JOC*Note*

Chiral *N*-Heterocyclic Carbene−Pd(0)-Catalyzed Asymmetric Diamination of Conjugated Dienes and Triene

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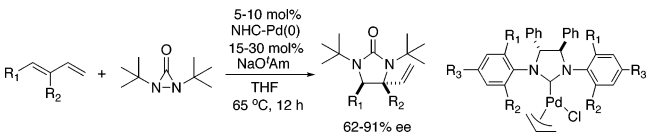

Studies show that a variety of conjugated dienes and triene can be enantioselectively diaminated using di-*tert*-butyldiaziridinone as nitrogen source and chiral *N*-heterocyclic carbene−Pd(0) complex as catalyst in good enantioselectivity (62−91% ee) with high regio- and diastereoselectivity.

N-Heterocyclic carbenes (NHCs) have emerged as highly effective ligands for a variety of metal-catalyzed transformations.[1] Compared to phosphines, carbene ligands usually form more stable complexes with metals and often do not require excess ligands. Their electron richness and steric bulkiness are also generally favorable to the oxidative addition and reductive elimination processes involved in many reactions.[1] In recent years, high levels of enantioselectivities have also been achieved for a wide variety of metal-catalyzed transformations with chiral NHCs as ligands,[2] such as iridium-catalyzed hydrogenation of alkenes,[3] ruthenium-catalyzed metathesis reactions,[4] copper-catalyzed allylic alkylations,[5] copper- and rhodium-catalyzed conjugated additions,[6] and rhodium- and ruthenium-catalyzed hydrosilylations.[7] Chiral NHC−Pd complexes have also been actively explored for asymmetric transformations such as α-arylation of amides,[8] oxidative kinetic resolution of secondary alcohols,[9] and allylic alkylation.[10,11] Recently, we reported a regio- and diastereoselective diamination of conjugated dienes and trienes using di-*tert*-butyldiaziridinone as nitrogen source and $Pd(PPh_3)_4$ as catalyst.[12,13−18] Subsequently, we have shown that NHC−Pd(0) complexes are also effective catalysts for this diamination process, giving similar reactivity and selectivity with less catalyst loading (Scheme 1).[19] In our efforts to develop an

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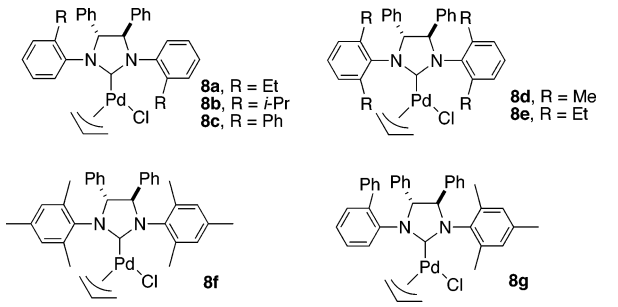
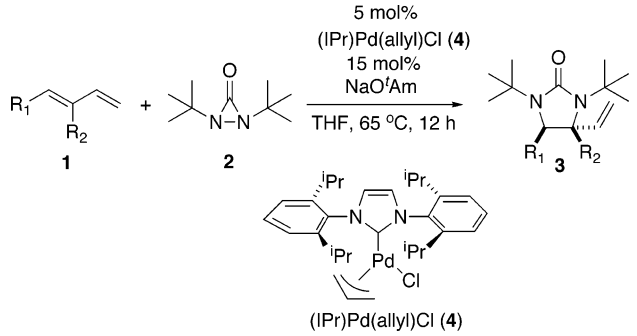
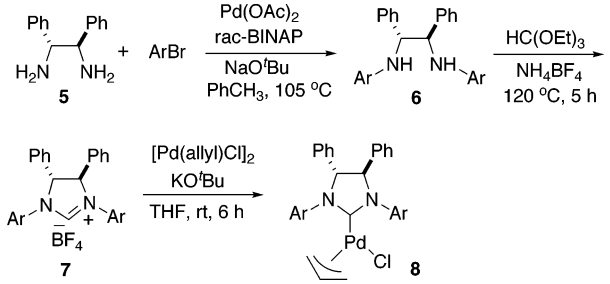


FIGURE 1. Chiral NHC−Pd complexes.

SCHEME 1



SCHEME 2



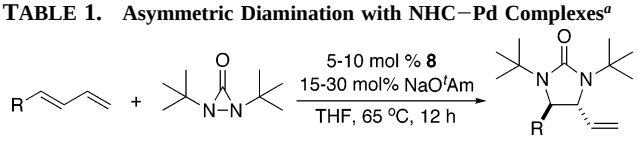
asymmetric version of this diamination, chiral NHC ligands have been examined along with chiral phosphine based ligands.[20] Herein we wish to report our preliminary studies on chiral NHC−Pd(0)-catalyzed diamination of dienes and triene.

Initial studies on asymmetric diamination were based on chiral *N*-aryl-substituted *N*-heterocyclic carbenes derived from (*R*,*R*)-diphenylethylenediamine, which were reported by Grubbs in the ruthenium-catalyzed ring-closing metathesis.[4a,c] On the basis of the reported procedures, imidazolium salts **7** were prepared from the chiral diamine in two steps (Scheme 2),[4a,c] and corresponding NHC−Pd(allyl)Cl complexes **8** were generated by treatment of the imidazolium salts and $[Pd(allyl)Cl]_2$ with KO^{t}Bu in THF[9a,21] (Scheme 2) (Figure 1).[22,23] The X-ray structure of NHC−Pd complex **8e** is shown in Supporting Information.

Asymmetric diamination was examined with catalysts generated in situ from NHC−Pd(allyl)Cl complexes **8a**−**g** (Figure 1) and NaO^{t}Am[24] using 1,3-hexadiene and 1-(*p*-methoxyphenyl)butadiene as substrates. The results are summarized in Table 1. Among the catalysts tested, complexes **8a**−**c**, bearing *ortho*-monosubstituted phenyl groups, gave 64−91% ee for 1,3-hexadiene (Table 1, entries 1−3). It appears that enantioselectivity increases with the size of the *ortho* substituent on the *N*-phenyl group. Unfortunately, these catalysts gave low conversions for both 1,3-hexadiene and 1-(*p*-methoxyphenyl)butadiene (Table 1, entries 1−3). A similar trend was also observed for a closely related unsymmetric NHC−Pd complex **8g** (Table 1, entry 10). Complexes **8d**−**f**, bearing *ortho*,*ortho*-disubstituted phenyl groups, gave higher conversions with less amount of catalyst (5 mol %) but lower ee's (Table 1, entries 4−9). The higher conversion obtained with these catalysts could be due to the steric hindrance of the carbene ligand, which may facilitate the reductive elimination step in the catalytic cycle.[19] As shown by the X-ray structure of **8e** (Supporting Information), ligands with *ortho*,*ortho*-disubstituted phenyl groups can provide a chiral environment around the Pd, thus giving reasonable enantioselectivity for the diamination. Lower ee's obtained with these ligands as compared to ligands with *ortho* monosubstituted phenyl groups in complexes such as **8b** and **8c** suggest that ligands with *ortho*,*ortho*-disubstituted phenyl groups are less efficient for stereodifferentiation than those with *ortho*-monosubstituted phenyl groups.

Although similar conversions were obtained for 1,3-hexadiene with **8d**−**f** (Table 1, entries 5, 7, and 9), catalyst **8e** showed higher reactivity than **8d** and **8f** for 1-(*p*-methoxyphenyl)-butadiene (Table 1, entries 5, 7, and 9). To further investigate the catalyst's reactivity and selectivity, diamination with **8e** was extended to other substrates. As shown in Table 2, various dienes

TABLE 1. Asymmetric Diamination with NHC−Pd Complexes[a]



		R = Et		R = *p*-MeOPh	
entry	catalyst	conv (%)[c]	ee (%)[d]	conv (%)[c]	ee (%)[e]
1	**8a**	28	64	<10	nd
2	**8b**	49	82	15	nd
3	**8c**	30	91	<10	nd
4	**8d**	81	71		
5[b]	**8d**	100	69	56	74
6	**8e**	85	70		
7[b]	**8e**	**100**	**71**	**100**	**73**
8	**8f**	78	73		
9[b]	**8f**	100	71	58	76
10	**8g**	48	90	<10	nd

[a] All reactions were carried out with diene (0.20 mmol), di-*tert*-butyldiaziridinone (**2**) (0.30 mmol), NaO^{t}Am (0.06 mmol), and NHC−Pd(allyl)Cl (0.02 mmol) in THF (0.1 mL) at 65 °C for 12 h in an NMR tube unless otherwise noted. [b] The reactions were carried out with NaO^{t}Am (0.03 mmol) and NHC−Pd(allyl)Cl (0.01 mmol) in a vial with stirring. (It was found that the conversion for diamination can be improved with **8d**−**f** when the reaction was carried out in a vial with stirring as compared to in an NMR tube. However, in the case of **8a**−**c** and **8g**, the conversion for diamination was not significantly improved with stirring.) [c] Conversion was determined by ^{1}H NMR analysis of the crude reaction mixture. [d] The ee was determined by chiral GC (Chiraldex B-DM column). [e] The ee was determined by chiral HPLC (Chiralpak AD-H column).

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(22) For a related chiral NHC-Pd complex, see ref 9a.

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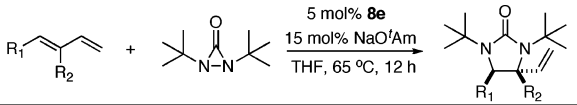
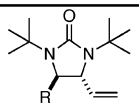
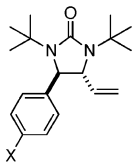
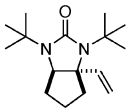
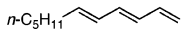
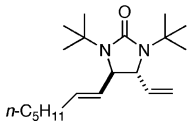
TABLE 2. Catalytic Asymmetric Diamination of Dienes and Triene[a]



entry	substrate	product	yield (%)[c]	Ee (%)
1	R = Me		88	76[d]
2[b]	R = Et		97	71[e]
3	R = *n*-C_5H_{11}		87	72[e]
4[b]	R = $PhCH_2CH_2$		95	70[f]
5[b]	R = *c*-C_6H_{11}		57	76[d]
6	X = H		76	74[f]
7	X = *p*-OMe		82	73[g]
8			82	62[e]
9			95	78[d]

[a] All reactions were carried out with diene or triene (0.6 mmol), di-*tert*-butyldiaziridinone (**2**) (0.9 mmol), NaO^{t}Am (0.09 mmol), and **8e** (0.03 mmol) in THF (0.1 mL) at 65 °C for 12 h. The absolute configurations are not determined, and the stereochemistry indicated represents the relative stereochemistry. [b] A mixture of *E* and *Z* isomers was used. For entry 2, diene (1.33 mmol, *E*/*Z* = 1/1.2; *E* isomer, 0.60 mmol); for entry 4, diene (1.09 mmol, *E*/*Z* = 1.2/1; *E* isomer, 0.60 mmol); for entry 5, diene (0.96 mmol, *E*/*Z* = 1.67/1; *E* isomer, 0.60 mmol). [c] Isolated yield based on diene or triene. [d] The ee was determined by chiral GC (Chiraldex B-DM column) after removal of *tert*-butyl groups. [e] The ee was determined by chiral GC (Chiraldex B-DM column). [f] The ee was determined by chiral HPLC (Chiralpak AD-H column) after removal of *tert*-butyl groups. [g] The ee was determined by chiral HPLC (Chiralpak AD-H column).

and a triene can be effectively diaminated in 57−97% yield and 62−78% ee. The diamination with **8e** proceeded highly regioselectively at the internal double bond with high diastereoselectivity, which is similar to the diamination using (IPr)-Pd(allyl)Cl (**4**) (Scheme 1).

In conclusion, it has been found that chiral NHC−Pd catalysts are promising for asymmetric diamination of conjugated dienes and triene using di-*tert*-butyldiaziridinone as nitrogen source, giving diamination products in good yields and ee's with high regio- and diastereoselectivities. The carbene structure has a large impact on both the reactivity and enantioselectivity. Catalysts such as **8d**−**f** are very active, giving high conversions for diamination with 5 mol % catalyst. High enantioselectivity (90−91% ee) can be obtained with catalysts **8c** and **8g** while the conversion is low. The information obtained in this study will be useful for the development of new NHC−Pd catalysts with both high reactivity and enantioselectivity via electronic and steric tuning of ligands. As compared to the chiral phosphine-based catalysts,[20] the NHC−Pd catalysts can potentially be more stable and active, thus requiring less catalyst loading. Further studies are currently underway.

Experimental Section

All diamination products in Table 2 are known and give satisfactory spectroscopic characterization.[20]

Representative Asymmetric Diamination Procedure (Table 2, Entry 6). A 2.0-mL vial was charged with complex **8e** (0.0201 g, 0.030 mmol), sodium *tert*-pentoxide (0.0099 g, 0.090 mmol), and a stirrer bar. The vial was sealed with a septum, evacuated, and then filled with argon three times. THF (0.1 mL) (freshly distilled from sodium) was then added via a syringe. After stirring at room temperature for 10 min, 1-phenylbutadiene (0.078 g, 0.60 mmol) was added (for a solid substrate, it was added earlier along with the Pd catalyst), followed by addition of di-*tert*-butyldiaziridinone (0.153 g, 0.90 mmol). Upon stirring at 65 °C for 12 h, the reaction mixture was purified by flash chromatography (silica gel, hexane/ether = 5/1) to give the diamination compound as a colorless oil (0.136 g, 76% yield, 74% ee). Colorless oil; $[\alpha]^{22}_D = +23.9°$ (*c* 1.04, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32−7.26 (m, 5H), 6.01 (ddd, *J* = 16.2, 9.6, 8.4 Hz, 1H), 5.18 (d, *J* = 16.2 Hz, 1H), 5.13 (d, *J* = 9.6 Hz, 1H), 4.14 (s, 1H), 3.63 (d, *J* = 8.4 Hz, 1H), 1.32 (s, 9H), 1.26 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 144.0, 140.9, 128.9, 127.8, 125.8, 115.8, 64.9, 63.3, 53.6, 53.4, 29.0, 28.8.

Table 2, Entry 1. Colorless oil; $[\alpha]^{22}_D = +24.9°$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87 (ddd, *J* = 17.1, 10.2, 8.4 Hz, 1H), 5.14 (d, *J* = 17.1 Hz, 1H), 5.04 (d, *J* = 10.2 Hz, 1H), 3.45 (d, *J* = 8.4 Hz, 1H), 3.24 (q, *J* = 6.3 Hz, 1H), 1.30 (s, 9H), 1.27 (s, 9H), 1.16 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.9, 140.0, 115.5, 63.6, 55.3, 53.0, 52.5, 29.1, 28.9, 21.2.

Table 2, Entry 2. Colorless oil; $[\alpha]^{22}_D = +7.7°$ (*c* 1.15, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87 (ddd, *J* = 17.4, 10.2, 8.4 Hz, 1H), 5.14 (d, *J* = 17.4 Hz, 1H), 5.04 (d, *J* = 10.2 Hz, 1H), 3.62 (d, *J* = 8.4 Hz, 1H), 3.01 (t, *J* = 5.7 Hz, 1H), 1.57−1.48 (m, 2H), 1.32 (s, 9H), 1.31 (s, 9H), 0.87 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.4, 140.8, 115.2, 60.9, 60.2, 53.1, 52.6, 29.1, 29.0, 27.3, 9.1.

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Supporting Information Available: Preparation procedures and characterization of chiral NHC−Pd(allyl)Cl complexes, characterization of diamination products, X-ray data of complex **8e**, ^{1}H and ^{13}C NMR spectra of chiral NHC−Pd(allyl)Cl complexes and diamination products, and data for determination of enantiomeric excess of diamination products. This material is available free of charge via the Internet at http://pubs.acs.org.

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