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An effective C–C double bond formation via Cu(I)-catalyzed dehydrogenation

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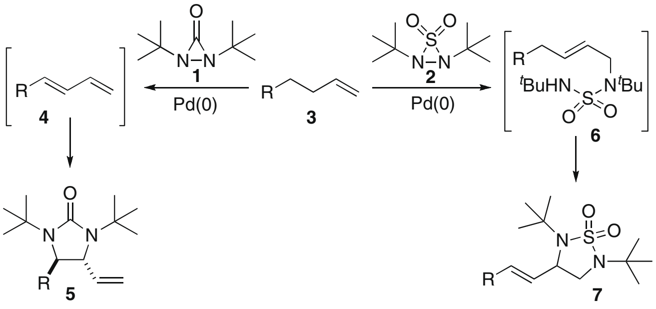
ABSTRACT

A dehydrogenation method using Cu(I) and either *N*,*N*-di-*tert*-butylthiadiaziridine 1,1-dioxide or *N*,*N*-di-*tert*-butyldiaziridinone is reported. The dehydrogenation allows a facile introduction of C–C double bond(s) into various carbocycles and heterocycles such as oxazolines and thiazolines.

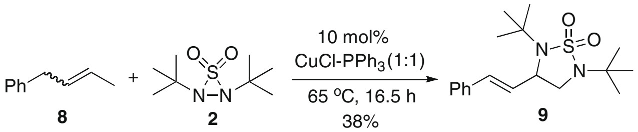
1. Introduction

Metal-mediated and metal-catalyzed diamination of olefins provides an attractive approach to vicinal diamines, and has been extensively investigated.[1] Various effective systems have been developed.[2–6] In our studies, we have shown that conjugated dienes and trienes can be effectively diaminated with complementary regioselectivity using Pd(0)[7] or Cu(I)[8] as catalyst and *N*,*N*-di-*tert*-butyldiaziridinone (**1**)[9,10] as nitrogen source. It has been shown that terminal olefins (**3**) can undergo dehydrogenative diamination with Pd(0)[11,12] as catalyst using *N*,*N*-di-*tert*-butyldiaziridinone (**1**) or *N*,*N*-di-*tert*-butylthiadiaziridine 1,1-dioxide (**2**)[13] as the nitrogen source (Scheme 1). These two dehydrogenative diaminations proceed via different mechanisms. In one mechanism, diene **4** is generated in situ and is subsequently diaminated regioselectively at the internal double bond to form **5**. In general, the diene intermediate could neither be isolated nor be detected. In the other mechanism, allyl sulfonamide **6** is initially formed and subsequently undergoes a Pd(II)-catalyzed cyclization to give **7**. The Cu(I)-catalyzed diamination is also effective toward activated terminal olefins such as styrenes, enynes, and enol ethers.[14–16] Herein, we wish to report that the system of CuCl with three-membered ring compound **1** or **2** also provides a valuable dehydrogenation method to introduce C–C double bonds.

In our efforts to expand the scope of our diamination methodologies, it was found that alkenes such as 1-phenyl-2-butene (**8**) undergo a dehydrogenative diamination to form **9** in 38% yield when treated with 10 mol% CuCl–PPh$_3$ and *N*,*N*-di-*tert*-butylthiadiaziridine 1,1-dioxide (**2**) (2.5 equiv) (Scheme 2). While an exact mechanism awaits further study, this dehydrogenative diamination is likely to proceed through a radical pathway as previously proposed (Scheme 3).[8,16–20] Reduction of the N–N bond of *N*,*N*-di-*tert*-butylthiadiaziridine 1,1-dioxide (**2**) by CuCl affords radical species **10**, which abstracts a hydrogen from alkene **8** to form radical **11** and copper complex **12**. Upon homolysis of the N–Cu bond of **12**, the resulting nitrogen radical abstracts another hydrogen from **11** to form diene **13** and di-*tert*-butyl sulfamide **14** and regenerate the



Scheme 1.



Scheme 2.

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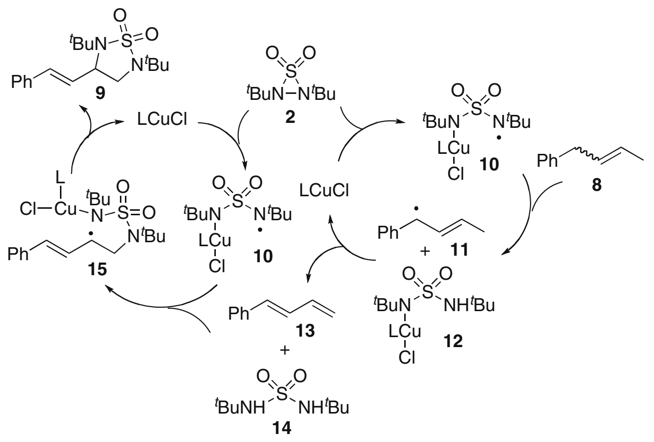


Scheme 3.

CuCl catalyst. Diene **13** is subsequently diaminated at the terminal double bond as previously described.[16] Efforts to isolate the diene by reducing the loading of **2** were unsuccessful, suggesting that the diene was being rapidly diaminated as it was generated. Our previous studies showed that reactive substrates for the Cu(I)-catalyzed diamination generally require the presence of a terminal double bond.[8,14,16] Therefore, it was envisioned that dehydrogenation products could be isolated if they have no terminal double bonds, thus providing a potentially useful method for the C–C double bond formation. Toward this end, various substrates were subjected to the dehydrogenation conditions.

Subjecting 1,4-diphenyl-2-butene to the reaction conditions (10 mol % CuCl–PPh$_3$, 2 equiv **2** at 65 °C without solvent) indeed led to the formation of 1,4-diphenylbutadiene as a major product, which was unreactive toward diamination under the reaction conditions. (*E*,*E*)-1,4-Diphenyl-butadiene was isolated in 50% yield (Table 1, entry 1, Method A). As shown in Table 1, dihydronaphthalenes, tetralin, and dihydrocoumarin were effective substrates for dehydrogenation (Table 1, entries 2–5). Further studies show that various heterocycles were efficiently dehydrogenated (Table 1, entries 6–10). The dehydrogenation provides a viable method to convert oxazolines and thiazolines to their respective oxazoles and thiazoles (Table 1, entries 8–10). *N*,*N*-Di-*tert*-butyldiaziridinone (**1**) can also be used for the dehydrogenation in most cases (Table 1, Method B). A representative example for the plausible catalytic cycle of the dehydrogenation using *N*,*N*-di-*tert*-butyldiaziridinone (**1**) is shown in Scheme 4.

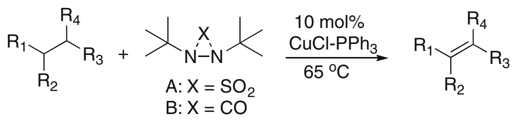
In summary, various substrates such as carbocycles and heterocycles can be effectively dehydrogenated under mild conditions using CuCl–PPh$_3$ and **1** or **2** to allow the introduction of C–C double bond(s).[21] This can be particularly useful in the generation of oxazoles and thiazoles from oxazolines and thiazolines, respectively.[22] As indicated in Scheme 3, this dehydrogenation involves a radical process, and as a result, effective substrates require one or more radical-stabilizing groups such as aromatic groups, alkenyl groups, and/or hetero atoms to facilitate radical generation.

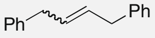
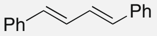
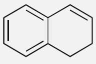
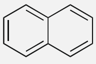
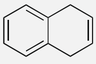
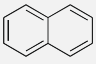
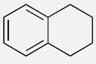
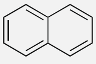
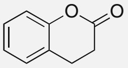
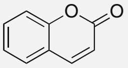
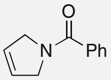
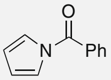
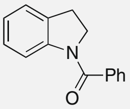
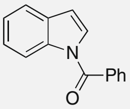
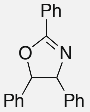
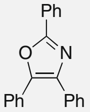
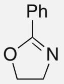
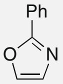
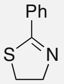
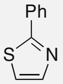
2. Experimental section

2.1. Dehydrogenative diamination of 1-phenyl-2-butene (8) (Scheme 2)

To an oven-dried 1.5-mL vial equipped with a magnetic stir bar were added CuCl (0.0015 g, 0.015 mmol) and PPh$_3$ (0.004 g, 0.015 mmol). The vial was sealed with a rubber septum, evacuated, and then filled with argon. This process was repeated three times.

Table 1
Cu(I)-catalyzed dehydrogenation

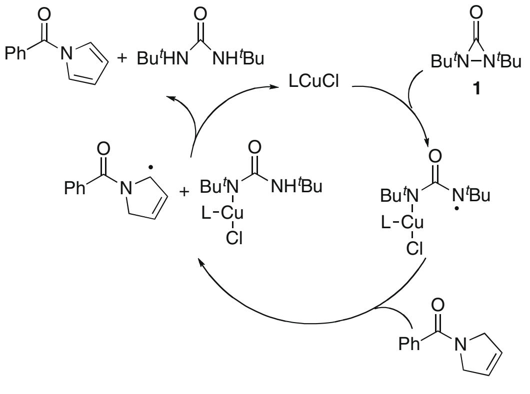


Entry	Substrate	Product	A[a] Yield[c] (%)	B[b] Yield[c] (%)
1	 Z/E = 8.4/1		50	
2			63	62
3			43	69
4			50	
5			60	48
6			59	70
7			70	65
8			78	95
9			73	68
10			62	80

[a] *Method A:* The reactions were carried out with substrate (0.3 mmol), *N*,*N*-di-*tert*-butylthiadiaziridine 1,1-dioxide (**2**) (0.6 mmol), and CuCl–PPh$_3$ (1:1) (0.03 mmol) at 65 °C under argon for 20 h unless otherwise stated. For entry 5, the reaction was run on 1/3 scale. For entry 9, the reaction was run on 1.5 scale. For entry 4, *N*,*N*-di-*tert*-butylthiadiaziridine 1,1-dioxide (**2**) (1.2 mmol) was employed.

[b] *Method B:* The reactions were carried out with substrate (1.0 mmol), *N*,*N*-di-*tert*-butyldiaziridinone (**1**) (2.0 mmol), and CuCl–PPh$_3$ (1:1) (0.1 mmol) in 0.26 mL CD$_2$Cl$_2$ at 65 °C under argon for 12 h unless otherwise stated. For entries 7 and 8, the reaction was run on 1/2 scale. For entries 5 and 10, the reaction was run in CDCl$_3$. For entry 9, the reaction was run on 4.48 mmol scale in 3 mL CHCl$_3$ for 14 h.

[c] Isolated yield based on substrate.



Scheme 4.

1-Phenyl-2-butene (**8**) (0.0198 g, 0.15 mmol) and dry C_6D_6 (0.060 mL) were then added. The vial was then immersed in an oil bath set at 65 °C. A solution of *N*,*N*-di-*tert*-butylthiadiaziridine 1,1-dioxide (**2**) (0.078 g, 0.375 mmol) in dry C_6D_6 (0.14 mL) was added to the reaction mixture dropwise with a syringe pump over 2.5 h. After the addition was complete, the reaction mixture was stirred for an additional 14 h. At this point, the crude reaction mixture was concentrated and then purified by flash column chromatography (SiO_2, hexanes, 50:1 hexanes/ether, 25:1 hexanes/ether, 10:1 hexanes/ether, v/v) to give the diamination product **9** as a white solid (0.019 g, 38%). mp 157–160 °C; IR (film): 1282, 1139 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.43–7.24 (m, 5H), 6.62–6.40 (m, 2H), 4.24–4.16 (m, 1H), 3.55 (dd, J = 8.6, 6.5 Hz, 1H), 3.09 (dd, J = 8.6, 3.6 Hz, 1H), 1.46 (s, 9H), 1.41 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.3, 131.7, 130.6, 128.9, 128.3, 126.8, 57.9, 56.5, 55.7, 47.5, 28.8, 27.6.

2.2. Representative dehydrogenation procedure using 2 (Table 1, entry 9, Method A)

To an oven-dried 1.5-mL vial equipped with a magnetic stir bar were added CuCl (0.0045 g, 0.045 mmol) and PPh_3 (0.012 g, 0.045 mmol). (Note: In cases where the substrate was a solid, it was added at this point.) The vial was sealed with a rubber septum, evacuated, and then filled with argon. This process was repeated three times. 2-Phenyl oxazoline (0.066 g, 0.45 mmol) was then added with a syringe. The reaction mixture was then stirred for 2 min, and *N*,*N*-di-*tert*-butylthiadiaziridine 1,1-dioxide (**2**) (0.186 g, 0.90 mmol) was added via a syringe. The vial was then immersed into an oil bath set at 65 °C and stirred for 20 h. The vial was cooled to room temperature and the residue was purified by flash column chromatography (SiO_2, hexanes, 50:1 hexanes/ether, 20:1 hexanes/ether, 12:1 hexanes/ether, v/v) to afford 2-phenyl oxazole as a colorless oil (0.0475 g, 73%). IR (film): 1587, 1557, 1483 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.08–8.02 (m, 2H), 7.72 (d, J = 0.9 Hz, 1H), 7.50–7.44 (m, 3H), 7.24 (d, J = 0.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 162.2, 138.8, 130.6, 129.0, 128.6, 127.7, 126.6.

2.3. Representative dehydrogenation procedure using 1 (Table 1, entry 9, Method B)

To an oven-dried 25 mL-round bottomed flask equipped with a magnetic stir bar were added CuCl (0.045 g, 0.45 mmol) and PPh_3 (0.12 g, 0.45 mmol) (Note: In cases where the substrate was a solid, it was added at this point). The flask was sealed with a rubber septum, evacuated, and then filled with argon. This process was repeated three times. $CHCl_3$ (3 mL) was then added with a syringe, followed by 2-phenyl oxazoline (0.66 g, 4.48 mmol). The reaction mixture was then immersed in an oil bath set at 65 °C, stirred for 2 min, and then *N*,*N*-di-*tert*-butyldiaziridinone (**1**) (1.63 g, 9.58 mmol) was added with a syringe pump over 10 h. After the addition was complete, the reaction mixture was stirred for an additional 4 h. At this point, the crude reaction mixture was concentrated and then purified by flash column chromatography (SiO_2, hexanes, 50:1 hexanes/ether, 25:1 hexanes/ether, 10:1 hexanes/ether, v/v) to afford 2-phenyl oxazole as a colorless oil (0.45 g, 68%).

Acknowledgments

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Supplementary data

Supplementary data (the preparation of *N*,*N*-di-*tert*-butylthiadiaziridine 1,1-dioxide (**2**), the characterization of dehydrogenation products, and the NMR spectra) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.01.114.

References and notes

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.
2. For examples of metal-mediated diaminations, see: Tl (a) Aranda, V. G.; Barluenga, J.; Aznar, F. *Synthesis* **1974**, 504; Os: (b) Chong, A. O.; Oshima, K.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, *99*, 3420; (c) Muñiz, K. *Eur. J. Org. Chem.* **2004**, 2243; Pd: (d) Bäckvall, J.-E. *Tetrahedron Lett.* **1978**, *19*, 163; Hg: (e) Barluenga, J.; Alonso-Cires, L.; Asensio, G. *Synthesis* **1979**, 962; Co: (f) Becker, P. N.; White, M. A.; Bergman, R. G. *J. Am. Chem. Soc.* **1980**, *102*, 5676; Mn: (g) Fristad, W. E.; Brandvold, T. A.; Peterson, J. R.; Thompson, S. R. *J. Org. Chem.* **1985**, *50*, 3647.
3. For 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 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.
5. 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.
6. For a recent example of 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.
7. For Pd(0)-catalyzed intermolecular diamination of conjugated dienes and trienes using *N*,*N*-di-*tert*-butyldiaziridinone, see: (a) Du, H.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2007**, *129*, 762; (b) Xu, L.; Du, H.; Shi, Y. *J. Org. Chem.* **2007**, *72*, 7038; (c) Du, H.; Yuan, W.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2007**, *129*, 11688; (d) Xu, L.; Shi, Y. *J. Org. Chem.* **2008**, *73*, 749; (e) Du, H.; Zhao, B.; Shi, Y. *Org. Synth.* **2009**, *86*, 315.
8. For Cu(I)-catalyzed intermolecular diamination of conjugated dienes and trienes using *N*,*N*-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.
9. Greene, F. D.; Stowell, J. C.; Bergmark, W. R. *J. Org. Chem.* **1969**, *34*, 2254.
10. 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.
11. For Pd(0)-catalyzed intermolecular allylic and homoallylic C-H diamination of terminal olefins using *N*,*N*-di-*tert*-butyldiaziridinone, see: (a) Du, H.; Yuan, W.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2007**, *129*, 7496; (b) Du, H.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2008**, *130*, 8590.
12. For Pd(0)-catalyzed dehydrogenative diamination of terminal olefins using *N*,*N*-di-*tert*-butylthiadiaziridine 1,1-dioxide, see: Wang, B.; Du, H.; Shi, Y. *Angew. Chem., Int. Ed.* **2008**, *47*, 8224.
13. For a leading reference on *N*,*N*-di-*tert*-butylthiadiaziridine 1,1-dioxide, see: Timberlake, J. W.; Alender, J.; Garner, A. W.; Hodges, M. L.; Özmeral, C.; Szilagyi, S.; Jacobus, J. O. *J. Org. Chem.* **1981**, *46*, 2082.
14. For Cu(I)-catalyzed intermolecular diamination of conjugated dienes, trienes, and activated terminal olefins using diaziridinimine, see Zhao, B.; Du, H.; Shi, Y. *Org. Lett.* **2008**, *10*, 1087.
15. For leading references on diaziridinimine, see: (a) Quast, H.; Schmitt, E. *Angew. Chem., Int. Ed.* **1969**, *8*, 448; (b) L'abbé, G.; Verbruggen, A.; Minami, T.; Toppet, S. *J. Org. Chem.* **1981**, *46*, 4478; (c) Mestres, R.; Palomo, C. *Synthesis* **1980**, 755.
16. For Cu(I)-catalyzed intermolecular diamination of activated terminal olefins using *N*,*N*-di-*tert*-butylthiadiaziridine 1,1-dioxide and *N*,*N*-di-*tert*-butyldiaziridinone, see: (a) Zhao, B.; Yuan, W.; Du, H.; Shi, Y. *Org. Lett.* **2007**, *9*, 4943; (b) Wen, Y.; Zhao, B.; Shi, Y. *Org. Lett.* **2009**, *11*, 2365.
17. For a leading review on metal-promoted radical reactions, see: Iqbal, J.; Bhatia, B.; Nayyar, N. K. *Chem. Rev.* **1994**, *94*, 519.
18. 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.
19. For leading references on nitrogen-centered radicals, see: (a) Stella, L.. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, 2001; Vol. 2, p 407; (b) Guin, J.; Mück-Lichtenfeld, C.; Grimme, S.; Studer, A. *J. Am. Chem. Soc.* **2007**, *129*, 4498.
20. 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.

21. For leading references on other dehydrogenation methods: (a) Fu, P. P.; Harvey, R. G. *Chem. Rev.* **1978**, *78*, 317; (b) Reetz, M. T.; Eibach, F. *Angew. Chem., Int. Ed.* **1978**, *17*, 278; NiO_2: (c) Evans, D. L.; Minster, D. K.; Jordis, U.; Hecht, S. M.; Mazzu, A. L., Jr.; Meyers, A. I. *J. Org. Chem.* **1979**, *44*, 497; Pd: (d) Shvo, Y.; Arisha, A. H. I. *J. Org. Chem.* **1998**, *63*, 5640; IBX: (e) Nicolau, K. C.; Zhong, Y.-L.; Baran, P. S. *J. Am. Chem. Soc.* **2000**, *122*, 7596; (f) Nicolau, K. C.; Montagnon, T.; Baran, P. S. *Angew. Chem., Int. Ed.* **2002**, *41*, 993.
22. For leading references on dehydrogenation of heterocyclic systems: DBU, $BrCCl_3$: (a) Williams, D. R.; Lowder, P. D.; Gu, Y-G.; Brooks, D. A. *Tetrahedron Lett.* **1997**, *38*, 331; (b) Phillips, A. J.; Uto, Y.; Wipf, P.; Reno, M. J.; Williams, D. R. *Org. Lett.* **2000**, *2*, 1165; NBS/$h\upsilon$: (c) Meyers, A. I.; Tavares, F. *Tetrahedron Lett.* **1994**, *35*, 2481.