

Intermolecular Hydroamination of Allenes with *N*-Unsubstituted Carbamates Catalyzed by a Gold(I) *N*-Heterocyclic Carbene Complex

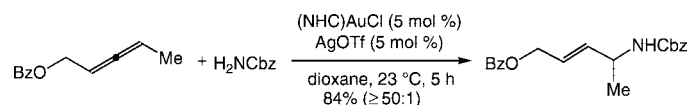
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ABSTRACT



Reaction of 2,3-pentadienyl benzoate with benzyl carbamate catalyzed by a 1:1 mixture of (NHC)AuCl and AgOTf in dioxane at 23 °C for 5 h led to isolation of (*E*)-4-(benzyloxycarbonylamino)-2-pentenyl benzoate in 84% yield as a single regio- and diastereomer. Gold(I)-catalyzed hydroamination was effective for a number of *N*-unsubstituted carbamates and a range of substituted allenenes.

Allylic amines are components of many naturally occurring and biologically active molecules and are versatile building blocks for the synthesis of complex nitrogen-containing molecules. As a result, considerable effort has been directed toward the development of general and selective methods for the synthesis of allylic amines.^{1,2} The transition-metal-catalyzed addition of the N–H bond of an amine or carboxamide derivative across the C=C bond of an allene represents an attractive and atom-economical approach to the synthesis of allylic amines.³ However, whereas general and efficient methods for the intramolecular hydroamination of allenenes have been developed,^{4,5} the intermolecular hydroamination of allenenes remains problematic, and no methods are available that effectively employ ammonia or ammonia

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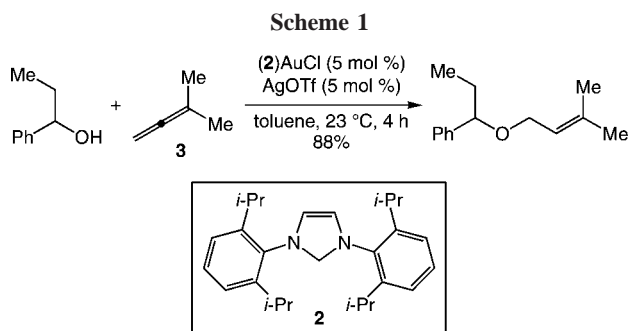
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equivalents as nucleophiles.^{6,7} Here we describe a general, regio- and stereoselective gold(I)-catalyzed protocol for the intermolecular hydroamination of allenes that employs *N*-unsubstituted carbamates as ammonia surrogates.

We have developed an effective protocol for the intramolecular hydroamination of *N*- γ - and δ -allenyl carbamates catalyzed by a mixture of the gold phosphine complex (1)AuCl [**1** = *P*-*t*-Bu₂-*o*-biphenyl]⁵ and AgOTf⁵ and a protocol for the intermolecular hydroalkoxylation of allenes with alcohols catalyzed by a mixture of the gold (NHC) complex (2)AuCl [**2** = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene] and AgOTf (Scheme 1).^{8,9} We therefore



targeted (1)AuCl and (2)AuCl as precatalysts for the intermolecular hydroamination of allenes with *N*-unsubstituted carbamates. In an initial experiment, reaction of 3-methyl-1,2-butadiene (**3**) and benzyl carbamate catalyzed by a 1:1 mixture of (1)AuCl and AgOTf in dioxane at 23 °C for 24 h led to 57% conversion to form the *N*-tertiary allylic carbamate **4a** as the exclusive product (Table 1, entry 1). Longer reaction time or employment of related gold phosphine catalysts led to no significant improvement in conversion (Table 1, entries 2–5). Conversely, reaction of **3** and benzyl carbamate with a catalytic mixture of (2)AuCl and AgOTf at 23 °C for 24 h led to 96% conversion to form

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Table 1. Gold(I)-Catalyzed Hydroamination of 3-Methyl-1,2-butadiene (**3**) with Benzyl Carbamate as a Function of Supporting Ligand

| entry | L | convn ^a (%) |
|-------|---|------------------------|
| 1 | 1 | 57 |
| 2 | PCy ₂ - <i>o</i> -biphenyl | 58 |
| 3 | PCy ₂ [2[2,5(OMe) ₂ C ₆ H ₃]C ₆ H ₄] | 47 |
| 4 | <i>Pt</i> Bu ₂ [2(2NMe ₂ C ₆ H ₃)C ₆ H ₄] | 0 |
| 5 | P(4MeOC ₆ H ₄) ₃ | 25 |
| 6 | 2 | 96 |

^a Conversion determined by GC analysis of the crude reaction mixture versus hexadecane internal standard.

4a as the exclusive product (Table 1, entry 6). Allylic carbamate **4a** was isolated in 93% yield from the corresponding preparative-scale reaction (Table 2, entry 1).

In addition to benzyl carbamate, 9-fluorenylmethyl carbamate and methyl carbamate reacted with **3** in the presence of (2)AuCl/AgOTf to form *N*-tertiary allylic carbamates **4b** and **4c**, respectively (Table 2, entries 2 and 3). Both the differentially 1,1-disubstituted allene **5** and trisubstituted allene **6** underwent intermolecular hydroamination to form the corresponding *N*-tertiary allylic carbamates (**7** and **8**) in modest yield as single regioisomers (Table 2, entries 4–6). Whereas hydroamination of the electron-deficient monosubstituted allene **9** led to exclusive formation of the *N*-primary (*E*)-allylic carbamate **10** (Table 2, entry 7), hydroamination of monoalkyl-substituted allene **11** formed a 1:1 mixture of *N*-secondary (**12a**) and *N*-primary (**12b**) allylic carbamates (Table 2, entry 8). 1,3-Disubstituted allenes **13–16** underwent hydroamination in good yield, with high *E*-selectivity, and in the case of differentially substituted allenes **14–16**, with exclusive attack of carbamate at the more electron-rich allene terminus (Table 2, entries 9–12). Reaction of enantiomerically enriched allene (*S*)-**15** (76% ee) with benzyl carbamate led to isolation of racemic **19** in 78% yield. This outcome is not surprising given the rapid (≤ 10 min) racemization of (*S*)-**15** under reaction conditions.⁸ Hydroamination of tetrasubstituted allene **21** formed *N*-tertiary allylic carbamate **22** in modest yield (Table 2, entry 13).

Noteworthy is the contrasting regioselectivity of the (2)AuCl/AgOTf-catalyzed intermolecular hydroamination and hydroalkoxylation of allenes. While both transformations favor addition of the nucleophile to the more electron-rich terminus of differentially 1,3-disubstituted allenes such as **14** and **15**, hydroalkoxylation displays much greater sensitivity to steric hindrance than does hydroamination, leading to preferential attack of alcohol at the less-substituted terminus of 1,1-disubstituted allenes such as **3** and trisubstituted allenes, as opposed to selective attack of carbamate at the more substituted allene terminus.¹⁰

Table 2. Intermolecular Hydroamination of Allenes with *N*-Unsubstituted Carbamates Catalyzed by a Mixture of (2)AuCl (5 mol %) and AgOTf (5 mol %) in Dioxane at 23 °C for 24 h.

| entry | allene | R of H ₂ NR | allylic carbamate | compd | yield (%) ^a |
|-----------------|--------|------------------------|-------------------|------------|------------------------|
| 1 | | Cbz | | 4a | 93 |
| 2 | | Fmoc | | 4b | 94 |
| 3 | | CO ₂ Me | | 4c | 87 |
| 4 | | Cbz | | 7a | 58 |
| 5 | | CO ₂ Me | | 7b | 58 |
| 6 | | Cbz | | 8 | 61 |
| 7 | | Cbz | | 10 | 75 |
| 8 | | Cbz | | 12a | 88 (1:1) |
| | | Cbz | | | |
| 9 | | Cbz | | 17 | 83 |
| 10 | | Cbz | | 18 | 84 |
| 11 ^b | | Cbz | | 19 | 80 |
| 12 | | Cbz | | 20 | 81 |
| 13 | | CO ₂ Me | | 22 | 61 |

^a Yields refer to isolated material of >95% purity. All *N*-allylic carbamates were formed in ≥98% regio- and diastereoisomeric purity unless noted otherwise. ^b Employment of enantiomerically enriched (*S*)-**15** (76% ee) formed racemic **19** in 78% yield.

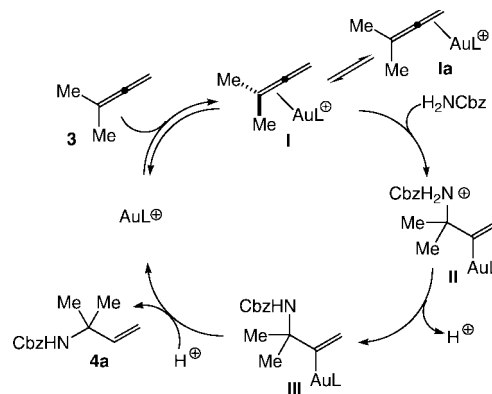
Stereochemical analysis of the gold(I)-catalyzed hydrofunctionalization of C–C multiple bonds has consistently supported outer-sphere pathways for C–X (X = N, O, C) bond formation.^{5,8,11} It therefore appears likely that the intermolecular hydroamination of allenenes catalyzed by (2)AuCl/AgOTf occurs via outersphere attack of the carbamate on

(10) It appears unlikely that these regiochemical differences can be attributed solely to the steric profile of the respective nucleophiles as reaction of **3** with 2-phenyl-1-ethanol catalyzed by (2)AuCl/AgOTf led to formation of a 4.4:1 mixture of 3-methyl-1-phenethoxy-2-butene and 1,1-dimethyl-1-phenethoxy-2-propene: Zhang, Z.; Widenhoefer, R. A. Unpublished results.

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gold π -allene complex **I** to initially form the cationic gold σ -alkenyl complex **II** that loses a proton to form **III** (Scheme 2). Protonolysis of the Au–C bond of **III** then releases the

Scheme 2



N-allylic carbamate with regeneration of the cationic Au(I) catalyst.¹² Available evidence regarding the gold(I)-catalyzed hydrofunctionalization of allenenes points to rapid and reversible formation of one or more gold π -allene complex followed by irreversible C–X bond formation.^{5,8,13} Therefore, the regioselectivity of gold(I)-catalyzed intermolecular hydroamination and hydroalkoxylation is presumably established via kinetic trapping of gold(I) π -allene complexes **I** and **Ia** with carbamate and alcohol, respectively, under Curtin–Hammett conditions (Scheme 2). However, the origins of this nucleophile-dependent selectivity remain unclear.¹⁰

In summary, we have developed a gold(I)-catalyzed protocol for the intermolecular hydroamination of allenenes. The protocol was effective for a number of *N*-unsubstituted carbamates and was effective for monosubstituted, 1,1- and 1,3-disubstituted, trisubstituted, and tetrasubstituted allenenes. We are currently working toward the development of enantioselective intermolecular allene hydroamination protocols and toward an understanding of the nucleophile-dependent regioselectivity of gold(I)-catalyzed allene hydrofunctionalization.

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Supporting Information Available: Experimental procedures and scans of NMR spectra for *N*-allylic carbamates. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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