

C–H Activation

A Silver-Catalyzed Intramolecular Amidation of Saturated C–H Bonds**

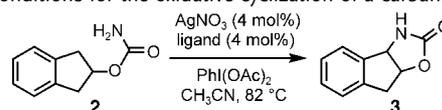
Yong Cui and Chuan He*

Oxidative insertion reactions into saturated C–H bonds to form amines and amine derivatives under transition-metal catalysis are attractive synthetic methodologies.^[1–14] Besides providing facile access to various organic structures, these reactions also offer opportunities to study the fundamental mechanism of C–H activation. It has been demonstrated that Rh- and Ru-based compounds mediate C–H amidation reactions particularly well.^[2,4,14–19] A dirhodium(II) tetracarboxylate system was shown to catalyze the intramolecular amidation of C–H bonds of carbamates and sulfamates with high regioselectivity and good to excellent diastereoselectivity.^[14–16] It is thought that a metal-bound nitrene species might be formed which then inserts oxidatively into saturated C–H bonds in these reactions. Despite extensive studies of metal-catalyzed amidations of C–H bonds, efficient and practical examples of such processes are limited. We report herein an efficient amidation reaction of saturated C–H bonds catalyzed by silver(I).

Silver complexes exhibit interesting activity, and silver-catalyzed organic transformations have attracted attention recently.^[20–23] In particular, several nonradical oxidative group-transfer reactions catalyzed by silver were discovered.^[24–27] We reported a disilver(I) compound (**1**, Scheme 1 a) that efficiently catalyzes the aziridination of olefins.^[26] Surprisingly, subsequent studies showed that only this disilver

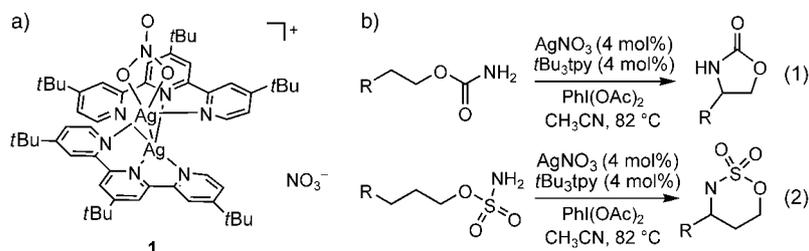
complex gave clean aziridine products in the silver-mediated reactions tested with a variety of different ligands. This led us to propose that the disilver structure may be important for the unique activity of this complex, and that the same compound may catalyze other reactions, such as the activation of saturated C–H bonds. After several experiments we found that **1** generated in situ catalyzed the efficient intramolecular amidation of saturated C–H bonds, as shown in Scheme 1 b. With the indanol-derived carbamate **2** as the substrate, AgNO₃ (4 mol %) with 4,4',4''-tri-*tert*-butyl-2,2':6',2''terpyridine (*t*Bu₃tpy, 4 mol %) as the catalyst, and PhI(OAc)₂ (2.0 equiv) as the oxidant, the cyclized product indanooxazolidin-2-one (**3**) was isolated from the reaction in acetonitrile in 83 % yield (Table 1 and entry 2 of Table 2). A color change

Table 1: Conditions for the oxidative cyclization of a carbamate.^[a]



Ligand	Yield [%]
pyridine	— ^[b]
4- <i>tert</i> -butylpyridine	— ^[b]
bipyridine	22
4,4'-di- <i>tert</i> -butylbipyridine	35
2,2':6',2''-terpyridine (tpy)	41
4,4',4''- <i>t</i> Bu ₃ tpy	89
4- <i>tert</i> -butylbis(oxazoline)	— ^[b]
4-phenylbis(oxazoline)pyridine	— ^[b]

[a] All reactions were conducted at 82 °C in CH₃CN with 2.0 equivalents of PhI(OAc)₂. The reported yields were determined by NMR spectroscopy by using mesitylene as an internal standard. [b] Product **3** was not observed.



Scheme 1. a) A unique disilver(I) catalyst [Ag₂(*t*Bu₃tpy)₂(NO₃)](NO₃) (**1**). b) Oxidative cyclization of carbamates [Eq. (1)] and sulfamates [Eq. (2)].

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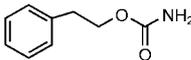
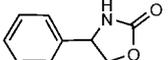
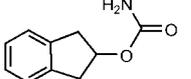
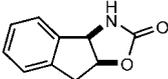
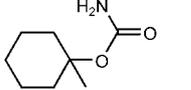
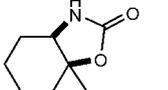
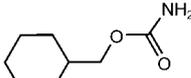
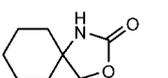
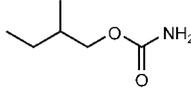
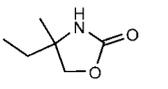
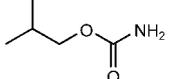
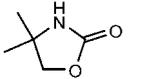
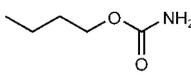
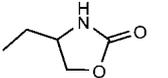
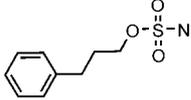
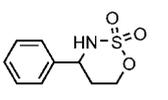
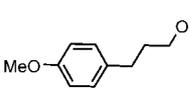
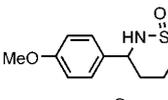
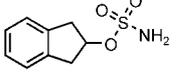
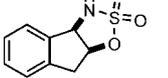
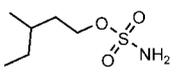
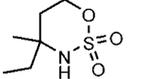
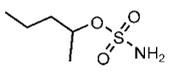
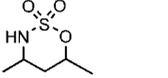
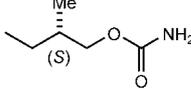
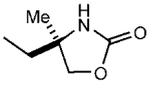
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from pale yellow to deep brown was observed during the course of the reaction, which may suggest the involvement of high-valent silver species.

Although different types of ligands were tested (Table 1), a clean reaction was observed and the product was obtained in high yield only when *t*Bu₃tpy was used, as had also been observed for the olefin aziridination reaction.^[26] Combinations of other ligands with silver(I) salts were either completely inactive or led to a low yield of the product. Sulfamate substrates were also tested, and very similar results were obtained. Although both silver and copper can catalyze olefin aziridination in the presence of *t*Bu₃tpy,^[26] copper, unlike silver, is not able to catalyze insertion into C–H bonds. It was reported that copper ions can mediate the amidation of saturated C–H bonds when an electron-deficient ligand is used.^[6] In this case a reactive electrophilic copper nitrene species may form. In the system described herein, it appears that the silver nitrene species are more oxidative than analogous copper species. The high oxidation potential often observed for silver complexes supports this notion.^[28]

A range of carbamates and sulfamates were tested, as shown in Table 2. Five-membered-ring and six-membered-ring insertion products were generated preferentially from

Table 2: Disilver(I)-catalyzed oxidative cyclization.^[a]

Entry	Substrate	Product	Yield [%]
1			81
2			83 ^[b]
3			85 ^[b]
4			85
5			76 (68) ^[c]
6			74 (70) ^[c]
7			58
8			87
9			78
10			65 (57) ^[b,c]
11			90
12			53 ^[c,d]
13			73

[a] All reactions were conducted at 82 °C in CH₃CN in the presence of AgNO₃, tBu₃tpy (4 mol%), and PhI(OAc)₂ (1.4 equiv for sulfamates and 2.0 equiv for carbamates). The yield of the isolated product is reported. [b] The *cis* product was obtained. [c] The reaction was carried out with 4-*tert*-butylpyridine (2 mol%); the yield determined by NMR spectroscopy for the reaction in the absence of 4-*tert*-butylpyridine is reported in parenthesis). [d] *syn/anti* = 2.2:1.0.

carbamates and sulfamates, respectively (in particular, see entries 7 and 12 of Table 2). Good to excellent yields comparable to or better than those found with other catalytic systems^[14–16] were observed with our silver catalyst. The addition of a stoichiometric amount of a base was not necessary. The addition of 2 mol% of 4-*tert*-butylpyridine led to better yields and cleaner products in several cases (Table 2,

entries 5, 6, 10, and 12). However, excess amounts of the monodentate ligand 4-*tert*-butylpyridine (10 equiv with respect to the silver catalyst) had a deleterious effect on the reaction. The exact role played by 4-*tert*-butylpyridine is not clear. Perhaps the binding of a monodentate ligand to one terminal side of disilver influences the activity on the other end. We also employed several amides as potential substrates. However, no product was observed under the various reaction conditions tested so far. Efforts to use catalyst **1** or other silver compounds to mediate insertion reactions of amides and other substrates are in progress.

A substrate derived from (*S*)-2-methyl-1-butanol was employed to probe the mechanism of this reaction and determine its stereoselectivity (Table 2, entry 13).^[14] A mixture of enantiomers would be expected as the product if a discrete radical species is the reactive intermediate. Retention of configuration should occur if a nitrene intermediate is produced and inserts directly into the C–H bond. The product of this reaction has the same optical rotation as an enantiomerically pure sample of the oxazolidinone^[14] shown in entry 13 of Table 2.^[29] The product obtained from the corresponding racemic starting material in a control experiment showed no optical rotation (Table 2, entry 5). This result indicates that the silver-catalyzed reaction is stereospecific. It also provides support for the involvement of a nitrene-type oxidant in the reaction, although the involvement of a short-lived radical as the reactive intermediate can not be excluded completely.

The disilver(I) catalyst **1** was probed by electrospray mass spectrometry (MS(ESI)) in acetonitrile. The molecular peak for the disilver(I) cation core [Ag₂(tBu₃tpy)₂NO₃]⁺ is clearly visible in the spectrum (Figure 1). Mononuclear silver(I)

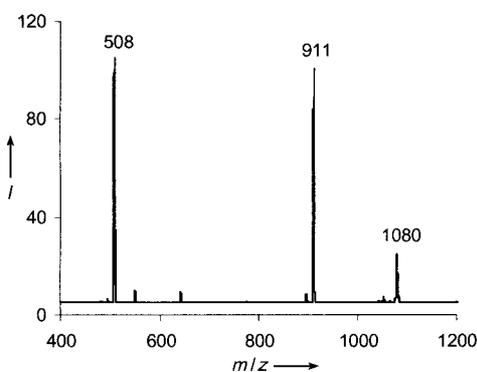


Figure 1. The MS(ESI) spectrum of complex **1** in CH₃CN. MS(ESI)⁺: calcd for [Ag₂(tBu₃tpy)₂NO₃]⁺: 1080, [Ag(tBu₃tpy)₂]⁺: 911, [Ag(tBu₃tpy)]⁺: 508.

species were also observed. These species perhaps result from the decomposition of **1** under the conditions of mass spectrometry; our previous NMR spectroscopic studies suggest that **1** remains a dimer in acetonitrile.^[26] The peak for the disilver cation core remained in the spectrum after compound **1** was treated with PhI=NTs (Ts = *p*-toluenesulfonyl) for 2 h at room temperature. A color change from pale yellow to brown occurred during the course of the reaction. A weak peak corresponding to a molecular weight of 1189 was

also observed, and assigned as the molecular peak of the disilver complex associated with the nitrenoid moiety =NTs. (The molecular weight of $\text{Ag}_2(\text{tBu}_3\text{tpy})_2$ with the nitrenoid =NTs is 1188.) When $\text{PhI}=\text{NSO}_2\text{Ph}$ was used, this peak shifted to 1175 as expected, which corresponds to the removal of a methyl group.^[30] There is no direct evidence to indicate that this species is a silver–nitrene intermediate. However, the results seem to suggest that the disilver structure can remain intact when in contact with the nitrenoid group. Evidently further mechanistic studies are required to fully elucidate the mechanism. We did not observe similar species upon the treatment of complex **1** with $\text{PhI}(\text{OAc})_2$ and carbamates. No color change occurred at room temperature after complex **1** was mixed with $\text{PhI}(\text{OAc})_2$ and a carbamate. In this case, the reaction intermediates may not be stable to analysis by mass spectrometry.

In summary, we have reported an efficient amidation reaction of saturated C–H bonds catalyzed by a unique disilver(i) complex. The results suggest the involvement of a silver–nitrene intermediate. The reaction is stereospecific and practical for constructing amine-containing organic molecules. Both the ligand tBu_3tpy and the silver salt are commercially available. With their inherent high oxidation potential, we believe silver ions are good oxidation catalysts that could exhibit other unique activities.

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- [30] The mass spectra are shown in the Supporting Information.