

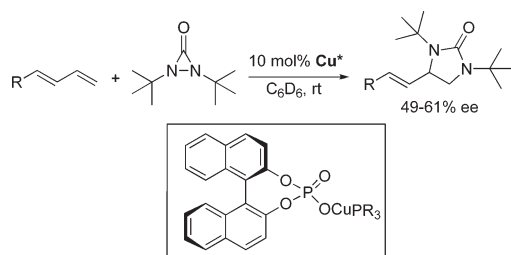
Cu(I)-Catalyzed Diamination of Conjugated Olefins with Tunable Anionic Counterions. A Possible Approach to Asymmetric Diamination

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Various achiral and chiral Cu(I) salts have been prepared from mesitylcopper(I) and investigated for the diamination of conjugated olefins with 1,3-di-*tert*-butyldiaziridinone as nitrogen source. It has been found that copper(I) phosphate has high catalytic activity for the diamination, and encouraging ee's have also been achieved with chiral phosphates as anionic counterions.

Vicinal diamines are contained in various biologically and chemically important molecules.¹ Diamination of olefins presents an attractive approach to these diamines and has recently received intensive interest. Various metal-promoted^{2,3}

(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. (d) de Figueiredo, R. M. *Angew. Chem., Int. Ed.* **2009**, *48*, 1190. (e) Cardona, F.; Goti, A. *Nat. Chem.* **2009**, *1*, 269.

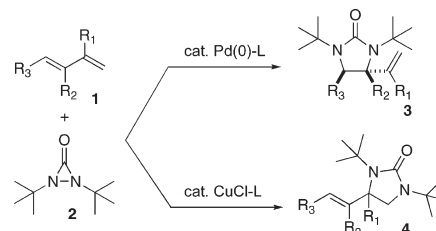
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(4) For recent Pd(II)- and Ni(II)-catalyzed intramolecular diamination of olefins, see: (a) Streuff, J.; Hövelmann, C. H.; Nieger, M.; Muñiz, K. *J. Am. Chem. Soc.* **2005**, *127*, 14586. (b) Muñiz, K.; Streuff, J.; Hövelmann, C. H.; Núñez, A. *Angew. 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. (e) Sibbald, P. A.; Michael, F. E. *Org. Lett.* **2009**, *11*, 1147.

and -catalyzed^{4–6} diaminations have been developed. Recently, we reported that conjugated dienes and trienes can be regioselectively diaminated with Pd(0)^{7,8} or Cu(I)⁹ as catalysts and di-*tert*-butyldiaziridinone^{10,11} as nitrogen source (Scheme 1). High enantioselectivity has also been achieved for the Pd(0)-catalyzed diamination process using tetramethylpiperidine-based phosphorus amidite ligands.^{7c,8b}

SCHEME 1



The Cu(I)-catalyzed diamination is consistent with a radical mechanism, which adds additional challenges to the development of its asymmetric process. Previously, we reported that encouraging ee's were obtained using (*R*)-DT-BM-SEGPHOS as chiral ligand (Scheme 2).^{9b} While the ee's can be further improved by optimizing and designing chiral

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(9) For Cu(I)-catalyzed intermolecular diamination of conjugated dienes and trienes using di-*tert*-butyldiaziridinone, see: (a) Yuan, W.; Du, H.; Zhao, B.; Shi, Y. *Org. Lett.* **2007**, *9*, 2589. (b) Du, H.; Zhao, B.; Yuan, W.; Shi, Y. *Org. Lett.* **2008**, *10*, 4231.

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

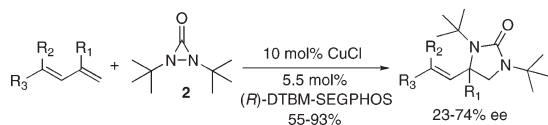
(11) For a leading review on diaziridinones, see: Heine, H. W. In *The Chemistry of Heterocyclic Compounds*; Hassner, A., Ed.; John Wiley & Sons, Inc.: Hoboken, NJ, 1983; p 547.

(12) For a leading review on chiral anion chemistry, see: Lacour, J.; Hebbe-Viton, V. *Chem. Soc. Rev.* **2003**, *32*, 373.

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(14) For examples of generation of RXCu from RXH and mesitylcopper(I), see: (a) Tsuda, T.; Watanabe, K.; Miyata, K.; Yamamoto, H.; Saegusa, T. *Inorg. Chem.* **1981**, *20*, 2728. (b) Lopes, C.; Håkansson, M.; Jagner, S. *Inorg. Chem.* **1997**, *36*, 3232. (c) Håkansson, M.; Lopes, C.; Jagner, S. *Organometallics* **1998**, *17*, 210. (d) Balogh-Hergovich, É.; Speier, G.; Huttner, G.; Zsolnai, L. *Inorg. Chem.* **1998**, *37*, 6535. (e) Polyakov, O. G.; Ivanova, S. M.; Gaudinski, C. M.; Miller, S. M.; Anderson, O. P.; Strauss, S. H. *Organometallics* **1999**, *18*, 3769. (f) Strieter, E. R.; Blackmond, D. G.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4120. (g) Mankad, N. P.; Rivard, E.; Harkins, S. B.; Peters, J. C. *J. Am. Chem. Soc.* **2005**, *127*, 16032. (h) Hong, S.; Huber, S. M.; Gagliardi, L.; Cramer, C. C.; Tolman, W. B. *J. Am. Chem. Soc.* **2007**, *129*, 14190. (i) Fürstner, A.; Stimson, C. C. *Angew. Chem., Int. Ed.* **2007**, *46*, 8845. (j) Oguadinma, P. O.; Schaper, F. *Organometallics* **2009**, *28*, 4089.

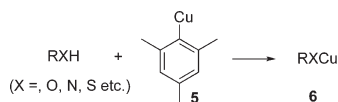
SCHEME 2



ligands, we have also been exploring the possibility of achieving asymmetric induction using Cu(I) catalysts bearing chiral anions.¹² Herein, we report our studies on this subject.

Various Cu(I) salts were prepared in situ from mesitylcopper(I) (**5**)¹³ and modifier RXH (Scheme 3).^{14,15} ¹H NMR studies with phenol, benzoic acid, and *N*-methylbenzenesulfonamide (Table 1, entries 7, 9, and 12) showed that the reactions between these additives and mesitylcopper(I) (**5**) were finished within 0.5 h. The catalytic activities of these in situ generated Cu(I) salts along with other common Cu(I) salts were investigated for diamination using 1-phenyl-1,3-butadiene (**1a**) as substrate. The results are summarized in Table 1. These Cu(I) salts exhibited moderate to excellent catalytic activity for diamination, giving product **4a** with very high regioselectivity. The electronic property of the anionic counterions has a large impact on the catalytic activity. In general, Cu(I) salts with more electronegative anionic counterions show better activities, with CuCl displaying the highest (Table 1, entry 1). A comparable activity was observed with copper(I) diphenylphosphate (Table 1, entry 14).

SCHEME 3



The catalytic activities displayed by these Cu(I) salts prompted us to investigate the possibility of the asymmetric process using Cu(I) salts generated from various chiral modifiers. Various chiral molecules containing OH or NH groups were converted in situ to the corresponding Cu(I) salts by reactions with mesitylcopper(I) (**5**) and were then examined for diamination using 1-phenyl-1,3-butadiene (**1a**) as substrate (Figure 1). Modifiers **Y1–Y6** gave low to moderate conversions and almost no ee's. However, BINOL-derived chiral phosphoric acid **Y7** gave diamination

TABLE 1. Diamination of 1-Phenyl-1,3-butadiene with Copper(I) Salts^a

Entry	CuX	Conv. (%) ^b
1	CuCl	98
2	CuBr·SMe ₂	66
3	CuI	89
4	CuCN	68
5	CuOTf	50
6		17
7		32
8		58
9		52
10		46
11		63
12		81
13		63
14		95

^aAll reactions were carried out with olefin (0.20 mmol), 1,2-di-*tert*-butyldiaziridinone (**2**) (0.30 mmol), CuX–PPh₃ (1:2) (0.020 mmol) in C₆D₆ (0.2 mL) at rt under argon for 24 h. For entries 6–14, catalyst RXCu was prepared in situ by stirring mesitylcopper(I) and RXH in dry C₆D₆ for 1 h, followed by treatment with PPh₃ at rt for 1 h. ^bConversion was determined by ¹H NMR of the crude reaction mixture.

(15) For our related work on generation of tunable cyclopropanation zinc reagents (RXZnCH₂Y) from RXH, see: (a) Yang, Z.; Lorenz, J. C.; Shi, Y. *Tetrahedron Lett.* **1998**, *39*, 8621. (b) Long, J.; Yuan, Y.; Shi, Y. *J. Am. Chem. Soc.* **2003**, *125*, 13632. (c) Lorenz, J. C.; Long, J.; Yang, Z.; Xue, S.; Xie, Y.; Shi, Y. *J. Org. Chem.* **2004**, *69*, 327. (d) Du, H.; Long, J.; Shi, Y. *Org. Lett.* **2006**, *8*, 2827.

(16) For examples of chiral phosphate-based asymmetric catalysis, see: (a) McCarthy, N.; McKervey, M. A.; Ye, T.; McCann, M.; Murphy, E.; Doyle, M. P. *Tetrahedron Lett.* **1992**, *33*, 5983. (b) Pirrung, M. C.; Zhang, J. *Tetrahedron Lett.* **1992**, *33*, 5987. (c) Hodgson, D. M.; Stuppel, P. A.; Pierard, F. Y. T. M.; Labande, A. H.; Johnstone, C. *Chem.—Eur. J.* **2001**, *7*, 4465. (d) Furuno, H.; Kambara, T.; Tanaka, Y.; Hanamoto, T.; Kagawa, T.; Inanaga, J. *Tetrahedron Lett.* **2003**, *44*, 6129. (e) Suzuki, S.; Furuno, H.; Yokoyama, Y.; Inanaga, J. *Tetrahedron: Asymmetry* **2006**, *17*, 504. (f) Mayer, S.; List, B. *Angew. Chem., Int. Ed.* **2006**, *45*, 4193. (g) Martin, N. J. A.; List, B. *J. Am. Chem. Soc.* **2006**, *128*, 13368. (h) Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, F. D. *Science* **2007**, *317*, 496. (i) Rueping, M.; Antonchick, A. P.; Brinkmann, C. *Angew. Chem., Int. Ed.* **2007**, *46*, 6903. (j) Mukherjee, S.; List, B. *J. Am. Chem. Soc.* **2007**, *129*, 11336. (k) Wang, X.; Reisinger, C. M.; List, B. *J. Am. Chem. Soc.* **2008**, *130*, 6070. (l) Hamilton, G. L.; Kanai, T.; Toste, F. D. *J. Am. Chem. Soc.* **2008**, *130*, 14984.

product **4a** in 93% conversion and 48% ee.^{16,17} Similar results were obtained with H₈–BINOL-based chiral phosphoric acid **Y10**. Introduction of substituents at 3,3' or 6,6' positions on the BINOL (**Y8** and **Y9**) resulted in lower ee's.¹⁸ TADDOL-derived phosphate **Y11** gave no asymmetric induction.

Chiral copper(I) phosphate can be obtained as an easily handled solid. For example, treating **Y7** with mesitylcopper(I) (**5**) in benzene at rt overnight afforded Cu**Y7** as a white solid in 69% yield (Scheme 4), which can be stored

(17) For a leading review on chiral phosphoric acid-catalyzed reactions, see: Akiyama, T. *Chem. Rev.* **2007**, *107*, 5744.

(18) When the diamination was carried out with (*R*)-3,3'-bis(2,4,6-triisopropylphenyl)-1,1'-binaphthyl-2,2'-diyl hydrogenphosphate (TRIP), 68% conversion and 0% ee were obtained.

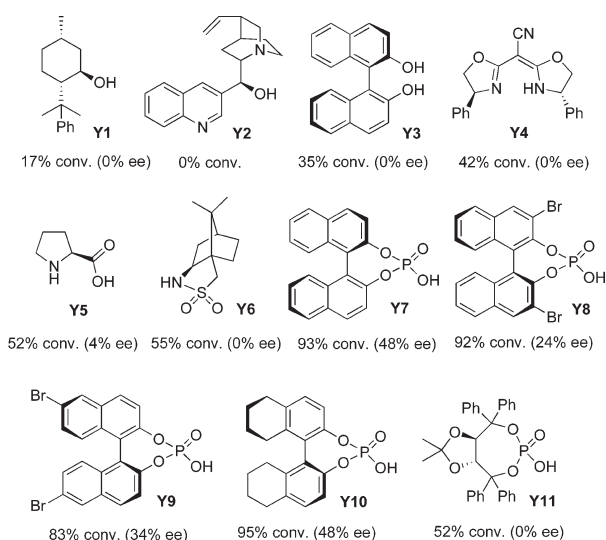
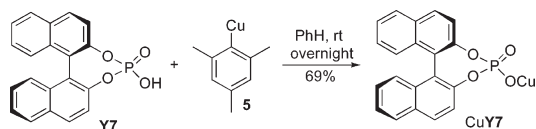


FIGURE 1. Asymmetric diamination of 1-phenyl-1,3-butadiene (**1a**) with chiral Cu(I) salts. All reactions were carried out with olefin (0.20 mmol), 1,2-di-*tert*-butyldiaziridinone (**2**) (0.40 mmol), and R*XCu–PPh₃ (1:2) (0.020 mmol) in C₆D₆ (0.2 mL) at rt under argon for 24 h. RXCu was prepared in situ by stirring mesitylcopper(I) and R*XH in dry C₆D₆ for 1 h, followed by treatment with PPh₃ at rt for 1 h. In the cases of **Y2**, **Y4**, and **Y5**, no PPh₃ was used.

SCHEME 4



in the freezer for three months without any obvious decomposition. The isolated CuY7 gave similar diamination results to the corresponding in situ generated Cu(I) salt.

With chiral catalyst CuY7 in hand, reaction conditions were further optimized for the diamination with 1-phenyl-1,3-butadiene (**1a**) by adding various achiral phosphine and nitrogen ligands. The ee for the diamination was improved to 55% using CuY7–tri(2-naphthyl)phosphine as catalyst in C₆D₆ at rt. When various conjugated dienes and a conjugated triene were subjected to these conditions, diamination products were obtained in good yields and encouraging ee's (49–61%) (Table 2).¹⁹ For aliphatic dienes such as (*E*)-deca-1,3-diene, however, only a trace amount of diamination product was detected from the crude ¹H NMR of the reaction mixture under similar reaction conditions.

In summary, various Cu(I) salts were investigated for the catalytic diamination of conjugated dienes with 1,3-di-*tert*-butyldiaziridinone (**2**) as nitrogen source. The anionic counterions are shown to have a large effect on the catalytic activity for the diamination. Like CuCl, copper(I) diphenyl phosphate generated from mesitylcopper(I) and the corresponding phosphoric acid, is shown to be a highly active catalyst. Encouraging ee's have been obtained when the diamination is carried out using chiral Cu(I) salt derived

TABLE 2. Catalytic Asymmetric Diamination of Conjugated Dienes and Triene^a

Entry	Substrate (1)	Product (4)	Yield (%) ^b	ee (%) ^c
1			64	55
2			70	58
3			77	61
4 ^d			67	49
5			69	49
6			45	55

^aAll reactions were carried out with olefin (0.20 mmol), 1,2-di-*tert*-butyldiaziridinone (**2**) (0.40 mmol), and CuY7–tri(2-naphthyl)phosphine (1:2) (0.020 mmol) in C₆D₆ (0.2 mL) at rt under argon for 30 h. ^bIsolated yield based on olefin. ^cThe ee was determined by chiral HPLC (Chiralpak AD-H column). ^dA mixture of isomers (*E*/*Z* = 1.9:1) was used; only a trace amount of *cis*-isomer in the diamination product was observed by ¹H NMR.

from BINOL-based chiral phosphoric acid, which provides a viable approach to an asymmetric diamination process. The applications of these chiral Cu(I) catalysts in other asymmetric reactions will be pursued.

Experimental Section

Representative Diamination Procedure with CuY7 Generated in Situ (Figure 1). A 1.5 mL vial containing a stir bar and (*R*)-(–)-1,1'-binaphthyl-2,2'-diyl hydrogen phosphate (**Y7**) (0.0070 g, 0.020 mmol) was evacuated and filled with Ar three times. Upon addition of dry C₆D₆ (0.1 mL) and mesitylcopper(I) solution (0.5 M in dry benzene, 0.04 mL, 0.020 mmol), the reaction mixture was stirred at rt for 1 h, followed by the addition of PPh₃ (0.0104 g, 0.040 mmol) solution in dry C₆D₆ (0.1 mL). After the mixture was stirred for an additional 1 h, 1-phenyl-1,3-butadiene (**1a**) (0.026 g, 0.20 mmol) and di-*tert*-butyldiaziridinone (**2**) (0.068 g, 0.40 mmol) were added. The reaction mixture was stirred at rt for 24 h. Diamination product **4a** was formed with 93% conversion (determined by ¹H NMR) and 48% ee.

Representative Diamination Procedure with CuY7 (Table 2, Entry 1). To a mixture of (*R*)-(–)-1,1'-binaphthyl-2,2'-diyl hydrogen phosphate (**Y7**) (1.04 g, 3.0 mmol) in dry benzene (6.0 mL) was added mesitylcopper(I) solution (0.5 M in dry benzene, 6.12 mL, 3.06 mmol) at room temperature over 5 min under argon atmosphere. The reaction mixture was stirred at rt overnight in the dark, filtered, and washed with dry benzene (2 mL) and hexane (3 mL × 2) to give CuY7 as a white solid (0.85 g, 69%).

(19) Our previous work (ref 9b) indicates that the ee of the solid diamination product could be improved by recrystallization if desired.

A 1.5 mL vial containing CuY7 (0.0082 g, 0.020 mmol) and tri(2-naphthyl)phosphine (0.0165 g, 0.040 mmol) was evacuated and filled with Ar three times. Upon addition of dry C₆D₆ (0.2 mL) and stirring at rt for 1 h, 1-phenyl-1,3-butadiene (**1a**) (0.026 g, 0.20 mmol) and di-*tert*-butyldiaziridinone (**2**) (0.068 g, 0.40 mmol) were added. The reaction mixture was stirred at rt for 30 h and purified by flash chromatography (petroleum ether/ethyl ether = 5:1, v/v) to give diamination product **4a** as a white solid (0.0385 g, 64% yield, 55% ee).

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Supporting Information Available: Characterization of diamination products and data for the determination of enantiomeric excess of diamination products along with the NMR spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.