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A Mild Cu(I)-Catalyzed Regioselective Diamination of Conjugated Dienes

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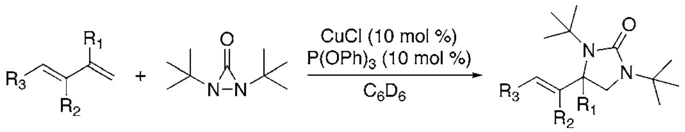
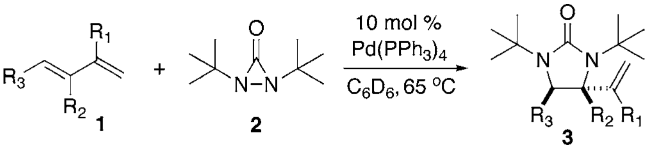
ABSTRACT



This paper describes a novel diamination process that uses CuCl as catalyst and di-*tert*-butyldiaziridinone as nitrogen source. A wide variety of conjugated dienes and a triene can be effectively diaminated in good yields with generally high regioselectivity under mild reaction conditions.

Metal-mediated and catalyzed diamination of olefins provides an effective approach to the synthesis of vicinal diamines which are very important functional moieties contained in various biologically active compounds and are widely used as chiral control elements in asymmetric synthesis.[1−6] Recently, we reported a Pd(0)-catalyzed regio- and stereoselective diamination of conjugated dienes and trienes using di-*tert*-butyldiaziridinone (**2**)[7,8] as the nitrogen source (Scheme 1).[9] In this reaction, the diamination occurred highly regioselectively at the internal double bond. In our efforts to search for complementary catalytic systems, we have found that the Cu(I)-catalyzed diamination occurs at the terminal double bond (Scheme 2), providing complementary regioselectivity to the Pd(0)-catalyzed diamination process. Herein we wish to report our preliminary efforts on this subject.

Scheme 1



Among various CuX (such as CuOAc, CuBr, CuI, CuCN, CuOTf)[10] and ligands examined,[11] a combination of CuCl and $P(OPh)_3$ (1:1) was found to be one of the most effective systems. For example, treating *trans*-1-phenylbutadiene with 10 mol % of CuCl−$P(OPh)_3$ (1:1) at room temperature for 6 h led to the diamination product in 75% yield (Table 1,

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(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 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.; 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.

(3) For a 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)- 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.

(5) For a recent Pd(II)-catalyzed intermolecular diamination of conjugated dienes, see: Bar, G. L. J.; Lloyd-Jones, G. C.; Booker-Milburn, K. I. *J. Am. Chem. Soc.* **2005**, *127*, 7308.

(6) For a recent Pd(II)-catalyzed intramolecular diamination of terminal olefins, see: Streuff, J.; Hövelmann, C. H.; Nieger, M.; Muñiz, K. *J. Am. Chem. Soc.* **2005**, *127*, 14586.

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

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

(9) Du, H.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2007**, *129*, 762.

(10) Little diamination was observed with $Cu(OAc)_2$, $CuSO_4$, and $Cu(OTf)_2$.

(11) In addition to PR_3 and $P(OR)_3$, nitrogen compounds such as pyridine, DABCO, DMAP, sparteine, oxazoline, etc. were also found to be capable ligands for CuX to promote the diamination.

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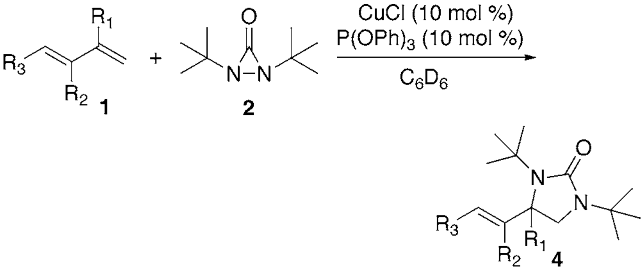
Scheme 2



entry 1).[12] The reaction occurred highly regioselectively at the terminal double bond.[5,13] As shown in Table 1, various other conjugated dienes can be regioselectively diaminated at the terminal double bond (Table 1, entries 2−7). When a conjugated triene was used, the diamination also occurred regioselectively at the terminal double bond (Table 1, entry 8). In all these cases (Table 1, entries 1−8), essentially only one regioisomer was obtained (the X-ray structures of **4b** and **4e** shown in Figure 1).[13] However, two regioisomers were obtained when *trans*-1,3-pentadiene was used (Table 1, entry 9). Interestingly, when *cis*-1,3-pentadiene was used, only one regioisomer was observed (Table 1, entry 10),[14] indicating that the *cis* double bond is much less reactive. For *cis*-1-phenylbutadiene, the terminal double bond was also diaminated, but isomerization of the *cis* double bond occurred during the reaction (Table 1, entry 11). The diamination also occurred for dienes containing geminal disubstituted terminal olefins (Table 1, entries 12−15).

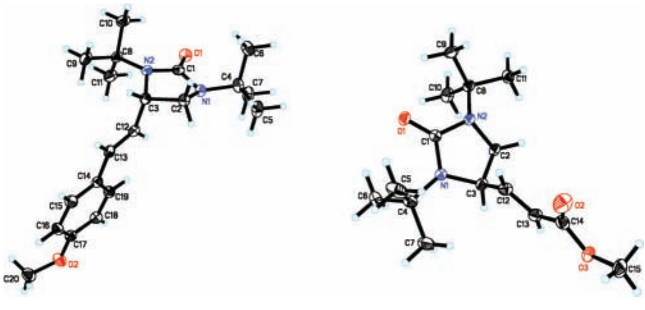
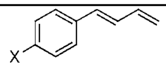
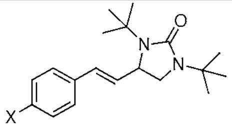
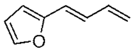
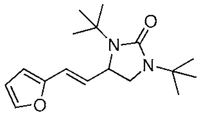
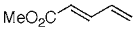
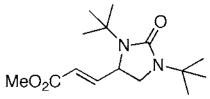
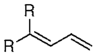
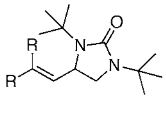
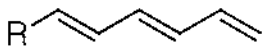
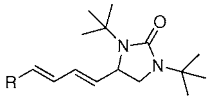
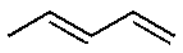
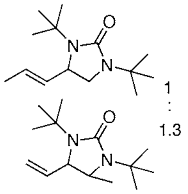
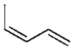
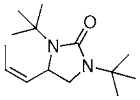
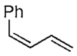
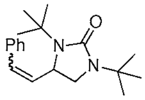
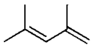
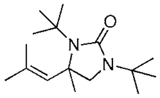
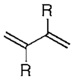
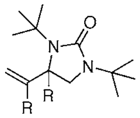


Figure 1. The X-ray structures of compounds **4b** and **4e**.

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

entry	substrate (**1**)	product (**4**)	yield (%)[c]
1	 **1a**, X = H		75
2	**1b**, X = OMe		82
3	**1c**, X = NO$_2$		73
4	 **1d**		73
5	 **1e**		50
6	 **1f**, R = Me		62
7	**1g**, R = Ph		83
8	 **1h**, R = *n*-C$_5$H$_{11}$		68
9	 **1i**		65
10[b]	 **1j**		58
11	 **1k**	 Z/E = 3.3/1	76
12	 **1l**		79
13	 **1m**, R = Me		89
14	**1n**, R = Ph		76
15	**1o**, R = OMe		52

[a] All reactions were carried out with diene or triene (0.6 mmol), di-*tert*-butyldiaziridinone (**2**) (0.9 mmol), CuCl (0.06 mmol), and P(OPh)$_3$ (0.06 mmol) in benzene-d_6 (1.5 mL) at rt under argon for 6 h unless otherwise stated. [b] The reaction was carried out at 65 °C for 6 h. [c] Isolated yield based on diene or triene.

While a precise reaction mechanism awaits further study, a plausible catalytic cycle is shown in Scheme 3. The CuCl first reductively cleaves the N−N bond of diaziridinone **2** to form radical species **5**.[15−18] Addition of **5** to diene **1** forms radical intermediate **6**. The homolytic cleavage of the Cu−N bond of **6** and formation of the C−N bond provide diami-

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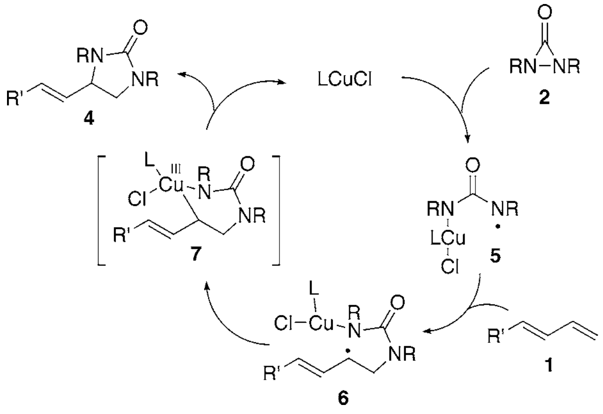
[12] **Representative diamination procedure (Table 1, entry 1):** A 10 mL test tube containing CuCl (0.006 g, 0.06 mmol) was evacuated and then filled with argon three times, followed by the addition of benzene-d_6 (dried over sodium metal) (1.5 mL), P(OPh)$_3$ (0.0186 g, 0.06 mmol), and *trans*-1-phenylbutadiene (0.078 g, 0.6 mmol) successively with stirring. Upon addition of di-*tert*-butyldiaziridinone (0.153 g, 0.9 mmol), the reaction mixture was stirred at room temperature for 6 h and purified by flash chromatography (silica gel, hexanes:ether = 7:1) to give the diamination product as a white solid (0.135 g, 75% yield).

[13] The other regioisomer was barely detectable by ^{1}H NMR of the crude reaction mixture if there was any.

[14] The *tert*-butyl groups of the diamination product (**4j**) can be readily removed with CF$_3$CO$_2$H at reflux for 6 h, giving a clean product in 93% yield (also see ref 9).

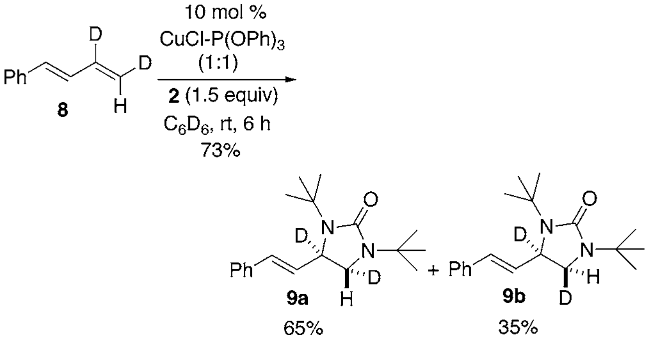
Scheme 3. A Proposed Catalytic Cycle for Diamination



nation product **4** and regenerate the CuCl catalyst. Alternatively, the carbon radical of **6** could coordinate with the Cu to form Cu(III)-like species **7**, which gives product **4** and regenerates the CuCl catalyst after reductive elimination.[19]

No isomerization of the *cis* double bond was observed for *cis*-1,3-pentadiene (Table 1, entry 10), suggesting that the formation of the C−N bond from radical **6** is faster than the bond rotation. In the case of *cis*-1-phenylbutadiene (Table 1, entry 11), the phenyl group further stabilizes radical **6**, thus prolonging its lifetime and causing double bond isomerization. This is also consistent with the observation that two isomers (**9a** and **9b**) were obtained for the diamination of deuterated *trans*-1-phenylbutadiene (**8**) (Scheme 4). It appears that the radical stability and possible steric effects are two important contributing factors for the observed regioselectivity.

Scheme 4



In summary, diamination for a variety of conjugated dienes and a triene has been effectively achieved at the terminal double bonds by using inexpensive CuCl as the catalyst and di-*tert*-butyldiaziridinone as the nitrogen source under mild reaction conditions with generally high regioselectivities. This CuCl-catalyzed diamination appears to be mechanistically distinct from the previous Pd(0)-catalyzed process and provides complementary regioselectivity.[9] Further studies of the reaction mechanism, investigation of different ligands and nitrogen sources, 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 Camille and Henry Dreyfus Foundation and the Monfort Foundation (CSU).

Supporting Information Available: The diamination procedure, the characterization of diamination products, the X-ray data of compounds **4b** and **4e**, and the NMR spectra of diamination products. This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) For a leading review on metal-promoted radical reactions, see: Iqbal, J.; Bhatia, B.; Nayyar, N. K. *Chem. Rev.* **1994**, *94*, 519.

(16) For leading reviews on CuX-catalyzed atom transfer reactions see: (a) Patten, T. E.; Matyjaszewski, K. *Acc. Chem. Res.* **1999**, *32*, 895. (b) Clark, A. J. *Chem. Soc. Rev.* **2002**, *31*, 1.

(17) For a leading review on nitrogen-centered radicals, see: Stella, L. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, P., Eds.; Wiley-VCH: Weinheim, Germany, 2001; Vol. 2, p 407.

(18) For leading references on Cu(I)-catalyzed homolytic cleavage of N−O bonds of oxaziridines, see: (a) Aubé, J.; Peng, X.; Wang, Y.; Takusagawa, F. *J. Am. Chem. Soc.* **1992**, *114*, 5466. (b) Black, D. StC.; Edwards, G. L.; Laaman, S. M. *Tetrahedron Lett.* **1998**, *39*, 5853.

(19) For a leading review on organocopper reagents, see: Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*. 135.