

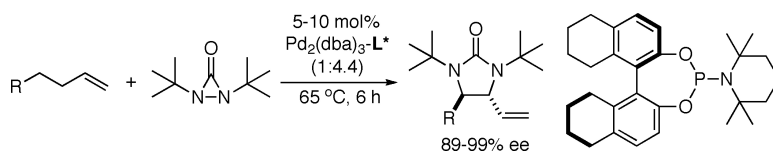
Communication

**Catalytic Asymmetric Allylic and Homoallylic Diamination
 of Terminal Olefins via Formal C#H Activation**

Haifeng Du, Baoguo Zhao, and Yian Shi

J. Am. Chem. Soc., **2008**, 130 (27), 8590-8591 • DOI: 10.1021/ja8027394 • Publication Date (Web): 13 June 2008

Downloaded from <http://pubs.acs.org> on February 8, 2009



More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Links to the 5 articles that cite this article, as of the time of this article download
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

[View the Full Text HTML](#)

Catalytic Asymmetric Allylic and Homoallylic Diamination of Terminal Olefins via Formal C–H Activation

Haifeng Du, Baoguo Zhao, and Yian Shi*

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

Received April 14, 2008; E-mail: yian@lamar.colostate.edu

Metal-promoted diamination of olefins provides an effective approach to the synthesis of vicinal diamines, which are present in various biologically active molecules and are used as chiral control elements in asymmetric synthesis.¹ Various diamination systems have been developed.^{1–7} Recently, we reported a Pd(0)-^{8,9} and Cu(I)¹⁰-catalyzed regio- and stereoselective diamination of conjugated dienes and trienes using di-*tert*-butyldiaziridinone (**2**)¹¹ as nitrogen source. We have also shown that readily available terminal olefins can be diastereoselectively diaminated at allylic and homoallylic carbons *via* formal C–H activation with Pd(PPh₃)₄ (Scheme 1).¹² Considering its synthetic potential, it is highly desirable to develop an asymmetric process for this diamination. Compared to asymmetric diamination of conjugated dienes as reported earlier,^{9a} the current formal C–H diamination requires a catalyst system which will be able to effectively convert the terminal olefin into a conjugated diene *in situ* besides being enantioselective. Herein we wish to report our preliminary progress on this subject.

Asymmetric C–H diamination was initially investigated using 1-hexene (**4**) as substrate with slow addition of di-*tert*-butyldiaziridinone (**2**) at 65 °C (Scheme 2) using phosphorus amidite ligand **L1** (previously used for the asymmetric diamination of conjugated dienes).^{9a} Ligand **L1** gave 92% ee for 1-hexene (**4**) but with moderate conversion (Scheme 2). To search for more effective ligands, various commercially available or easily prepared chiral ligands^{13,14} were then examined for the diamination of 1-hexene under the conditions shown in Scheme 2. Studies show that conversions and ee's of the diamination were highly dependent on the ligands used (Supporting Information). Overall, H₈-BINOL-based phosphorus amidite ligand **L2** gave the highest conversion for the reaction. Studies show that the reaction conversion was significantly influenced by the Pd/ligand ratio with 1:2.2 being optimal. ³¹P NMR studies also indicate that complexes with one Pd and two ligands were formed regardless of the Pd/ligand ratio (Supporting Information).

Asymmetric C–H diamination of various terminal olefins with Pd₂(dba)₃ and **L2** was investigated. As shown in Table 1, all the diamination reactions occurred highly regio- and diastereoselectively at allylic and homoallylic carbons of terminal olefins, giving diamination products in good yields (50–85%) and high enantioselectivities (89–94% ee) (Table 1, entries 1–10). The olefin geometry for *cis*- and *trans*-1,5-undecadiene was maintained during the reaction (Table 1, entries 7 and 8). Both (*R*)- and (*S*)-5-(trimethylsiloxy)-1-hexene were also diaminated in good yields with high diastereoselectivities (Table 1, entries 11 and 12), indicating that the stereochemistry of diamination products was primarily determined by the chiral catalyst, and the stereogenic center of the substrate had only a small effect on diastereoselectivities. The diamination product in entry 11 was desilylated. The absolute configuration of the resulting alcohol (**6**) was determined to be (2*R*,3*S*,4*R*) by its X-ray structure (Figure 1). When 1,9-decadiene (**7**) was subjected to the diamination conditions (Scheme 3),

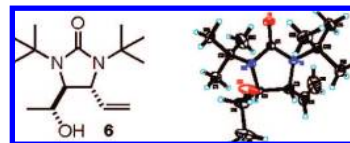
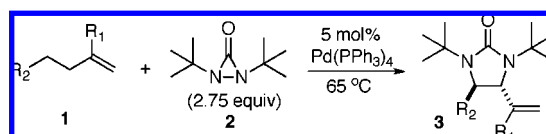
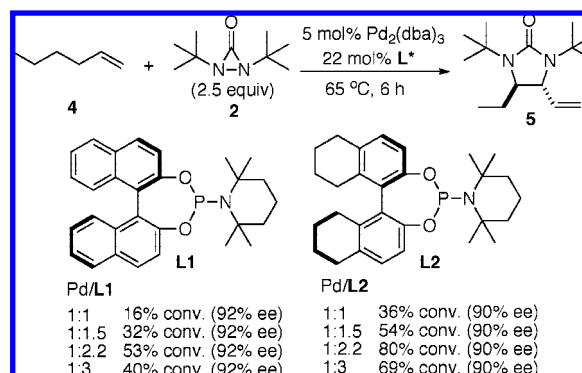


Figure 1. The X-ray structure of **6**.

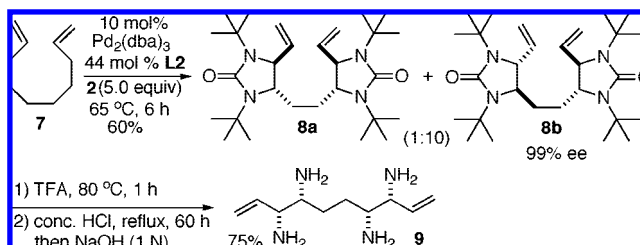
Scheme 1



Scheme 2



Scheme 3



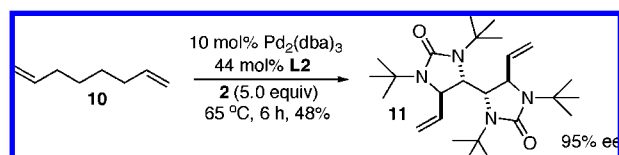
bisdiamination compound **8b** was obtained in 60% yield and 99% ee¹⁵ along with small amount of meso compound **8a**.¹⁶ Treating **8b** with CF₃COOH, concd HCl, and 1 N aqueous NaOH led to the formation of optically active tetraamine **9** in 75% yield. When the reaction was carried out with 1,7-octadiene (**10**), compound **11** was obtained as a single diastereomer in 48% yield and 95% ee¹⁵ (Scheme 4). Since the bisdiaminations in Schemes 3 and 4 involved multiple transformations, a higher catalyst loading was needed.

In summary, a catalytic asymmetric allylic and homoallylic diamination for a variety of readily available terminal olefins has been successfully achieved using di-*tert*-butyldiaziridinone (**2**) as

Table 1. Catalytic Asymmetric C–H Diamination of Terminal Olefins^a

Entry	Substrate	Product ^b	Yield (%) ^c	ee (%) ^d
1	R = Et		50	90
2	R = <i>n</i> -C ₅ H ₁₁		71	91
3	R = CH ₂ Ph		67	93 ^{e,f}
4	R = <i>i</i> -Pr		51	94 ^g
5	R = Ph		80	90 ^c
6			80	92
7	<i>n</i> -C ₅ H ₁₁		81	90 ^g
8	<i>n</i> -C ₅ H ₁₁		69	89
9			85	91
10			67	92
11			70	97:3 ^{h,i} (dr)
12			66	94:6 ^h (dr)

^a All reactions were carried out with olefin (0.80 mmol), **2** (2.0 mmol, 2.5 equiv), Pd₂(dba)₃ (0.04 mmol), and ligand **L2** (0.176 mmol) at 65 °C for 6 h. ^b The structures represent only proposed absolute configurations by analogy. ^c Isolated yield based on olefin. ^d The ee was determined by chiral GC (Chiraldex B-DM column) unless otherwise stated. ^e The ee was determined by chiral HPLC (Chiralpak AD column) after the removal of *t*-butyl groups. ^f The (*R,R*) configuration was determined by comparing the optical rotation with the reported one (see ref 9a). ^g The ee was determined by chiral GC (Chiraldex B-DM column) after the removal of *t*-butyl groups. ^h The ratio was determined by achiral GC (VA-5MS column). ⁱ The (*2R,3S,4R*) configuration was determined by the X-ray structure of diamination product after the removal of TMS group.

Scheme 4

nitrogen source with a catalyst generated from Pd₂(dba)₃ and H₈-BINOL-derived phosphorus amidite ligand **L2**, giving diamination products in good yields with high regio-, diastereo-, and enantioselectivities. For substrates bearing two terminal double bonds,

four C–N bonds can be stereoselectively constructed in one step by formally replacing four sp³ C–H bonds.¹⁷ Compared to the asymmetric diamination of conjugated dienes, the current asymmetric diamination uses readily available terminal olefins without the need to prepare conjugated dienes. This advantage is even more apparent in the cases of bisdiaminations where the stereoselective preparation of sensitive conjugated tetraenes is not necessary. Further development of a more effective asymmetric catalytic process and expansion of the substrate scope as well as synthetic application are currently underway.

Acknowledgment. We are grateful for the generous financial support from the Camille and Henry Dreyfus Foundation and the General Medical Sciences of the National Institutes of Health (GM083944-01).

Supporting Information Available: Experimental procedures, ligand studies, characterizations, X-ray structures of **L1**, **L2**, and **6**, and data for determination of enantiomeric excess of diamination products along with the NMR spectra of compounds. 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: Organic Chemistry* **2005**, *18*, 555. (c) Kotti, S. R. S.; Timmons, C.; Li, G. *Chem. Biol. Drug. Des.* **2006**, *67*, 101.
- (2) For examples of metal-mediated diaminations, see: 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. *Eur. J. Org. Chem.* **2004**, 2243. Pd: (f) Bäckvall, J.-E. *Tetrahedron Lett.* **1978**, 163. Ti: (g) Aranda, V. G.; Barluenga, J.; Aznar, F. *Synthesis* **1974**, 504.
- (3) For recent Cu(II)-mediated intramolecular diamination, see: (a) Zabawa, T. P.; Kasi, D.; Chemler, S. R. *J. Am. Chem. Soc.* **2005**, *127*, 11250. (b) Zabawa, T. P.; Chemler, S. R. *Org. Lett.* **2007**, *9*, 2035.
- (4) For Rh(II)-, Fe(III)-catalyzed diamination with TsNCl₂, 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.
- (5) For a recent Pd(II)-catalyzed intermolecular diamination of conjugated dienes, see: (a) Bar, G. L. J.; Lloyd-Jones, G. C.; Booker-Milburn, K. I. *J. Am. Chem. Soc.* **2005**, *127*, 7308.
- (6) For recent Pd(II)- and Ni-catalyzed intramolecular diamination of olefins, see: (a) Streuff, J.; Hövelmann, C. H.; Nieger, M.; Muñiz, K. *J. Am. Chem. Soc.* **2005**, *127*, 14586. (b) Muñiz, K.; Streuff, J.; Hövelmann, C. H.; Núñez, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 7125. (c) Muñiz, K. *J. Am. Chem. Soc.* **2007**, *129*, 14542. (d) Muñiz, K.; Hövelmann, C. H.; Streuff, J. *J. Am. Chem. Soc.* **2008**, *130*, 763.
- (7) For leading references on asymmetric diamination using bisimidoosmium as reagent, see: (a) Muñiz, K.; Nieger, M. *Synlett* **2003**, 211. (b) Muñiz, K.; Nieger, M. *Chem. Commun.* **2005**, 2729.
- (8) (a) Du, H.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2007**, *129*, 762. (b) Xu, L.; Du, H.; Shi, Y. *J. Org. Chem.* **2007**, *72*, 7038.
- (9) For an asymmetric process, see: (a) Du, H.; Yuan, W.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2007**, *129*, 11688. (b) Xu, L.; Shi, Y. *J. Org. Chem.* **2008**, *73*, 749.
- (10) Yuan, W.; Du, H.; Zhao, B.; Shi, Y. *Org. Lett.* **2007**, *9*, 2589.
- (11) Greene, F. D.; Stowell, J. C.; Bergmark, W. R. *J. Org. Chem.* **1969**, *34*, 2254.
- (12) Du, H.; Yuan, W.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2007**, *129*, 7496.
- (13) For leading references on BINOL-based phosphorus amidite ligands, see: (a) de Vries, A. H. M.; Meetsma, A.; Feringa, B. L. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2374. (b) Sewald, N.; Wendisch, V. *Tetrahedron: Asymmetry* **1998**, *9*, 1341. (c) Arnold, L. A.; Imbos, R.; Mandoli, A.; de Vries, A. H. M.; Naasz, R.; Feringa, B. L. *Tetrahedron* **2000**, *56*, 2865.
- (14) For leading references on H₈-BINOL-based phosphorus amidite ligands, see: (a) Zeng, Q.; Liu, H.; Cui, X.; Mi, A.; Jiang, Y.; Li, X.; Choi, M. C. K.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2002**, *13*, 115. (b) Duursma, A.; Minnaard, A. J.; Feringa, B. L. *Tetrahedron* **2002**, *58*, 5773.
- (15) The ee was determined by chiral HPLC (Chiralcel OD column) after the removal of *t*-butyl groups.
- (16) A 1:1 mixture of **8a** and **8b** was obtained using Pd(PPh₃)₄ (see ref 12).
- (17) For leading reviews on C–H amination, see: (a) Espino, C. G.; Du Bois, J. In *Modern Rhodium-Catalyzed Organic Reactions*; Evans, P. A., Ed.; Wiley-VCH: Weinheim, Germany, 2005; Chapter 17. (b) Davies, H. M. L.; Long, M. S. *Angew. Chem., Int. Ed.* **2005**, *44*, 3518. (c) Dick, A. R.; Sanford, M. S. *Tetrahedron* **2006**, *62*, 2439.

JA8027394