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Cu(I)-Catalyzed Intermolecular Diamination of Activated Terminal Olefins

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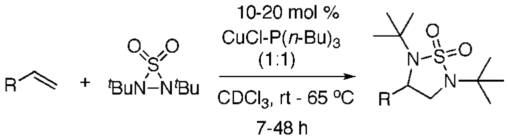
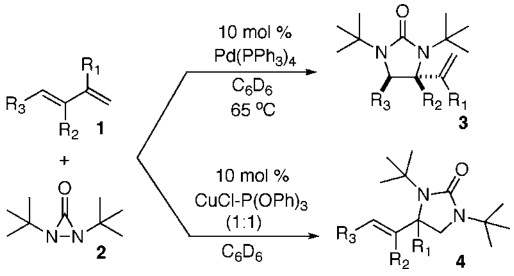
ABSTRACT



This paper describes a novel intermolecular diamination process with CuCl as catalyst and di-*tert*-butylthiadiaziridine 1,1-dioxide as nitrogen source. A variety of activated terminal olefins can be effectively diaminated in good yields under mild reaction conditions.

Vicinal diamines are present in various biologically active compounds and are widely used as chiral control elements in asymmetric synthesis.[1] Metal-mediated and -catalyzed diamination of olefins provides an attractive approach to synthesis of 1,2-diamines and has been actively pursued,[1−6] including very recent reports on Pd(II)-catalyzed intermolecular diamination of conjugated dienes[4] as well as Cu(II)-mediated[5] and Pd(II)-catalyzed[6] intramolecular diamination of terminal olefins. Recently, we reported a Pd(0)-[7,8] and Cu(I)[9]-catalyzed regio- and stereoselective diamination of conjugated dienes and trienes using di-*tert*-butyldiaziridinone (**2**)[10,11] as the nitrogen source (Scheme 1). Generally, catalytic intermolecular diamination of terminal olefins is still chal-

Scheme 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.

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(4) Bar, G. L. J.; Lloyd-Jones, G. C.; Booker-Milburn, K. I. *J. Am. Chem. Soc.* **2005**, *127*, 7308.

(5) (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.

(6) Streuff, J.; Hövelmann, C. H.; Nieger, M.; Muñiz, K. *J. Am. Chem. Soc.* **2005**, *127*, 14586.

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

(8) For a related diamination of terminal olefins at allylic and homoallylic carbons via C−H activation, see: Du, H.; Yuan, W.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2007**, *129*, 7496.

(9) Yuan, W.; Du, H.; Zhao, B.; Shi, Y. *Org. Lett.* **2007**, *9*, 2589.

(10) Greene, F. D.; Stowell, J. C.; Bergmark, W. R. *J. Org. Chem.* **1969**, *34*, 2254.

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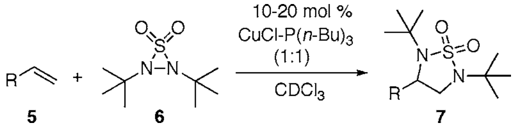
10.1021/ol702061s CCC: $37.00

lenging. Herein we wish to report our preliminary efforts on this subject.

Initial studies were carried out with styrene as substrate and di-*tert*-butyldiaziridinone (**2**) as nitrogen source. Little diamination was observed with $Pd(PPh_3)_4$ as catalyst, but a low yield of the diamination product was obtained when the reaction was carried out with $CuCl-P(OPh)_3$ as catalyst. After much experimentation, the diamination was further improved by using di-*tert*-butylthiadiaziridine 1,1-dioxide (**6**)[12] as the nitrogen source and $CuCl-P(n\text{-}Bu)_3$ as the catalyst in $CDCl_3$ (Scheme 2). As shown in Table 1, various styrenes with different substituents can be diaminated smoothly in moderate to good yields (Table 1, entries 1−9) (the X-ray structure of compound **7h** is shown in Figure 1).[13] It appears that styrenes with electron-donating groups are better substrates than those with electron-withdrawing groups. Naphthylethene and various heteroarylethenes are also effective substrates (Table 1, entries 10−14). Certain enyne and vinyl enol ether can also be diaminated (Table 1, entries 15 and 16). However, terminal olefins such as 1-octene and ethyl acrylate are not effective substrates toward diamination.

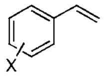
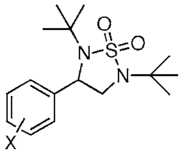
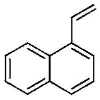
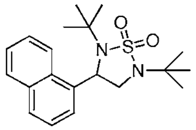
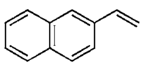
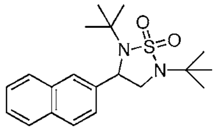
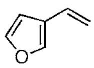
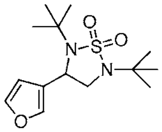
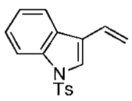
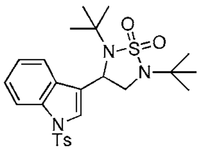
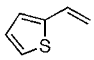
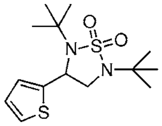
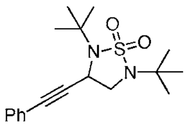
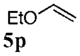
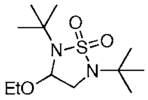
Scheme 2



The deprotection of diamination product **7** is illustrated in Scheme 3. The *tert*-butyl groups of compound **7a** were smoothly removed with CF_3CO_2H at room temperature. When **7a** was treated with concentrated HCl and $BaCO_3$ at 60 °C, both *tert*-butyl and sulfonyl groups were removed cleanly.[14]

When deuterated styrene **10** was subjected to the diamination condition, a mixture of two isomers (**11a** and **11b**) was obtained (Scheme 4). While a precise reaction mechanism awaits further study, this diamination appears to proceed via a radical mechanism as proposed previously[9] (Scheme 5). The CuCl probably first reduces the N−N bond of di-*tert*-butylthiadiaziridine 1,1-dioxide (**6**) to form radical

Table 1. Catalytic Diamination of Terminal Olefins[a]

entry	substrate (**5**)	product (**7**)	yield (%)[d]
1	 **5a**, X = H		65
2[b]	**5b**, X = *p*-OMe		74
3	**5c**, X = *p*-F		61
4	**5d**, X = *p*-^{t}Bu		75
5	**5e**, X = *p*-Ph		75
6[c]	**5f**, X = *p*-NO_2		49
7	**5g**, X = *o*-Cl		67
8	**5h**, X = *m*-Br		63
9[b]	**5i**, X = 3-Br, 4-OMe		67
10[c]	 **5j**		91
11[c]	 **5k**		88
12	 **5l**		45
13[c]	 **5m**		80
14	 **5n**		74
15	 **5o**		88
16[b]	 **5p**		59

[a] All reactions were carried out with olefin (0.4 mmol), di-*tert*-butylthiadiaziridine 1,1-dioxide **(6)** (0.6 mmol), $CuCl-P(n\text{-}Bu)_3$ (1:1) (0.08 mmol) in $CDCl_3$ (0.1 mL) at 50 °C under argon for 24 h unless otherwise stated. For entry 2, 7 h; for entry 15, 48 h at rt; for entry 16, 14 h at 65 °C with olefin (0.6 mmol) and **6** (0.4 mmol) in an NMR tube without stirring. [b] With $CuCl-P(n\text{-}Bu)_3$ (1:1) (0.04 mmol). [c] In 0.2 mL of $CDCl_3$. [d] Isolated yield based on olefin except entry 16 where the yield is based on **6**.

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(12) Prepared based on reported procedure: Timberlake, J. W.; Alender, J.; Garner, A. W.; Hodges, M. L.; Özmeral, C.; Szilagyi, S.; Jacobus, J. O. *J. Org. Chem.* **1981**, *46*, 2082.

(13) **A representative diamination procedure (Table 1, entry 1):** To a 1.5 mL vial equipped with a stirrer bar was added CuCl (0.008 g, 0.08 mmol). The sealed vial was evacuated and filled with Ar three times, followed by addition of $CDCl_3$ (0.1 mL) and tri-*n*-butylphosphine (0.020 mL, 0.08 mmol). After the mixture was stirred at room temperature for 10 min, styrene (**5a**) (0.042 g, 0.40 mmol) and di-*tert*-butylthiadiaziridine 1,1-dioxide (**6**) (0.124 g, 0.60 mmol) were added (for solid olefins, they were added together with CuCl). The reaction mixture was stirred at 50 °C for 24 h and purified by flash chromatography (silica gel, petroleum ether: ethyl acetate:chloroform = 15:1:1.5) to give the diamination product **7a** as a white solid (0.080 g, 65%).

(14) The deprotection with $BaCO_3$·HCl has also been investigated with additional substrates. For example, both the *tert*-butyl and sulfonyl groups of compound **7h** were cleanly removed in 91% yield. Compound **7k** was deprotected in 70% yield with a slightly modified procedure (small amount of ethanol was added to improve solubility of **7k** and the reaction time was extended to 24 h). However, compounds **7*l*−n** decomposed under this deprotection condition. For a reductive deprotection of sulfamide with $LiAlH_4$, see ref 5a.

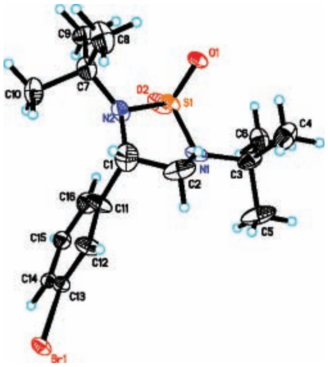
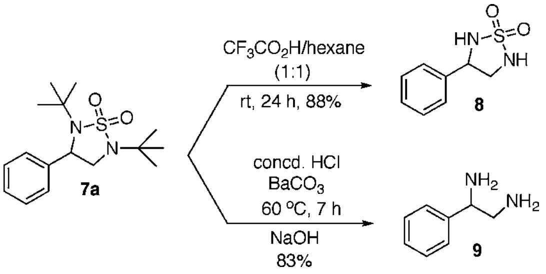
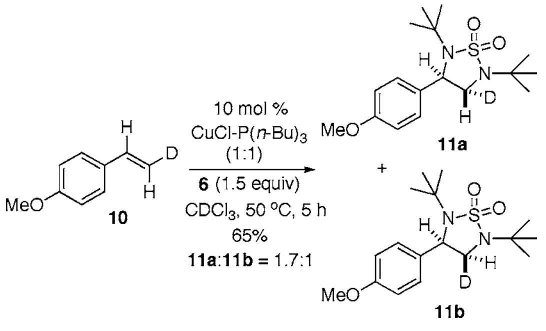


Figure 1. The X-ray structure of compound **7h**.

Scheme 3

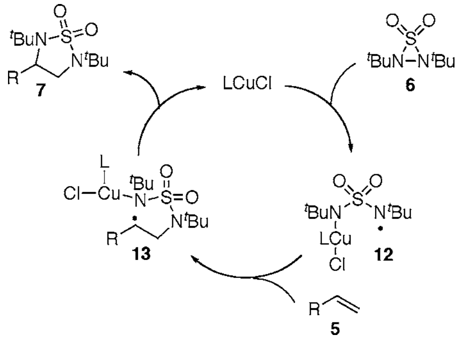


Scheme 4



species **12**.[15−18] Addition of **12** to olefin **5** forms radical intermediate **13**, which undergoes C−N bond formation to give diamination product **7** and regenerates the CuCl catalyst.[19] The higher reactivities displayed with electron-rich olefins (e.g., Table 1, entries 2 and 16) as compared to electron-poor olefins are consistent with the electrophilic nature of nitrogen radical **12**.[17]

Scheme 5. A Proposed Catalytic Cycle for Diamination



In summary, diamination for a variety of conjugated terminal olefins has been effectively achieved with CuCl as catalyst and di-*tert*-butylthiadiaziridine 1,1-dioxide (**6**) as nitrogen source under mild reaction conditions, providing various 1,2-diamines that are present in various biologically active compounds.[20] The diamination is likely to proceed via a nitrogen radical intermediate. Further studies of the reaction mechanism, investigation of different catalysts and nitrogen sources, and expansion of the substrate scope as well as development of an asymmetric process are currently underway.

Acknowledgment. We are grateful for the generous financial support from the Camille and Henry Dreyfus Foundation and the Monfort Foundation (CSU).

Supporting Information Available: The diamination and deprotection procedures, the characterization of diamination products, and the X-ray data of compounds **7h** along with the ^{1}H and ^{13}C NMR spectra of **7**, **8**, **9**, and **11**. 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 leading references 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. (b) Guin, J.; Mück-Lichtenfeld, C.; Grimme, S.; Studer, A. *J. Am. Chem. Soc.* **2007**, *129*, 4498.

(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) Aubé, J. *Chem. Soc. Rev.* **1997**, *26*, 269. (c) Black, D. StC.; Edwards, G. L.; Laaman, S. M. *Tetrahedron Lett.* **1998**, *39*, 5853. (d) Black, D. StC.; Edwards, G. L.; Laaman, S. M. *Synthesis* **2006**, 1981.

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

(20) For examples, see: (a) Casapullo, A.; Bifulco, G.; Bruno, I.; Riccio, R. *J. Nat. Prod.* **2000**, *63*, 447. (b) Miyake, F. Y.; Yakushijin, K.; Horne, D. A. *Org. Lett.* **2002**, *4*, 941. (c) Kumar, V.; Guo, D.; Cassel, J. A.; Daubert, J. D.; DeHaven, R. N.; DeHaven-Hudkins, D. L.; Gauntner, E. K.; Gottshall, S. L.; Greiner, S. L.; Koblish, M.; Little, P. J.; Mansson, E.; Maycock, A. L. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1091.