Although platinum-catalyzed intramolecular hydroamination displayed good functional-group compatibility, the procedure required reaction temperatures of 120 °C and displayed a limited substrate scope.^[2] Preliminary mechanistic experiments pointed to protonolysis of heterobicyclic amine complex **3** with an amine hydrochloride as the turnoverlimiting step in the Pt-catalyzed conversion of **1** into **2** $[Eq. (2)].^{[2]}$ On the basis of this insight, we reasoned that

$$\begin{array}{ccc}
\text{Cl.} & \text{PPPn}_{3} \\
\text{Bn.} & \text{Pt} \\
\text{HNR}_{3}\text{Cl.} \\
\text{dioxane, 120 °C} \\
\text{Ph} \\
\text{Ph} \\
\text{3} \\
\begin{array}{c}
\text{Bn.} \\
\text{HNR}_{3}\text{Cl.} \\
\text{Ph} \\
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\begin{array}{c}
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employment of a less basic amine derivative might lead to a more efficient and more general hydroamination protocol. Indeed, herein we report a mild and effective Au-catalyzed protocol for the intramolecular hydroamination of alkenyl carbamates to form protected nitrogen heterocycles.

Although tosylamides have been employed to good effect in the catalytic amination of C–C multiple bonds,^[3] the strongly reducing conditions required for subsequent deprotection compromises the utility of these transformations.^[4,5] For this reason, we targeted benzyl carbamates, which undergo deprotection under mild conditions,^[4] as nucleophiles for the catalytic intramolecular hydroamination of unactivated olefins. Selective hydroamination of alkenyl carbamates has previously been achieved only through employment of a stoichiometric amount of Hg^{II} followed by reduction.^[6,7] Unfortunately, attempted hydroamination of carbamate **4** employing the catalyst system optimized for the hydroamination of **1** required 120°C and formed protected pyrrolidine **5** in only 50% yield (determined by ¹H NMR spectroscopic analysis) [Eq. (1)].^[8]

A number of recent reports have documented the utility of cationic Au^I-phosphine complexes as catalysts for the addition of carbon^[9,10] and oxygen^[11-13] nucleophiles to alkenes and alkynes.^[14,15] For this reason, we considered that cationic Au^I-phosphine complexes might also catalyze the addition of nitrogen nucleophiles to unactivated olefins. An initial experiment was encouraging and treatment of 4 with a catalytic 1:1 mixture of [Au(PPh₃)Cl] and AgOTf in toluene at 100°C for 24 h led to 5 in 59% yield (¹H NMR; Table 1, entry 1). Subsequent experimentation led to identification of a significantly more active catalyst system for the conversion of 4 into 5 that employed a catalytic 1:1 mixture of [Au{P- $(tBu)_2(o-biphenyl)$]Cl (6) and AgOTf in dioxane at 100°C (Table 1, entries 2-8).^[16] This catalyst system was also effective at lower temperatures and, in a preparative-scale reaction, treatment of 4 with a catalytic 1:1 mixture of 6 and AgOTf (5 mol %) in dioxane at 60 °C for 18 h led to 5 in 97 % yield (Table 2, entry 1). Comparison of $P(tBu)_2(o-biphenyl)$ and PMe₂Ph as ligands for the Au^I-catalyzed hydroamination of 4 suggests that steric rather than electronic factors are responsible for the high efficiency of the former ligand (Table 1, entries 7 and 8).

Neither the rate nor the yield of the Au^I-catalyzed conversion of 4 into 5 was affected by the presence of water (1 equiv) (Table 2, entry 2). Gold-catalyzed intramolecular

Hydroamination (2)

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Gold(I)-Catalyzed Intramolecular Hydroamination of Alkenyl Carbamates**

Xiaoqing Han and Ross A. Widenhoefer*

Intramolecular hydroamination of unactivated olefins has received considerable attention as an attractive and potentially expedient route to the synthesis of functionalized nitrogen heterocycles.^[1] However, despite this prolonged focus, a general and efficient procedure has not been realized.^[1] In response to this limitation, we recently reported a platinum-catalyzed procedure for the intramolecular hydroamination of unactivated olefins with secondary alkyl amines.^[2] As an example, reaction of *N*-benzyl-4-pentenylamine (**1**) with a catalytic 1:2 mixture of $[{PtCl_2(H_2C=CH_2)}_2]$ and PPh₃ at 120 °C for 16 h led to isolation of pyrrolidine **2** in 75 % yield (88 % by GC) [Eq. (1)].



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 - Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.



Communications

Table 1: Effect of phosphine and solvent on the Aul-catalyzed hydroamination of 4.

	Ph Ph 4 [Au(PR ₃)Cl] (5 AgOTf (5 m 100 °C, 2	5 mol%) nol%) 24 h Ph 5	Me
Entry	PR ₃	Solvent	Yield [%] ^[a]
1	PPh ₃	toluene	59
2	PPh₃	CH₃CN	49
3	PPh ₃	$C_2H_4Cl_2$	33
4	PPh ₃	dioxane	75
5	$P(4-C_6H_4OMe)_3$	dioxane	70
6	$P(4-C_6H_4CF_3)_3$	dioxane	23
7	PMe ₂ Ph	dioxane	7
8	P(tBu)₂(o-biphenyl)	dioxane	98

[a] Yield determined by ¹H NMR spectroscopic analysis of the crude reaction mixture. Tf=trifluoromethanesulfonyl.

> hydroamination was compatible with a range of labile carbamate groups including Boc, Moz, and Fmoc (Table 2, entries 3-5). The protocol tolerates substitution at C1, C2, C3, or C4 of the 4-pentenyl chain, often with encouraging levels of diastereoselectivity (Table 2, entries 6-11). Gold-catalyzed intramolecular hydroamination of alkenyl carbamates is also effective for cyclization of unsubstituted 4-pentenyl derivatives (Table 2, entry 12). Furthermore, Au^I-catalyzed hydroamination of alkenyl carbamates can be applied to the synthesis of aromatic and aliphatic heterobicyclic compounds and to the synthesis of piperidine derivatives (Table 2, entries 13-15). Notably, unsubstituted, C1monosubstituted, and monocyclic 4-pentenylbenzylamines failed to undergo Pt-catalyzed hydroamination; C2-monosubstituted 4-pentenylbenzylamines and 5hexenylbenzylamines undergo Pt-catalyzed cyclization in modest yield.

Information regarding the mechanisms of the Au^Icatalyzed addition of nucleophiles to C-C multiple bonds is limited. Teles et al. proposed an inner-sphere mechanism for the Au^I-catalyzed intermolecular addition of alcohols to alkynes on the basis of ab initio calculations.^[11] Conversely, stereochemical analysis of the Au^I-catalyzed intramolecular addition of alcohols and activated methylene compounds to alkynes were in accord with outer-sphere attack of the nucleophile on a Au^I-complexed alkyne.^[9,12] On the basis of these latter precedents, we favor a mechanism for the Au^I-catalyzed hydroamination of 4 involving outer-sphere attack of the carbamate nitrogen atom on the Au-complexed olefin of I coupled with loss of HCl to form the neutral alkyl-gold complex II (Scheme 1). Protonolysis of the Au-C bond of II would then release pyrrolidine 5 and regenerate the cationic monophosphine gold catalyst.

In summary, we have developed an effective Au^Icatalyzed protocol for the intramolecular hydroamination of alkenyl carbamates to form protected nitrogen heterocycles. This protocol allows the intramolecular hydroamination of unactivated olefins under milder conditions and with broader substrate scope than was previously realized with latetransition-metal catalyst systems.[17]

Table 2:	Hydroamination	of alkenyl	carbamates	catalyzed	by a 1:1	mixture of
Au[P(tBı	u)2(o-biphenyl)]Cl	(6) and A	gOTf (5 mol	%) in dio	kane.	

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Entry	Alkene	Heterocycle	Temp [°C]	Time [h]	Yield [%] ^[a]
	Ph Ph	Ph Ph			
1 2 3 4 5	R = Cbz R = Cbz R = Boc R = Moz R = Fmoc		60 60 60 60 60	18 18 20 16 24	97 96 ^(b) 96 95 93
	NHCbz R	Cbz N Me			
6 7	R = H R = Me		60 80	23 40	96 88
	NHCbz OR	Cbz N Me OR			
8 9	R = H R = Ac		60 60	22 18	91 (3.6:1) 63 (3.0:1)
10	Ar	Ar Cbz Me	100	39	93 (3.5:1)
	$Ar = 4-C_6$	H₄OMe			
11	Me_NHCbz	Me Cbz Me	100	55	91 (1.5:1) ^[c]
12	NHCbz	Cbz N Me	100	68	87 ^[c]
13	NHCbz	Cbz N Me	100	47	59 ^[c]
14	NHCbz	Cbz Me	100	30	95 (2.5:1)
15	NHCbz	NCbz Me	100	26	84

[a] Isolated material of \geq 95% purity. [b] Reaction run in the presence of H₂O (1 equiv). [c] Reaction run with 10 mol% of 6. Cbz = benzyloxycarbonyl, Boc = *tert*-butoxycarbonyl, Moz = *p*-methoxybenzyloxycarbonyl, Fmoc = 9-fluorenylmethyloxycarbonyl.

Experimental Section

5: A mixture of 4 (0.17 g, 0.45 mmol), 6 (12 mg, 0.022 mmol), and AgOTf (6 mg, 0.02 mmol) in dioxane (0.45 mL) was degassed by means of one freeze-pump-thaw cycle, pressurized with nitrogen, and stirred at 60°C for 18 h. The crude reaction mixture was purified by



 $\textit{Scheme 1.}\ Proposed mechanism for the Aul-catalyzed conversion of 4 into 5.$

chromatography (hexanes/EtOAc 20:1) to give 5 (160 mg, 97 %) as a viscous, colorless oil.

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