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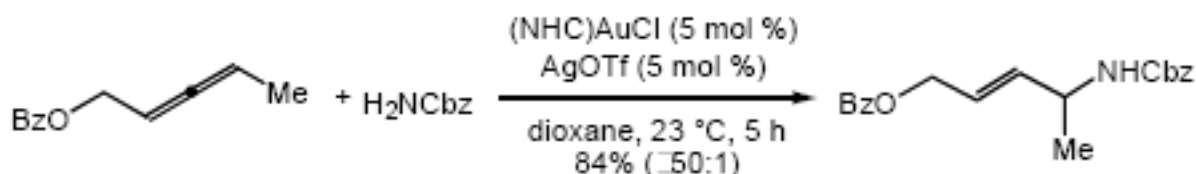
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Intermolecular Hydroamination of Allenes with *N*-Unsubstituted Carbamates Catalyzed by a Gold(I) *N*-Heterocyclic Carbene Complex

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Abstract



Reaction of 2,3-pentadienyl benzoate and benzyl carbamate with a catalytic 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 allenens.

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 allenens have been developed,^{4,5} the intermolecular hydroamination of allenens remains problematic and no methods are available that effectively employ ammonia or ammonia equivalents as nucleophiles.^{6,7} Here we describe a general, regio- and stereoselective gold(I)-catalyzed protocol for the intermolecular hydroamination of allenens 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 = *Pt*-Bu₂*o*-biphenyl]⁵ and AgOTf and a protocol for the intermolecular hydroalkoxylation of allenens 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 allenens 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

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

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 **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 (**7-8**) 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 mono-alkyl-substituted allene **11** formed a 1:1 mixture of *N*-primary (**12a**) and *N*-secondary (**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 hinderance 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

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 allenes catalyzed by (2)AuCl/AgOTf occurs via outer-sphere attack of the carbamate on 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 *N*-allylic carbamate with regeneration of the cationic Au(I) catalyst.¹² Available evidence regarding the gold(I)-catalyzed hydrofunctionalization of allenes 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 allenes. 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 allenes. 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.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

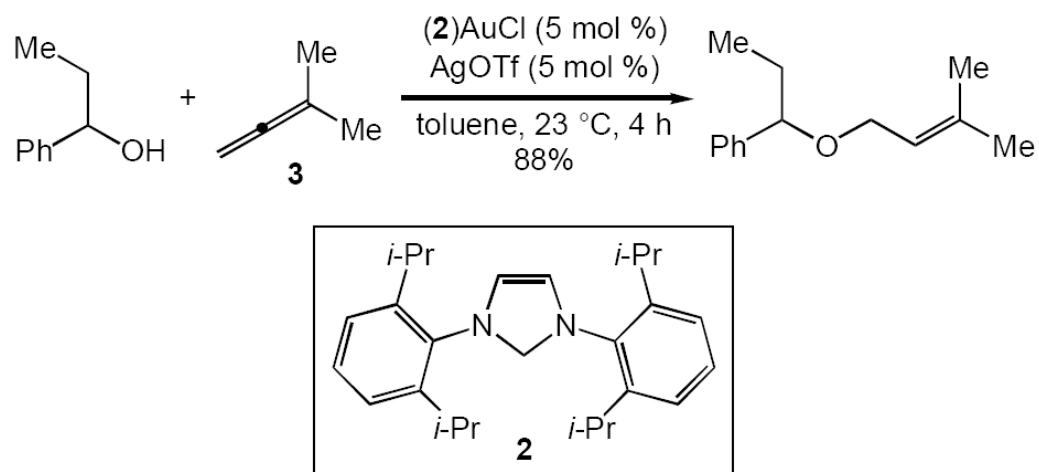
Acknowledgments

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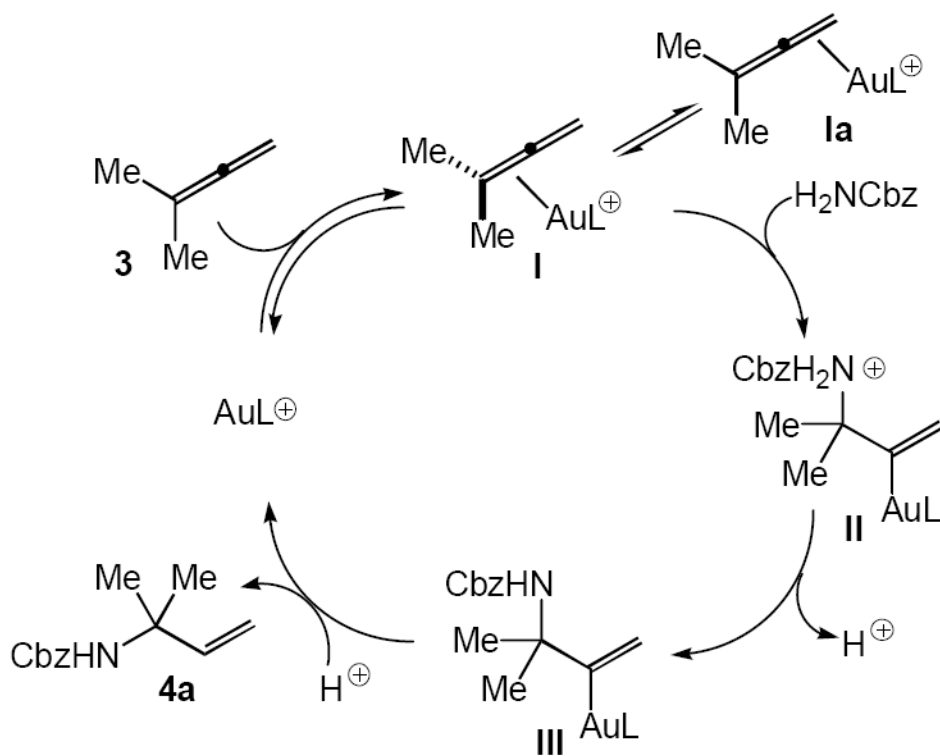
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10. It appears unlikely that these regiochemical differences can be attributed solely to the steric profile of the respective nucleophiles as reaction of **3** with 2-phenyl-1-ethanol catalyzed by (2)AuCl/AgOTf led to formation of a 4.4:1 mixture of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



Scheme 2.

Table 1


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

Reaction scheme: 3-methyl-1,2-butadiene (**3**) + H₂N-Cbz $\xrightarrow[\text{24 h}]{\text{LAuCl (5 mol %), AgOTf (5 mol %), dioxane, 23 °C}}$ 3-methyl-1,2-butanimine (**4a**)

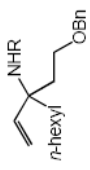
entry	L	convn (%) ^a
1	1	57
2	PCy ₂ -o-biphenyl	58
3	PCy ₂ {2-[2,5-(OMe) ₂ C ₆ H ₃]C ₆ H ₄ }	47
4	Pr-Bu ₂ [2-(2-NMe ₂ C ₆ H ₃)C ₆ H ₄]	0
5	P(4-MeOC ₆ H ₄) ₃	25
6	2	96

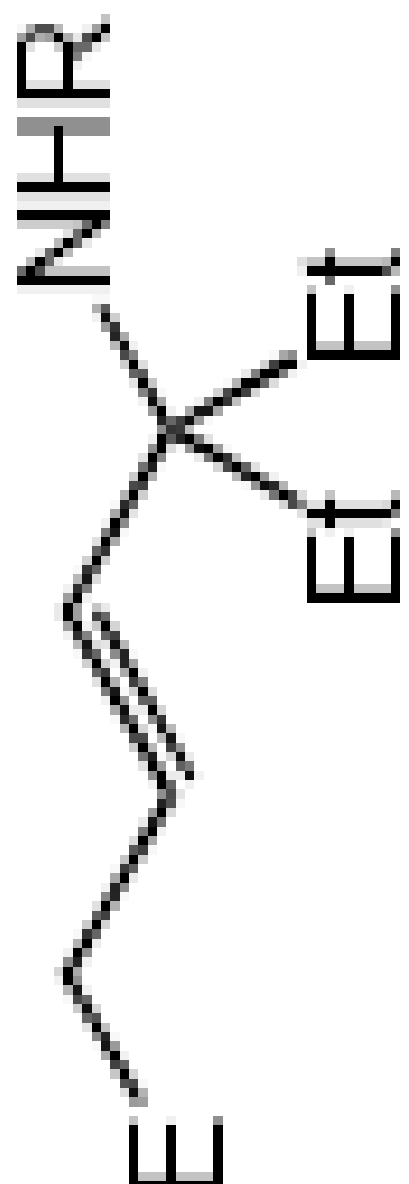

^a Conversion determined by GC analysis of the crude reaction mixture versus hexadecane internal standard.

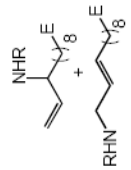
y a Mixture of (2)AuCl (5 mol %) and AgOTf

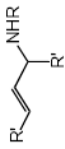
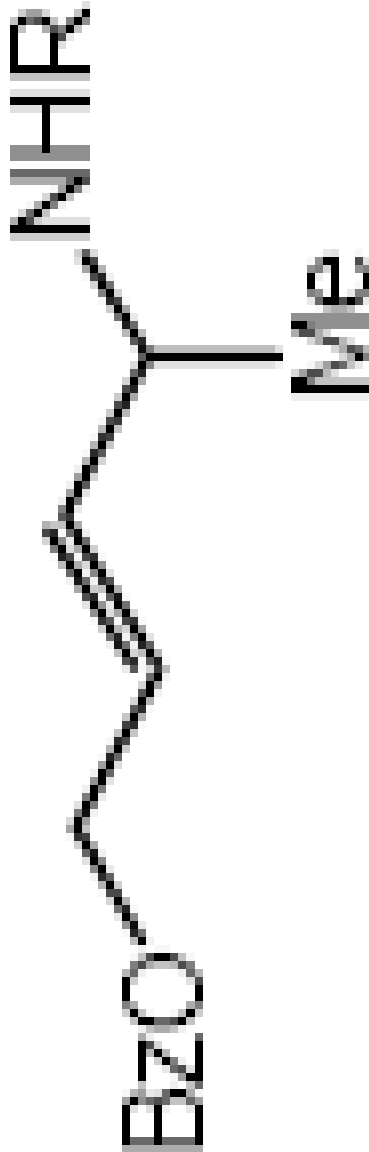
R of H ₂ NR	allylic carbamate	compd	yield (%) ^a
Cbz		4a	93
Fmoc		4b	94
CO ₂ Me		4c	87

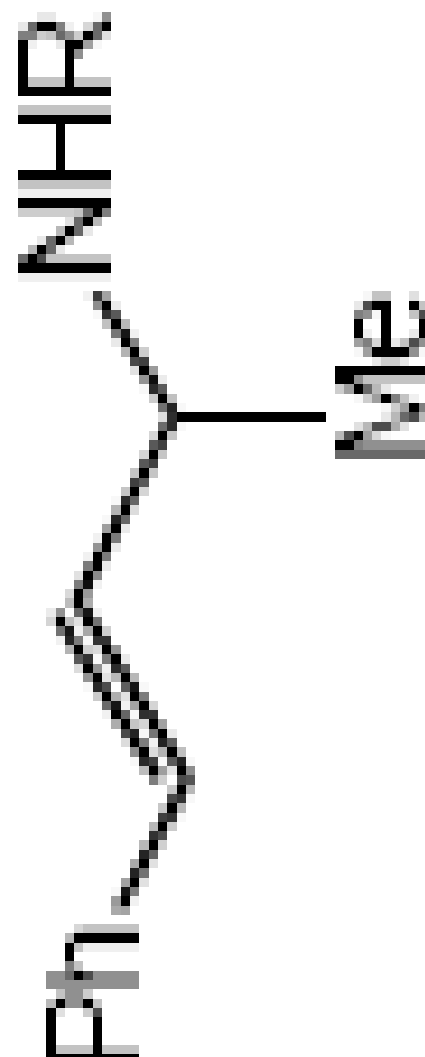
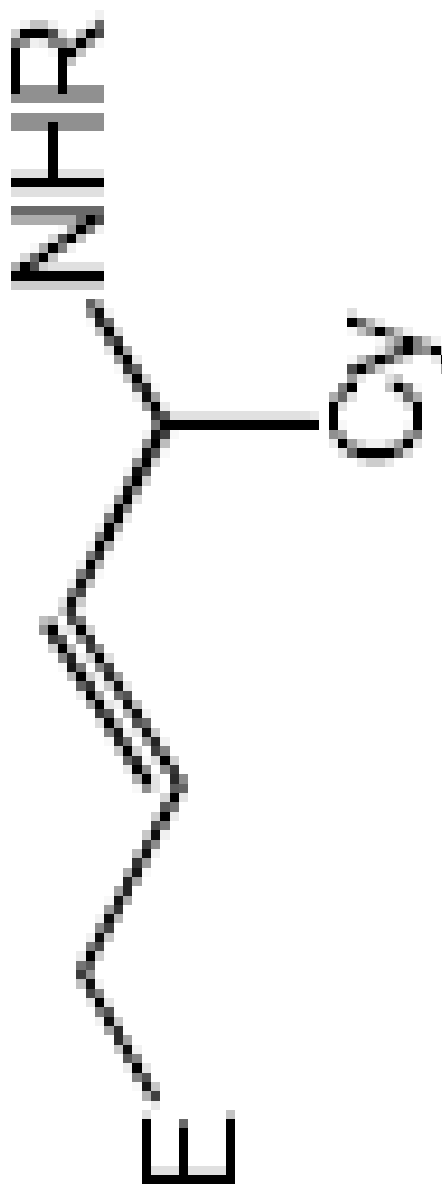


R of H ₂ NR	allylic carbamate	compd	yield (%) ^d
Cbz		7a	58
CO ₂ Me		7b	58

R of H ₂ NR	allylic carbamate	compd	yield (%) ^d
Cbz		8	61
Cbz		10	75

R of H ₂ NR	allylic carbamate	compd	yield (%) ^d
Cbz		12a } } 12b	88(1:1)

R of H ₂ NR	allylic carbamate	compd	yield (%) ^d
Cbz		17	83
Cbz		18	84

R of H ₂ NR	allylic carbamate	compd	yield (%) ^d
Cbz		19	80
Cbz		20	81

R of H ₂ NR	allylic carbamate	compd	yield (%) ^d
CO ₂ Me	<chem>CN(C)C(C)C(=O)OC</chem>	22	61

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noted otherwise.