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

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Abstract

This paper describes a catalytic asymmetric diamination process for terminal olefins at allylic and homoallylic carbons via formal C-H activation using di-*t*-butyldiaziridinone as nitrogen source with catalyst generated from $\text{Pd}_2(\text{dba})_3$ and chiral phosphorus amidite ligand. A wide variety of readily available terminal olefins can be effectively diaminated in good yields with high regio-, diastereo-, and enantioselectivities.

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 $\text{Pd}(0)$ -^{8,9} and Cu(I) ¹⁰-catalyzed regio- and stereoselective diamination of conjugated dienes and trienes using di-*t*-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 $\text{Pd}(\text{PPh}_3)_4$ (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-*t*-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, H_8 -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. ^{31}P 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 amination of various terminal olefins with $\text{Pd}_2(\text{dba})_3$ and **L2** was investigated. As shown in Table 1, all the amination reactions occurred highly regio- and diastereoselectively at allylic and homoallylic carbons of terminal olefins, giving amination 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 aminated in good yields with high diastereoselectivities (Table 1, entries 11–12), indicating that the stereochemistry of amination products was primarily determined by the chiral catalyst, and the stereogenic center of the substrate had only a small effect on diastereoselectivities. The amination 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 amination conditions (Scheme 3), bisamination compound **8b** was obtained in 60% yield and 99% ee¹⁵ along with small amount of meso compound **8a**.¹⁶ Treating **8b** with CF_3COOH , conc. 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 bisaminations in Scheme 3 and Scheme 4 involved multiple transformations, thus a higher catalyst loading was needed.

In summary, a catalytic asymmetric allylic and homoallylic amination for a variety of readily available terminal olefins has been successfully achieved using di-*t*-butyldiaziridinone (**2**) as nitrogen source with a catalyst generated from $\text{Pd}_2(\text{dba})_3$ and H_8 -BINOL derived phosphorus amidite ligand **L2**, giving amination 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 sp^3 C-H bonds.¹⁷ Compared to the asymmetric amination of conjugated dienes, the current asymmetric amination uses readily available terminal olefins without the need to prepare conjugated dienes. This advantage is even more apparent in the cases of bisaminations 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.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
The X-ray structure of 6

Scheme 1.

Pd/L1

1:1	16% conv. (92% ee)
1:1.5	32% conv. (92% ee)
1:2.2	53% conv. (92% ee)
1:3	40% conv. (92% ee)

Pd/L2

1:1	36% conv. (90% ee)
1:1.5	54% conv. (90% ee)
1:2.2	80% conv. (90% ee)
1:3	69% conv. (90% ee)

Scheme 2.

Scheme 3.

Scheme 4.

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

Entry	Substrate	Product ^b
1	R = Et
2	R = <i>n</i> C ₅ H ₁₁	
3	R = CH ₂ Ph	
4	R = <i>i</i> -Pr	
5	R = Ph	

Entry	Substrate	Product ^b
6
7	$n\text{-C}_5\text{H}_{11}$

EntrySubstrate

Product^b

8

9

10

Entry	Substrate	Product ^b
11
12

^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.