. Drug Discovery Der.* **2008**, *11*, 870.
2. Selected articles for Pd-catalyzed cyclization of bisallenes: (a) Kang, S.-K.; Baik, T.-G.; Kulak, A. N.; Ha, Y.-H.; Lim, Y.; Park, J. *J. Am. Chem. Soc.* **2000**, *122*, 11529. (b) Hong, Y.-T.; Yoon, S.-K.; Kang, S.-K.; Yu, C.-M. *Eur. J. Org. Chem.* **2004**, 4628. (c) Jiang, X.; Cheng, X.; Ma, S. *Angew. Chem. Int. Ed.* **2006**, *45*, 8009. (d) Shu, W.; Jia, G.; Ma, S. *Angew. Chem. Int. Ed.* **2009**, *48*, 2788. (e) Lian, X.; Ma, S. *Chem. Eur. J.* **2010**, *16*, 7960.
3. Selected articles for Au-catalyzed cyclization of bisallenes: Kim, S. M.; Park, J. H.; Kang, Y. K.; Chung, Y. K. *Angew. Chem. Int. Ed.* **2009**, *48*, 4532.
4. Selected articles for Rh-catalyzed cyclization of bisallenes: (a) Ma, S.; Lu, P.; Lu, L.; Hou, H.; Wei, J.; He, Q.; Gu, Z.; Jiang, X.; Jin, X. *Angew. Chem. Int. Ed.* **2005**, *44*, 5275. (b) Lu, P.; Ma, S. *Org. Lett.* **2007**, *9*, 2095. (c) Kawamura, T.; Inagaki, F.; Narita, S.; Takahashi, Y.; Hirata, S.; Kitagaki, S.; Mukai, C. *Chem. Eur. J.* **2010**, *16*, 5173.
5. Trost, B. M.; Xie, J. *J. Am. Chem. Soc.* **2006**, *128*, 6044.
6. (a) Zhao, D.; Oisaki, K.; Kanai, M.; Shibasaki, M. *Tetrahedron Lett.* **2006**, *47*, 1403. (b) Zhao, D.; Oisaki, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2006**, *128*, 14440.
7. (a) Skucas, E.; Bower, J. F.; Krische, M. J. *J. Am. Chem. Soc.* **2007**, *129*, 12678. (b) Bower, J. F.; Skucas, E.; Patman, R. L.; Krische, M. J. *J. Am. Chem. Soc.* **2007**, *129*, 15134. (c) Patman, R. L.; Bower, J. F.; Kim, I. S.; Krische, M. J. *Aldrichimica Acta* **2008**, *41*, 95. (d) Hong, J.-T.; Wang, X.; Kim, J.-H.; Kim, K.; Yun, H.; Jang, H.-Y. *Adv. Synth. Catal.* **2010**, *352*, 2949.
8. Substituents at the allene terminus are known to slow down the decomposition of the allene. (a) Franzén, J.; Löfstedt, J.; Dorange, I.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **2002**, *124*, 11246. (b) Zhu, G.; Zhang, Z. *Org. Lett.* **2004**, *6*, 4041.