J|A|C|S
COMMUNICATIONS

A Facile Pd(0)-Catalyzed Regio- and Stereoselective Diamination of Conjugated Dienes and Trienes

Haifeng Du, Baoguo Zhao, and Yian Shi*

Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523

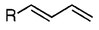
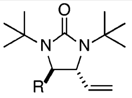
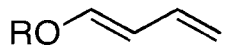
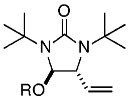
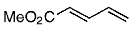
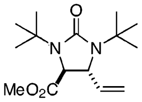
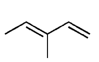
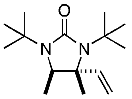
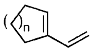
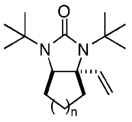
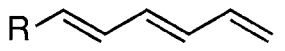
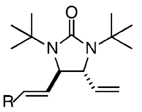
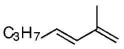
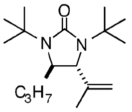
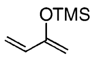
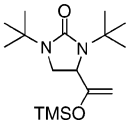
Received November 10, 2006; E-mail: yian@lamar.colostate.edu

Vicinal diamines are very important functional moieties which are present in various biologically active compounds and have also been widely used as chiral control elements in asymmetric synthesis.[1] Diamination of olefins presents an attractive strategy for the synthesis of vicinal diamines. Various metal-free[1,2] or metal-mediated[1,3,4] processes have been developed. Metal-catalyzed diaminations have also been reported.[5,6] Very recently, it has been shown that both intermolecular diamination of conjugated dienes[6a] and intramolecular[6b] diamination of terminal olefins with ureas can be achieved using Pd(II) as catalyst. For the intermolecular process, the diamination occurred regioselectively at less-substituted double bonds of dienes. In these cases, the amination is likely to proceed via a Pd(II)-promoted aza-Wacker-type process (trans-aminopalladation),[3g,6,7] followed by the replacement of the C−Pd bond with a C−N bond.[3g,6,7]

As part of our general interest in synthetic transformations of dioxirane[8] and its nitrogen analogues, we have been exploring a possible metal-catalyzed diamination of olefins via an oxidative addition to the N−N bond of diaziridine **1** to form diamido species **2**, followed by a migratory insertion to a double bond to form **3**[9] and a subsequent reductive elimination to form **4** (Scheme 1). Herein we wish to report our preliminary efforts on this subject.

The diamination was examined with olefins and di-*t*-butyldiaziridinone (**6**)[10,11] using Pd(PPh$_3$)$_4$ as catalyst. Among the olefins tested, conjugated dienes were found to be very effective substrates (Scheme 2). For example, subjecting *trans*-1,3-pentadiene (**5a**) to the reaction conditions (Scheme 2) for 30 min led to a clean diamination product (**7a**) in 94% yield (Table 1, entry 1). The reaction occurred highly regioselectively at the internal double bond and highly stereoselectively as well.[12] As shown in Table 1, this diamination can be extended to a variety of dienes including both electron-rich (Table 1, entries 8 and 9) and electron-deficient dienes (Table 1, entry 10). Trisubstituted double bonds can also be diaminated (Table 1, entries 11−13). When a conjugated triene was used, the diamination occurred cleanly at the middle double bond (Table 1, entries 14−15). In all these cases (Table 1, entries 1−15), essentially only one regio- and stereoisomer was obtained.[12] It appears that only trans- and trisubstituted double bonds react under the reaction conditions. For example, no diamination was observed when *cis*-1,3-pentadiene was used. Therefore, when a mixture of *E* and *Z* dienes were used (Table 1, entries 2, 7, and 11), only the *E* isomer reacted and the *Z* isomer was enriched after the reaction. The diamination also occurred for the dienes containing geminal disubstituted double bonds (Table 1, entries 16 and 17). In these two cases, the reaction occurred also regioselectively and stereoselectively.[13] The stereochemistry of the diamination products (**7**) was tentatively assigned by comparing the NOE of compounds **7b**, **g**, **h**, and **p** (Table 1, entries 2, 7, 8, and 16) with **7q** (Table 1, entry 17) (see Supporting Information). The X-ray structure of compound **7n** (Table 1, entry 14) further supports the assigned stereochemistry (Scheme 3).

Table 1. Catalytic Diamination of Dienes and Trienes[a]

Entry	Substrate (**5**)	Product (**7**)	Time	Yield (%)[e]
				
1	**5a**, R = Me		30 min	94
2[b]	**5b**, R = Et		40 min	94
3	**5c**, R = C_5H_{11}		1 h	91
4	**5d**, R = CH_2OBn		30 min	76
5	**5e**, R = Ph		40 min	90
6	**5f**, R = *p*-MeO-Ph		30 min	94
7[b]	**5g**, R = 2-furyl		30 min	78
				
8[c,d]	**5h**, R = Me		15 min	95
9[c,d]	**5i**, R = TMS		15 min	88
10	 **5j**		2 h	62
11[b]	 **5k**		5 h	88
				
12	**5l**, n = 1		30 min	72
13	**5m**, n = 2		30 min	86
				
14	**5n**, R = Me		30 min	86
15	**5o**, R = C_5H_{11}		30 min	81
16	 **5p**		2.5 h	46
17	 **5q**		1 h	90

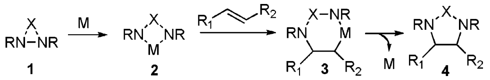
---

[a] All reactions were carried out with di-*t*-butyldiaziridinone (**6**) (0.2 mmol), diene or triene (0.24 mmol, 1.2 equiv), and Pd(PPh$_3$)$_4$ (0.02 mmol) in benzene-d_6 (0.6 mL) in an NMR tube at 65 °C under argon unless otherwise stated. [b] A mixture of *E* and *Z* isomers was used. For entry 2, diene (0.53 mmol, *E*/*Z* = 1/1.2, *E* isomer: 0.24 mmol); for entry 7, diene (0.48 mmol, *E*/*Z* = 1/1, *E* isomer: 0.24 mmol); for entry 11, diene (0.34 mmol, *E*/*Z* = 2.5/1, *E* isomer: 0.24 mmol). [c] Containing <10% *Z* isomer. [d] Compounds are acid sensitive and were purified on less acidic silica gel (Iatrobeads 6RS-8060, Mitsubishi Kagaku Iatron, Inc. Japan). [e] Isolated yield based on **6**.

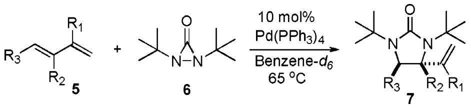
The deprotection of compound **7b** (Table 1, entry 2) was investigated. Treating **7b** with CF$_3$CO$_2$H (TFA) at 75−80 °C for 2

10.1021/ja0680562 CCC: $37.00

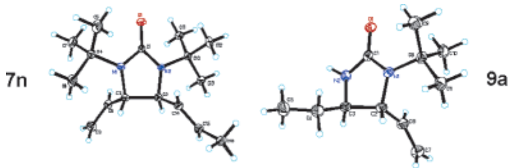
Scheme 1



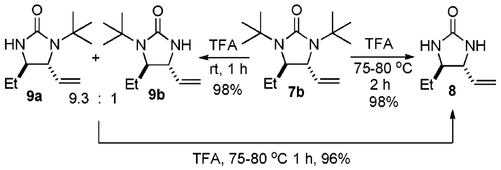
Scheme 2



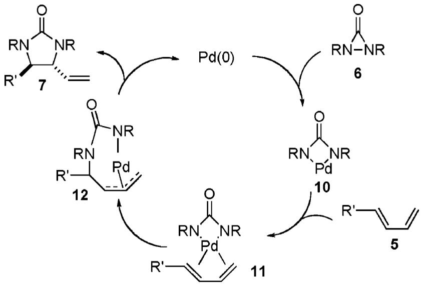
Scheme 3. The X-ray Structures of Compounds **7n** and **9a**



Scheme 4



Scheme 5. A Proposed Catalytic Cycle for Diamination



h gave a clean deprotection product **8** in 98% yield (Scheme 4). Interestingly, monodeprotection was also possible when the reaction was carried out at room temperature, giving **9a** as major product (Scheme 4). The structure of **9a** was determined by X-ray (Scheme 3). The selective monodeprotection provides opportunities to introduce different groups on the two nitrogens if it is desired.

While a precise reaction mechanism awaits further study, a plausible catalytic cycle is shown in Scheme 5. The Pd(0) first inserts into the N−N bond of diaziridinone **6** to form a four-membered Pd(II) species (**10**).[14] Upon complexing with diene **5** and a migratory insertion, compound **10** is then converted into π-allyl Pd complex **12**,[15] which then undergoes a reductive elimination to form product **7** and regenerate the Pd(0) catalyst.[16]

In summary, a diamination for a variety of conjugated dienes and trienes has been effectively achieved using di-*t*-butyldiaziridinone as the nitrogen source and Pd(PPh$_3$)$_4$ as catalyst, giving the diamination products in good yields with high regio- and stereoselectivities. This Pd(0)-catalyzed diamination is mechanistically distinct from the Pd(II)-catalyzed process, thus resulting in different regioselectivity.[6] Further studies of the reaction mechanism, development of a more effective catalytic process with different nitrogen sources and metal catalysts, and expansion of the substrate scope as well as the asymmetric process are currently underway.

Acknowledgment. We are grateful to the generous financial support from the Monfort Foundation (CSU).

Supporting Information Available: The diamination and deprotection procedures, the characterization of diamination products, and the X-ray data of compounds **7n** and **9a**. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) For leading reviews, see: (a) Lucet, D.; Gall, T. L.; Mioskowski, C. *Angew. Chem., Int. Ed.* **1998**, *37*, 2580. (b) Mortensen, M. S.; O'Doherty, G. A. *Chemtracts: Org. Chem.* **2005**, *18*, 555. (c) Kotti, S. R. S. S.; Timmons, C.; Li, G. *Chem. Biol. Drug Des.* **2006**, *67*, 101.

(2) For leading references on recent Ritter-type diamination see: (a) Li, G.; Kim, S. H.; Wei, H-X. *Tetrahedron Lett.* **2000**, *41*, 8699. (b) Booker-Milbum, K. I.; Guly, D. J.; Cox, B.; Procopiou, P. A. *Org. Lett.* **2003**, *5*, 3313.

(3) For examples of metal-mediated diaminations, see the following. Co: (a) Becker, P. N.; White, M. A.; Bergman, R. G. *J. Am. Chem. Soc.* **1980**, *102*, 5676. Hg: (b) Barluenga, J.; Alonso-Cires, L.; Asensio, G. *Synthesis* **1979**, 962. Mn: (c) Fristad, W. E.; Brandvold, T. A.; Peterson, J. R.; Thompson, S. R. *J. Org. Chem.* **1985**, *50*, 3647. Os: (d) Chong, A. O.; Oshima, K.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, *99*, 3420. (e) Muñiz, K.; Nieger, M. *Synlett* **2003**, 211. (f) Muñiz, K.; Nieger, M. *Chem. Commun.* **2005**, 2729. Pd: (g) Bäckvall, J.-E. *Tetrahedron Lett.* **1978**, 163. Tl: (h) Aranda, V. G.; Barluenga, J.; Aznar, F. *Synthesis* **1974**, 504.

(4) For a recent Cu(II)-mediated intramolecular diamination, see: Zabawa, T. P.; Kasi, D.; Chemler, S. R. *J. Am. Chem. Soc.* **2005**, *127*, 11250.

(5) For Rh(II) and Fe(III)-catalyzed diamination with TsNCl$_2$ see: (a) Li, G.; Wei, H.-X.; Kim, S. H.; Carducci, M. D. *Angew. Chem., Int. Ed.* **2001**, *40*, 4277. (b) Wei, H.-X.; Kim, S. H.; Li, G. *J. Org. Chem.* **2002**, *67*, 4777.

(6) (a) Bar, G. L. J.; Lloyd-Jones, G. C.; Booker-Milbun, K. I. *J. Am. Chem. Soc.* **2005**, *127*, 7308. (b) Streuff, J.; Hövelmann, C. H.; Nieger, M.; Muñiz, K. *J. Am. Chem. Soc.* **2005**, *127*, 14586.

(7) For leading reviews, see: (a) Hegedus, L. S. *Tetrahedron* **1984**, *40*, 2415. (b) Müller, T. E.; Beller, M. *Chem. Rev.* **1998**, *98*, 675.

(8) Shi, Y. *Acc. Chem. Res.* **2004**, *37*, 488.

(9) For examples of less common *cis*-aminopalladation, see: (a) Isomura, K.; Okada, N.; Saruwatari, M.; Yamasaki, H.; Taniguchi, H.; *Chem. Lett.* **1985**, 385. (b) Ney, J. E.; Wolfe, J. P. *Angew. Chem. Int. Ed.* **2004**, *43*, 3605. (c) Brice, J. L.; Harang, J. E.; Timokhin, V. I.; Anastasi, N. R.; Stahl, S. S. *J. Am. Chem. Soc.* **2005**, *127*, 2868. (d) Liu, G.; Stahl, S. S. *J. Am. Chem. Soc.* **2006**, *128*, 7179.

(10) Prepared on the basis of the reported method: Greene, F. D.; Stowell, J. C.; Bergmark, W. R. *J. Org. Chem.* **1969**, *34*, 2254.

(11) For a leading review on diaziridinones, see: Heine, H. W. In *The Chemistry of Heterocyclic Compounds*; Hassner, A., Ed.; John Wiley & Sons, Inc: New York, 1983; pp 547.

(12) Other regio- and stereoisomers were barely detectable by ^{1}H NMR of the crude reaction mixture if there was any.

(13) When isoprene was used, however, a mixture of two regioisomers (2.3: 1) was formed in 90% yield after 1 h reaction. The diamination slightly preferred the more substituted double bond in this case.

(14) The insertion of Ni and Pd to the N−N bond of diaziridinone has been reported, see: Komatsu, M.; Tamabuchi, S.; Minakata, S.; Ohshiro, Y. *Heterocycles* **1999**, *50*, 67. However, to the best our knowledge, the reaction of the resulting complex **10** with an olefin has not been reported.

(15) For a recent leading review on π-allyl Pd chemistry, see: Trost, B. M. *J. Org. Chem.* **2004**, *69*, 5813.

(16) For a recent book, see: Tsuji, J. *Palladium Reagents and Catalysts: New Perspective for the 21st Centur*y; John Wiley & Sons Ltd: New York, 2004.

JA0680562