JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Communication
pubs.acs.org/JACS

Copper-Catalyzed Aerobic [3+2]-Annulation of *N*-Alkenyl Amidines

Yi-Feng Wang,[†] Xu Zhu,[†] and Shunsuke Chiba*

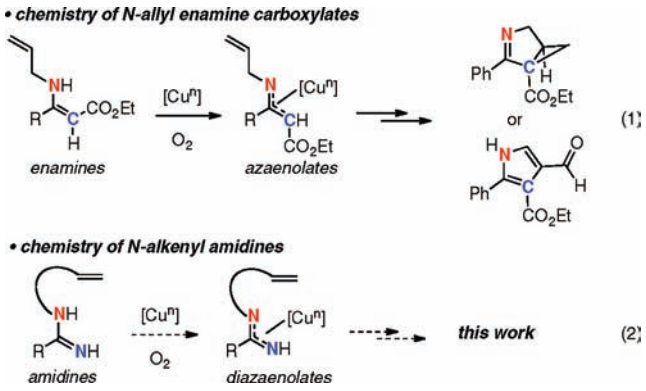
Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, Singapore 637371, Singapore

Supporting Information

ABSTRACT: A method for the synthesis of bi- and tricyclic amidines has been developed through copper-catalyzed aerobic [3+2]-annulation reaction of *N*-alkenyl amidines. These cyclic amidines could be converted into mono-benzyl-protected vicinal diamines by the reduction with aluminum hydride.

Nitrogen-containing heterocycles (azaheterocycles) are an omnipresent component of numerous natural alkaloids and potent pharmaceutical drugs.[1] Although diverse synthetic approaches toward azaheterocycles have been exploited,[2] there remains a need for conceptually novel and versatile methodologies for chemical synthesis of azaheterocycles from readily available building blocks. Herein, we report a copper-catalyzed aerobic [3+2]-annulation of *N*-alkenyl amidines that includes 1,2-diamination of alkenes.

We have been interested in copper-mediated oxidative functionalization of carbon−carbon unsaturated bonds under aerobic conditions,[3,4] and we recently reported the reactions of *N*-allyl enamine carboxylates for intramolecular cyclopropanation and carbooxygenation, giving 3-azabicyclo[3.1.0]hex-2-enes and 4-formylpyrroles, respectively (eq 1).[3a] Amidines could

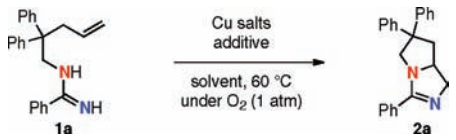


be easily prepared by addition reactions of amines to the corresponding carbonitriles or imidates.[5] Stimulated by the structural analogy of amidines with enamine carboxylates, we could envision unique oxidative amination processes to occur by copper-mediated aerobic reactions of *N*-alkenyl amidines via putative copper diazaenolates (eq 2).

We began our investigation with the copper-mediated aerobic reactions of *N*-(2,2-diphenyl-4-pentenyl)amidine (**1a**) (Table 1). Interestingly, when **1a** was treated with 1.1 equiv of CuBr·SMe$_2$ and 2,2′-bipyridine in DMSO at 60 °C under an O$_2$ atmosphere, an intramolecular 1,2-diamination product, bicyclic amidine (tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazole, **2a**), was isolated in 29% yield (entry 1). The unprecedented 1,2-diamination reaction of the C=C bond[6−13] to form bicyclic amidine **2a** prompted us to optimize the reaction conditions further. While CuCl did not provide **2a** at all (entry 2), the yield of product **2a** was improved to 51% by using CuI (entry 3). It was found that the reaction could be completed even by using a catalytic amount of CuI (entry 4), and DMF was proved to be an optimal solvent for this transformation (entry 5). The catalytic loading of CuI could be reduced to 10 mol %, in which bicyclic amidine **2a** was obtained in 87% yield with 10 mol % of 2,2′-bipyridine in DMF (entry 7). Under a N$_2$ atmosphere, no reaction was observed along with 93% yield recovery of **1a** after 23 h (entry 8). In the absence of 2,2′-bipyridine as a ligand, the reaction became sluggish and the yield of **2a** dropped (entry 9). The reaction with 1,10-phenanthroline afforded amidine **2a** only in 39% yield (entry 10). It is noted that Cu(II) complexes such as CuBr$_2$ did not afford product **2a** at all (entry 11).[14]

Using the CuI−2,2′-bipyridine catalytic system (Table 1, entry 7), we examined the generality of this [3+2]-annulation

Table 1. Optimization of Reaction Conditions[a]



entry	Cu salts (equiv)	additive (equiv)	solvent	time (h)	yield (%)[b]
1	CuBr·SMe$_2$ (1.1)	2,2′-bipyridine (1.1)	DMSO	23	29
2	CuCl (1.1)	2,2′-bipyridine (1.1)	DMSO	8	trace
3	CuI (1.1)	2,2′-bipyridine (1.1)	DMSO	8	51
4	CuI (0.2)	2,2′-bipyridine (0.4)	DMSO	16	55
5	CuI (0.2)	2,2′-bipyridine (0.4)	DMF	9	38
6	CuI (0.1)	2,2′-bipyridine (0.2)	DMF	23	80
7	CuI (0.1)	2,2′-bipyridine (0.1)	DMF	23	87
8[c]	CuI (0.1)	2,2′-bipyridine (0.1)	DMF	23	0 (93)[d]
9	CuI (0.1)	–	DMF	30	75
10	CuI (0.1)	1,10-phenanthroline (0.1)	DMF	23	39
11	CuBr$_2$ (0.1)	2,2′-bipyridine (0.1)	DMF	23	0 (53)[d]

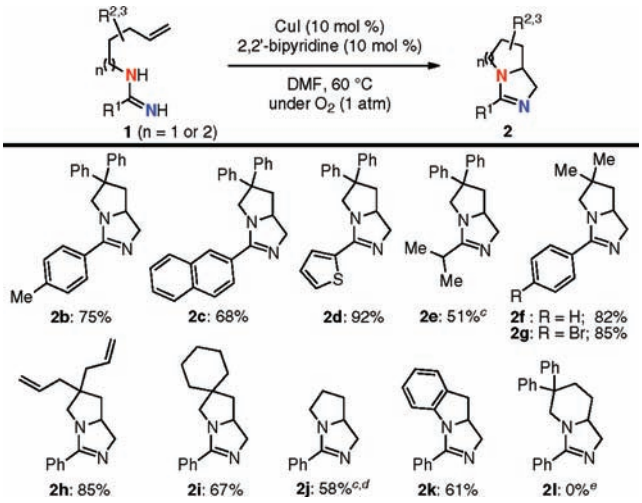
[a]Unless otherwise noted, the reactions were carried out using 0.3−0.5 mmol of amidine **1a** in solvent (0.1 M) at 60 °C under an O$_2$ atmosphere. [b]Isolated yields. [c]The reaction was carried out under a N$_2$ atmopshere. [d]Recovery yields of **1a**.

Received: December 25, 2011
Published: January 31, 2012

   dx.doi.org/10.1021/ja2120629 | *J. Am. Chem. Soc.* 2012, 134, 3679−3682

of *N*-alkenyl amidines. By varying substituents R^1 of *N*-4-pentenyl amidines **1** (Chart 1), it was shown that various aro-

Chart 1. Scope of the [3+2]-Annulation of *N*-Alkenyl Amidines[a,b]



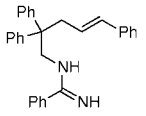
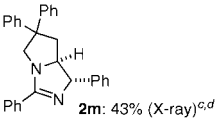
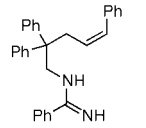
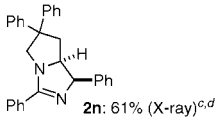
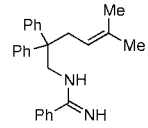
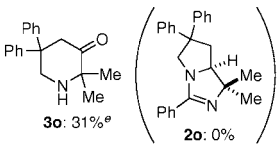
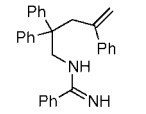
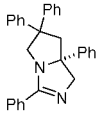
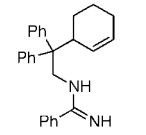
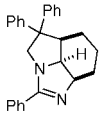
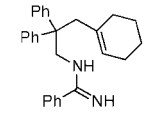
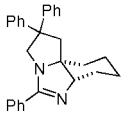
[a]Unless otherwise noted, the reactions were carried out using 0.3−0.5 mmol of amidine **1** using 10 mol % of CuI and 2,2′-bipyridine in DMF (0.1 M) at 60 °C under an O_2 atmosphere. [b]Isolated yields were recorded above. [c]The reaction was run using 40 mol % of CuI and 2,2′-bipyridine. [d]**2j** was obtained in 63% yield using 1.1 equiv of CuI and 1.1 equiv of 2,2′- bipyridine. [e]Unidentified complex mixtures were formed.

matic rings including bromophenyl and thienyl groups (for **2g** and **2d**) were tolerated, and an alkyl substituent (for **2e**) could be introduced. 4-Pentenyl tethers of amidines **1** could include not only 2,2-diphenyl (for **2a**−**g**) but also 2,2′-dimethyl (for **2f**,**g**), 2,2-diallyl (for **2h**), and cyclohexyl (for **2i**) moieties. Even simple *N*-pentenyl amidine **1j** cyclized to give **2j** in 58% yield, while 40 mol % of CuI-2,2′-bipyridine was required. This method allowed for construction of a dihydro-1*H*-imidazo[1,5-a]indole structure (for **2k**) in good yield. The reaction of *N*-5-hexenyl amidine, however, did not afford a [3+2]-annulation product such as **2l**.

Next, the effect of substituent on the alkenyl moiety for the present [3+2]-annulation was examined (Table 2). The reactions of both (*E*)- and (*Z*)-*N*-5-phenyl-4-pentenyl derivatives **1m** and **1n** provided a single diastereomer of **2m** and **2n**, respectively with retention of the configuration of the alkenyl moieties (entries 1 and 2),[15] which may suggest that the present [3+2]-annulation proceeds in a concerted manner. The reaction of *N*-5,5-dimethyl-4-pentenyl amidine **1o** afforded no [3+2]-annulation product even by using a stoichiometric amount of CuI and 2,2′-bipyridine (entry 3). In this case, cyclic α-amino ketone **3o** was isolated in 31% yield through aminooxygenation of the C=C bond.[16] In the case of *N*-4-phenyl-4-pentenyl amidine **1p**, desired bicyclic amidine **2p** could be obtained in 85% yield (entry 4). The reactions of amidines **1q** and **1r** bearing a cyclohexene tether proved the further potential of this method, affording highly strained fused tricyclic amidines **2q** and **2r**, respectively (entries 5 and 6).

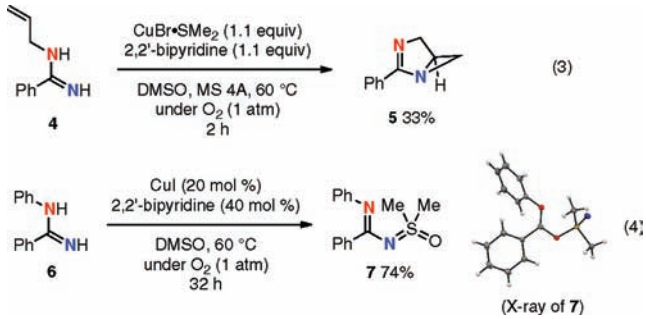
The reaction of *N*-allyl amidine **4** was also examined (eq 3).[17] In this case, bicyclic aziridine **5** was isolated in 33% yield, although a stoichiometric use of $CuBr{\cdot}SMe_2$ and 2,2′-bipyridine in DMSO was required to complete the reaction.[18] It was

Table 2. Scope of the [3+2]-Annulation of *N*-Alkenyl Amidines[a,b]

entry	*N*-alkenyl amidines **1**		products[b]
1		**1m**	 **2m**: 43% (X-ray)[c,d]
2		**1n**	 **2n**: 61% (X-ray)[c,d]
3		**1o**	 **3o**: 31%[e] **2o**: 0%
4		**1p**	 **2p**: 85%
5		**1q**	 **2q**: 75% (X-ray)[d]
6		**1r**	 **2r**: 79% (X-ray)[c,d]

[a]Unless otherwise noted, the reactions were carried out using 0.3−0.5 mmol of *N*-alkenyl amidines **1** with 10 mol % of CuI and 10 mol % of 2,2′-bipyridine in DMF at 60 °C under an O_2 atmosphere. [b]Isolated yields were recorded above. [c]The reaction was carried out using 40 mol % of CuI and 40 mol % of 2,2′-bipyridine. [d]The structures were secured by X-ray crystallographic analysis, see Supporting Information. [e]The reaction was carried out using 1.1 equiv of CuI and 1.1 equiv of 2,2′-bipyridine.

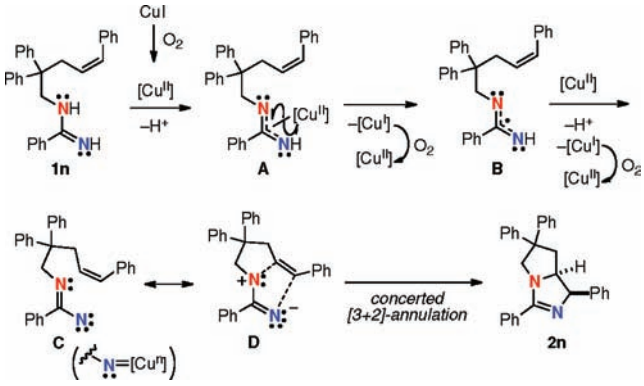
interestingly found that treatment of *N*-phenyl amidine **6** with 20 mol % of CuI and 40 mol % of 2,2′-bipyridine in DMSO under an O_2 atmosphere delivered sulfoxyimine **7** in 74% yield, probably via trap of the putative nitrene species generated during the catalytic process with DMSO (eq 4).[19,20]



Based on these results, a proposed mechanistic possibility is outlined in Scheme 1. In this senario, $Cu^{I}I$ is first oxidized by molecular oxygen to form a higher oxidation state Cu^{II} superoxo or peroxo species (described as $[Cu^{II}]$).[21] One-electron oxidation of *N*-alkenyl amidine **1** with the resulting Cu^{II} species

dx.doi.org/10.1021/ja2120629 | J. Am. Chem. Soc. 2012, 134, 3679−3682

Scheme 1. Proposed Reaction Mechanism for the [3+2]-Annulation of *N*-Alkenyl Amidines

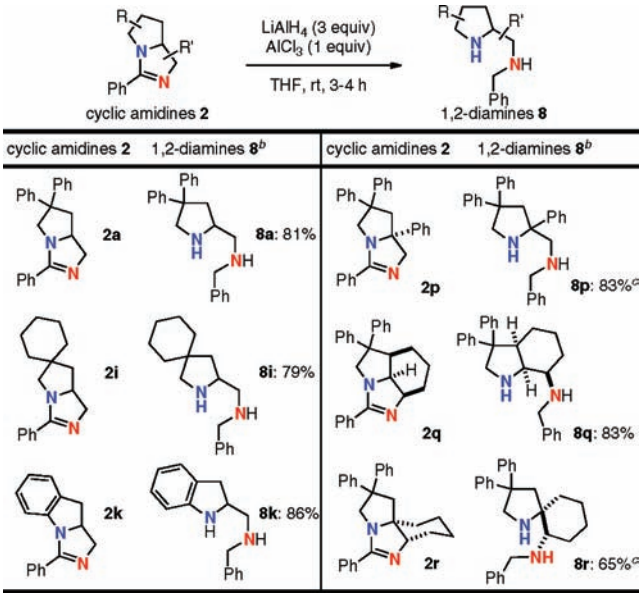


through copper diaza-enolate **A** proceeds to give 1,3-diazaallyl radical **B**, which may be further oxidized by another Cu^{II} species to generate nitrene intermediate (copper nitrene complex) **C**.[22,23] Presumably, nitrene intermediate **C** could potentially possess chemical reactivity as a 1,3-dipole with resonance form **D**, which would induce the concerted [3+2]-cycloaddition with an intramolecular alkenyl moiety to give cyclic amidine **2** with retention of the configuration of the alkene (for Table 2, entries 1 and 2). The results in eqs 3 (aziridination) and 4 (sulfoxyimine formation) also implied generation of the putative nitrene species like **C**. The catalytic cycle could be maintained by oxygen oxidation of the resulting Cu^{I} species to the Cu^{II}.

Vicinal diamine functionalities are privileged as the structual elements in biologically active molecules as well as ligands for transition metal catalysts.[24] Having developed a preparation method of bi- and tricyclic amidines, we finally explored concise reductive transformation of them to vicinal diamines.[25,26] It was found that reduction by aluminum hydride (AlH_3, prepared *in situ* from $LiAlH_4$ and $AlCl_3$)[27] proceeded smoothly to give monobenzyl-protected vicinal diamines, in which the benzyl group was attached exclusively on the tethered nitrogen (marked in red) along with formation of another secondary amine on the pyrrolidine ring (marked in blue) (Chart 2). By using this reductive transformation, monocyclic pyrrolidines **8a** and **8p**, azaspiro[4,5]decanes **8i** and **8r**,[28] dihydro-1*H*-indole **8k**, and octahydro-1*H*-indole (bicyclic pyrrolidines) **8q** with the vicinal diamine moiety could be efficiently constructed.

In summary, unprecedented chemical reactivity of *N*-alkenyl amidines under copper-catalyzed aerobic conditions have been exploited for the synthesis of bi- and tricyclic amidines. The reaction might be characterized as a concerted [3+2]-annulation via putative nitrene species, which might be generated under the mild oxidative reaction conditions with molecular oxygen. Moreover, concise reductive conversion of the bi- and tricyclic amidines into mono-benzyl-protected vicinal diamines has been demonstrated using aluminum hydride. Further investigation of the scope, detailed mechanisms, and synthetic applications of the present strategy to other azaheterocycles as well as development of asymmetric intermolecular diaminations is currently underway.

Chart 2. Reductive Transformation of Cyclic Amidines[a]



[a]Unless otherwise noted, the reactions were carried out by first treatment of $AlCl_3$ (1 equiv) in THF with $LiAlH_4$ (3 equiv) at 0 °C followed by addition of cyclic amidines **2** and stirring at room temperature. See Supporting Information for more details. [b]Isolated yields were recorded above. [c]The reaction were carried out using 3 equiv of $AlCl_3$ and 9 equiv of $LiAlH_4$ for 48 h.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures and characterization of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

shunsuke@ntu.edu.sg

Author Contributions

†These authors contributed equally to this paper.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by funding from Nanyang Technological University and the Singapore Ministry of Education. We thank Dr. Yongxin Li and Dr. Rakesh Ganguly (Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University) for assistance in X-ray crystallographic analysis.

■ REFERENCES

(1) For recent reviews, see: (a) Thomas, G. L.; Johannes, C. W. *Curr. Opin. Chem. Biol.* **2011**, *15*, 516. (b) Tohme, R.; Darwiche, N.; Gali-Muhtasib, H. *Molecules* **2011**, *16*, 9665. (c) Dandapani, S.; Marcaurelle, L. A. *Curr. Opin. Chem. Biol.* **2010**, *14*, 362. (d) Welsch, M. E.; Snyder, S. A.; Stockwell, B. R. *Curr. Opin. Chem. Biol.* **2010**, *14*, 347. (e) Carey, J. S.; Laffan, D.; Thomson, C.; Williams, M. T. *Org. Biomol. Chem.* **2006**, *4*, 2337.

(2) For recent reviews, see: (a) *Progress in Heterocyclic Chemistry*; Gribble, G. W., Joule, J. A., Eds.; Elsevier: Oxford, 2008; Vol. *20* and others in this series. (b) *Comprehensive Heterocyclic Chemistry III*; Katritzky, A. R., Ramsden, C. A., Scriven, E. F. V., Taylor, R. J. K., Eds.; Pergamon:

Oxford, 2008. (c) *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. A., Scriven, E. F. V., Taylor, R. J. K., Eds.; Pergamon: Oxford, 2008. (d) *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., McKillop, A., Eds.; Pergamon: Oxford, 1996 and references therein. (e) Eicher, T.; Hauptmann, S. *The Chemistry of Heterocycles*; Wiley-VCH: Weinheim, 2003.

(3) (a) Toh, K. K.; Wang, Y.-F.; Ng, E. P. J; Chiba, S. *J. Am. Chem. Soc.* **2011**, *133*, 13942. (b) Zhang, L.; Ang, G. Y.; Chiba, S. *Org. Lett.* **2010**, *12*, 3682. (c) Chiba, S.; Zhang, L.; Lee, J.-Y. *J. Am. Chem. Soc.* **2010**, *132*, 7266.

(4) For recent selected reports on copper-catalyzed aerobic oxidative transformation, see: (a) Zhang, C.; Xu, Z.; Zhang, L.; Jiao, N. *Angew. Chem., Int. Ed.* **2011**, *50*, 11088. (b) Wang, H.; Wang, Y.; Liang, D.; Liu, L.; Zhang, J.; Zhu, Q. *Angew. Chem., Int. Ed.* **2011**, *50*, 5678. (c) Wang, J.; Wang, J.; Zhu, Y.; Lu, P.; Wang, Y. *Chem. Commun.* **2011**, *47*, 3275. (d) King, A. E.; Huffman, L. M.; Casitas, A.; Costas, M.; Ribas, X.; Stahl, S. S. *J. Am. Chem. Soc.* **2010**, *132*, 12068. (e) Zhang, C.; Jiao, N. *J. Am. Chem. Soc.* **2010**, *132*, 28. (f) Ueda, S.; Nagasawa, H. *J. Org. Chem.* **2009**, *74*, 4272. (g) Hewgley, J. B.; Stahl, S. S.; Kozlowski, M. C. *J. Am. Chem. Soc.* **2008**, *130*, 12232. (h) Brasche, G.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 1932. (i) Chen, X.; Hao, X.-S.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2006**, *128*, 6790.

(5) Caron, S.; Wei, L.; Douville, J.; Ghosh, A. *J. Org. Chem.* **2010**, *75*, 945 and references therein.

(6) For reviews, see: (a) Cardona, F.; Goti, A. *Nature Chem.* **2009**, *1*, 269. (b) de Figueiredo, R. M. *Angew. Chem., Int. Ed.* **2009**, *48*, 1190.

(7) For selected recent examples of Pd(II) and Ni(II)-catalyzed diamination of alkenes, see: (a) Sibbald, P. A.; Michael, F. E. *Org. Lett.* **2009**, *11*, 1147. (b) Hövelmann, C. H.; Streuff, J.; Brelot, L.; Muñiz, K. *Chem. Commun.* **2008**, 2334. (c) Muñiz, K.; Streuff, J.; Chávez, P.; Hövelmann, C. H. *Chem. Asian J.* **2008**, *3*, 1248. (d) Muñiz, K.; Hövelmann, C. H.; Campos-Gómez, E.; Barluenga, J.; González, J. M.; Streuff, J.; Nieger, M. *Chem. Asian J.* **2008**, *3*, 776. (e) Muñiz, K.; Hövelmann, C. H.; Streuff, J. *J. Am. Chem. Soc.* **2008**, *130*, 763. (f) Muñiz, K. *J. Am. Chem. Soc.* **2007**, *129*, 14542. (g) Muñiz, K.; Streuff, J.; Hövelmann, C. H.; Núñez, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 7125. (h) Streuff, J.; Hövelmann, C. H.; Nieger, M.; Muñiz, K. *J. Am. Chem. Soc.* **2005**, *127*, 14586. (i) Bar, G. L. J.; Lloyd-Jones, G. C.; Booker-Milburn, K. I. *J. Am. Chem. Soc.* **2005**, *127*, 7308.

(8) For Au(I)-catalyzed diamination of alkenes and allenes, see: (a) Iglesias, A.; Muñiz, K. *Chem.—Eur. J.* **2009**, *15*, 10563. (b) Li, H.; Widenhoefer, R. A. *Org. Lett.* **2009**, *11*, 2671.

(9) For Cu(II)-mediated diamination of alkenes, see: (a) Sequeira, F. C.; Turnpenny, B. W.; Chemler, S. R. *Angew. Chem., Int. Ed.* **2010**, *49*, 6365. (b) Zabawa, T. P.; Chemler, S. R. *Org. Lett.* **2007**, *9*, 2035. (c) Zabawa, T. P.; Kasi, D.; Chemler, S. R. *J. Am. Chem. Soc.* **2005**, *127*, 11250.

(10) For recent selected examples of Cu(I)-catalyzed diamination of alkenes using di-*tert*-butyldiaziridinone and its derivatives, see: Zhao, B.; Peng, X.; Zhu, Y.; Ramirez, T. A.; Cornwall, R. G.; Shi, Y. *J. Am. Chem. Soc.* **2011**, *133*, 20890. (b) Zhao, B.; Peng, X.; Cui, S.; Shi, Y. *J. Am. Chem. Soc.* **2010**, *132*, 11009. (c) Wen, Y.; Zhao, B.; Shi, Y. *Org. Lett.* **2009**, *11*, 2365. (d) Zhao, B.; Du, H.; Shi, Y. *Org. Lett.* **2008**, *10*, 1087. (e) Zhao, B.; Yuan, W.; Du, H.; Shi, Y. *Org. Lett.* **2007**, *9*, 4943. (f) Yuan, W.; Du, H.; Zhao, B.; Shi, Y. *Org. Lett.* **2007**, *9*, 2589.

(11) For recent selected examples of Pd(0)-catalyzed diamination of alkenes using di-*tert*-butyldiaziridinone, see: (a) Zhao, B.; Du, H.; Cui, S.; Shi, Y. *J. Am. Chem. Soc.* **2010**, *132*, 3523. (b) Du, H.; Yuan, W.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2007**, *129*, 11688. (c) Du, H.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2007**, *129*, 762.

(12) For metal-catalyzed diamination of alkenes with $TsNCl_2$ or $TsNBr_2$, see: (a) Han, J.; Li, T.; Pan, Y.; Kattuboina, A.; Li, G. *Chem. Biol. Drug Des.* **2008**, *71*, 71. (b) Timmons, C.; Mcpherson, L. M.; Chen, D.; Wei, H.-X.; Li, G. *J. Peptide Res.* **2005**, *66*, 249. (c) Wei, H.-X.; Kim, S. H.; Li, G. *J. Org. Chem.* **2002**, *67*, 4777. (d) Wei, H.-X.; Siruta, S.; Li, G. *Tetrahedron Lett.* **2002**, *43*, 3809. (e) Li, G.; Wei, H.-X.; Kim, S. H.; Carducci, M. D. *Angew. Chem., Int. Ed.* **2001**, *40*, 4277.

(13) For recent examples of metal-free diamination of alkenes, see: (a) Röben, C.; Souto, J. A.; González, Y.; Lishchynskyi, A.; Muñiz, K. *Angew. Chem., Int. Ed.* **2011**, *50*, 9478. (b) Li, H.; Widenhoefer, R. A. *Tetrahedron* **2010**, *66*, 4827. (c) Booker-Milburn, K. I.; Guly, D. J.; Cox, B.; Procopiou, P. A. *Org. Lett.* **2003**, *5*, 3313.

(14) Liebeskind reported Cu(I)-catalyzed aerobic C−C bond-forming cross-coupling reactions of thiol esters and boronic acids, which did not proceed with Cu(II) complexes efficiently, see: (a) Liebeskind, L. S.; Yang, H.; Li, H. *Angew. Chem., Int. Ed.* **2009**, *48*, 1417. (b) Villalobos, J. M.; Srogl, J.; Liebeskind, L. S. *J. Am. Chem. Soc.* **2007**, *129*, 15734.

(15) These are contrasting results to our previous copper-mediated aerobic cyclopropanation from *N*-3-phenylallyl enamine carboxylates, where both (*E*)- and (*Z*)-isomers provided nearly 1:1 mixtures of diastereomers, see ref 3a.

(16) It was confirmed that the reaction of alkenyl primary amine, *N*-5,5-dimethyl-4-penten-1-amine under the present reaction conditions did not provide cyclic α-amino ketone **3o**. The reaction mechanism for the formation of α-amino ketone **3o** from amidine **1o** is under investigation.

(17) Zhang and Zhu reported copper-catalyzed aerobic reactions of *N*-allyl amidines, that afforded formylimidazoles via carbooxygenation of the alkene, see ref 4b.

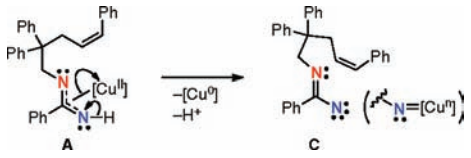
(18) For selected reports on copper-mediated aziridination of alkenes, see: (a) Lebel, H.; Parmentier, M. *Pure Appl. Chem.* **2010**, *82*, 1827. (b) Xu, Q.; Appella, D. H. *Org. Lett.* **2008**, *10*, 1497. (c) Lebel, H.; Lectard, S.; Parmentier, M. *Org. Lett.* **2007**, *9*, 4797. (d) Gillespie, K. M.; Crust, E. J.; Deeth, R. J.; Scott, P. *Chem. Commun.* **2001**, 785. (e) Brandt, P.; Södergren, M. J.; Andersson, P. G.; Norrby, P.-O. *J. Am. Chem. Soc.* **2000**, *122*, 8013. (f) Li, Z.; Quan, R. W.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5889.

(19) For a review on synthesis of sulfoxyimine using nitrene species, see: Okamura, H.; Bolm, C. *Chem. Lett.* **2004**, *33*, 482.

(20) Buchwald reported the reaction of *N*-phenyl amidine **6** under 15 mol % $Cu(OAc)_2$ and 5 equiv of AcOH in DMSO at 100 °C under an O_2 atmosphere, that provided benzimidazole via aromatic C-H amination, while our reaction afforded sulfoxyimine **7** exclusively. For Buchwald's benzimidazole synthesis, see ref 4h.

(21) Cu^{II} superoxo or peroxo species generated from CuI and molecular oxygen might play a vital role in the present process because the reaction with $CuBr_2$ did not give any desired product **2a** at all (see Table 1, entry 11). For recent reviews on copper−dioxygene systemes, see: (a) Rolff, M.; Tuczek, F. *Angew. Chem., Int. Ed.* **2008**, *47*, 2344. (b) Lewis, E. A.; Tolman, W. B. *Chem. Rev.* **2004**, *104*, 1047. (c) Gamez, P.; Aubel, P. G.; Driessen, W. L.; Reedijk, J. *Chem. Soc. Rev.* **2001**, *30*, 376. (d) Fontecave, M.; Pierre, J.-L. *Coord. Chem. Rev.* **1998**, *170*, 125.

(22) Alternatively, direct formation of nitrene **C** from copper diazaenolates **A** could be proposed with elimination of Cu^0 species and proton.



A C

(23) Addition of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) did not retard the present reactions. For example, the reactions of Table 1, entry 7, and eq 4 in the presence of 1.2 equiv of TEMPO provided **2a** and **7** in 85% (23 h) and 69% (32 h), respectively.

(24) For reviews, see: (a) Kizirian, J.-C. *Chem. Rev.* **2008**, *108*, 140. (b) Kotti, S. R. S. S.; Timmons, C.; Li, G. *Chem. Biol. Drug Des.* **2006**, *67*, 101. (c) Viso, A.; de la Pradilla, R. F.; García, A.; Flores, A. *Chem. Rev.* **2005**, *105*, 3167. (d) Lucet, D.; Gall, T. L.; Mioskowski, C. *Angew. Chem., Int. Ed.* **1998**, *37*, 2580.

(25) These cyclic amidines resisted to hydrolysis by acid and base. For reports on hydrolysis of cyclic amidine derivatives by hydrolysis for preparation of vicinal diamines, see: Jung, S.-H.; Kohn, H. *J. Am. Chem. Soc.* **1985**, *107*, 2931.

(26) Corey reported treatment of cyclic amidine with aluminium amalgam followed by aqueous acid provided vicinal diamine, see: Corey, E. J.; Kühnle, N. M. *Tetrahedron Lett.* **1997**, *38*, 8631.

(27) Brown, H. C.; Yoon, N. M. *J. Am. Chem. Soc.* **1966**, *88*, 1464.

(28) 1-Azaspiro[4,5]decan-6-amine derivatives such as **8r** have shown antinociceptive activity, see: Fujimoto, R. A.; Boxer, J.; Jackson, R. H.; Simke, J. P.; Neale, R. F.; Snowhill, E. W.; Barbas, B. J.; Williams, M.; Sills, M. A. *J. Med. Chem.* **1989**, *32*, 1259.