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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 carbo- and heterocycles such as oxazolines and thiazolines.

Keywords

dehydrogenation; diamination; *N,N*-di-*tert*-butylthiadiaziridine 1,1-dioxide; *N,N*-di-*tert*-butyldiaziridinone

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 not be isolated nor 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, enol ethers, etc.^{14,15,16} 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-PPh₃ and *N,N*-di-*tert*-butylthiadiaziridine 1,1-dioxide (**2**)

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Supplementary Data

The preparation of *N,N*-di-*tert*-butylthiadiaziridine 1,1-dioxide (**2**), the characterization of dehydrogenation products, and the NMR spectra (25 pages).

(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 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-PPh₃, 2 equivalents **2** at 65 °C without solvent) indeed led to the formation of 1,4-diphenylbutadiene as major product, which was unreactive towards 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-PPh₃ 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, or hetero atoms to facilitate radical generation.

Experimental Section

Dehydrogenative diamination of 1-phenyl-2-butene (**8**)

(Scheme 2). To an oven-dried 1.5 mL vial equipped with a magnetic stir bar was added CuCl (0.0015 g, 0.015 mmol) and PPh₃ (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. 1-Phenyl-2-butene (**8**) (0.0198 g, 0.15 mmol) and dry C₆D₆ (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 C₆D₆ (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 was concentrated and then purified with flash column chromatography (SiO₂, 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, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 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.

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 was added CuCl (0.0045 g, 0.045 mmol) and PPh₃ (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, 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* syringe. The vial was then immersed into an oil bath set at 65 °C and stirred for 20 h. The vial was cooled to rt and the residue was purified by flash column chromatography (SiO₂, 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, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 162.2, 138.8, 130.6, 129.0, 128.6, 127.7, 126.6.

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 was added CuCl (0.045 g, 0.45 mmol) and PPh₃ (0.12 g, 0.45 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, then filled with argon. This process was repeated three times. CHCl₃ (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 was concentrated and then purified with flash column chromatography (SiO₂, 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%).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Scheme 1.

Scheme 2.

Scheme 3.

Table 1

Cu(I)-Catalyzed Dehydrogenation

Entry	Substrate
1	Z/E = 8.4/1
2
3

Entry	Substrate
4	
5

Entry

Substrate

6

Entry	Substrate
7

Entry

Substrate

8

Entry

Substrate

9

Entry	Substrate
10	<p>Chemical structure of 1-phenyl-2,5-dihydrothiazole, a five-membered ring containing sulfur (S) and nitrogen (N) atoms, with a phenyl group (Ph) attached to the carbon atom adjacent to the nitrogen.</p>

^a **Method A:** Reactions were carried out with substrate (0.3 mmol), *N,N*-di-*tert*-butylthiadiaziridine 1,1-dioxide (**2**) (0.6 mmol), and CuCl-PPh₃ (1:1) (0.03 mmol) at 65 °C under argon for 20 h unless otherwise stated. For entry 5, the reaction was carried out on 1/3 scale. For entry 9, 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:** Reactions were carried out with substrate (1.0 mmol), *N,N*-di-*tert*-butyldiaziridinone (**1**) (2.0 mmol), and CuCl-PPh₃ (1:1) (0.1 mmol) in 0.26 mL CD₂Cl₂ at 65 °C under argon for 12 h unless otherwise stated. For entries 7 and 8, reaction was run on 1/2 scale. Entries 5 and 10 were run in CDCl₃. Entry 9 was run on 4.48 mmol scale in 3 mL CHCl₃ for 14 h.

^c Isolated yield based on substrate.