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Highly Active Au(I) Catalyst for the Intramolecular *exo*-Hydrofunctionalization of Allenes with Carbon, Nitrogen, and Oxygen Nucleophiles

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Abstract: Reaction of benzyl (2,2-diphenyl-4,5-hexadienyl)carbamate (**4**) with a catalytic 1:1 mixture of Au[P(*t*-Bu)$_2$(*o*-biphenyl)]Cl (**2**) and AgOTf (5 mol %) in dioxane at 25 °C for 45 min led to isolation of benzyl 4,4-diphenyl-2-vinylpyrrolidine-1-carboxylate (**5**) in 95% yield. The Au(I)-catalyzed intramolecular hydroamination of *N*-allenyl carbamates tolerated substitution at the alkyl and allenyl carbon atoms and was effective for the formation of piperidine derivatives. γ-Hydroxy and δ-hydroxy allenes also underwent Au-catalyzed intramolecular hydroalkoxylation within minutes at room temperature to form the corresponding oxygen heterocycles in good yield with high *exo*-selectivity. 2-Allenyl indoles underwent Au-catalyzed intramolecular hydroarylation within minutes at room temperature to form 4-vinyl tetrahydrocarbazoles in good yield. Au-catalyzed cyclization of *N*-allenyl carbamates, allenyl alcohols, and 2-allenyl indoles that possessed an axially chiral allenyl moiety occurred with transfer of chirality from the allenyl moiety to the newly formed stereogenic tetrahedral carbon atom.

Introduction

Nitrogen[1] and oxygen[2] heterocycles are common structural components of a wide range of naturally occurring and biologically active molecules. Therefore, the development of new and efficient methods for the synthesis of heterocyclic compounds is of central importance in organic synthesis.[3] An attractive and atom-economical route to the synthesis of functionalized heterocycles is via the transition metal-catalyzed addition of the X−H bond of a carbon, nitrogen, or oxygen nucleophile across the C=C bond of a pendant alkene (hydrofunctionalization). Unfortunately, due to a number of factors including the high thermodynamic stability of most X−H σ-bonds and the inherent nucleophilicity of simple alkenes, effective transition metal-catalyzed protocols for the intramolecular hydrofunctionalization of unactivated alkenes with C-,[4,5] N-,[6−9] or O-nucleophiles[10,11] remain scarce.

The C=C π-bond of an allene is ∼10 kcal/mol less stable than is the C=C π-bond of a simple alkene.[12] For this reason, the transition metal-catalyzed hydrofunctionalization of allenes with carbon and heteroatom nucleophiles has been investigated

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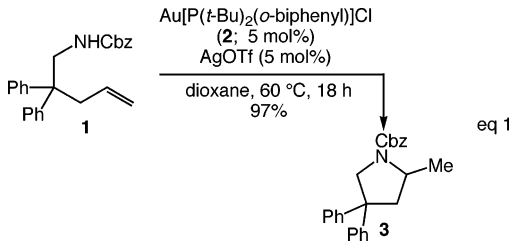
as a means to circumvent some of the difficulties associated with catalytic alkene hydrofunctionalization.[13] However, whereas Ag(I), Au(III), and Cu(I) complexes catalyze the *endo*-hydrofunctionalization of allenes with N-,[14] O-,[15,16] and S-[17] nucleophiles, the *exo*-hydrofunctionalization of allenes with carbon and heteroatom nucleophiles remains problematic. Although the Ag(I)-catalyzed *exo*-hydroamination[18] and *exo*-hydroalkoxylation[19] of allenes and the Pd(II)-catalyzed *exo*-hydroamination[20,21] and *exo*-hydroalkylation[21,22] of allenes have been reported, these protocols suffer from a number of shortcomings including limited substrate scope, low reactivity, and/or modest turnover numbers.[23,24] Similarly, d^0-lanthanide complexes are active catalysts for the *exo*-hydroamination of γ- and δ-amino allenes,[25,26] but the synthetic utility of these protocols is compromised by the poor functional group compatibility and excessive air- and moisture-sensitivity of the oxophilic catalyst.

As part of a program directed toward the development of new catalytic methods for the transition metal-catalyzed hydrofunctionalization of unactivated alkenes with carbon,[5] nitrogen,[8,9] and oxygen[11] nucleophiles, we recently reported the gold-catalyzed intramolecular *exo*-hydroamination of *N*-alkenyl carbamates.[9,27−33] As an example of this protocol, treatment of the *N*-5-hexenyl carbamate **1** with a catalytic 1:1 mixture of Au[P(*t*-Bu)$_2$(*o*-biphenyl)]Cl (**2**) and AgOTf (5 mol %) in dioxane at 60 °C for 18 h led to isolation of protected pyrrolidine **3** in 97% yield (eq 1). Employment of the sterically hindered *o*-biphenyl ligand was crucial for high activity; cyclization of **1** catalyzed by a 1:1 mixture of Au(PPh$_3$)Cl and AgOTf (5 mol %) reached only 75% conversion after 24 h at 100 °C. The high activity of the **2**/AgOTf catalyst system with respect to the *exo*-hydroamination of *N*-alkenyl carbamates suggested that **2**/AgOTf might also catalyze the *exo*-hydroamination of *N*-allenyl carbamates under mild conditions. Indeed, here we report that a 1:1 mixture of **2** and AgX (X = OTf, OTs) is an exceptionally active catalyst system for the *exo*-hydroamination of *N*-allenyl carbamates and also for the *exo*-hydroalkoxylation of allenyl alcohols and the *exo*-hydroarylation of 2-allenyl indoles.



Results and Discussion

***exo*-Hydroamination of *N*-Allenyl Carbamates.** Mixtures of **2** and AgOTf in dioxane catalyzed the *exo*-hydroamination of 4,5-hexadienyl carbamates within minutes at room temperature. For example, reaction of *N*-allenyl carbamate **4** with a

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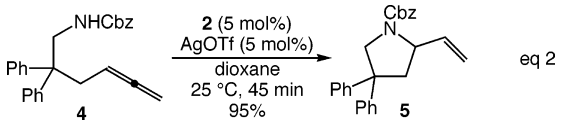
catalytic 1:1 mixture of **2** and AgOTf (5 mol %) in dioxane at room temperature for 45 min led to isolation of 2-vinyl pyrrolidine **5** in 95% yield (eq 2). In comparison, treatment of **4** with a catalytic amount of AgOTf (5 mol %) at room temperature for 2 days led to no detectable consumption of **4**.[34]



eq 2

Gold-catalyzed *exo*-hydroamination was also effective for Boc and Fmoc-substituted *N*-allenyl carbamates (Table 1, entries 1 and 2). The protocol tolerated substitution at the C(1) or C(3) position of the 4,5-hexadienyl chain with modest to good levels of diastereoselectivity (Table 1, entries 3 and 4). The protocol tolerated substitution at the internal and terminal allenyl carbon atoms and was also effective for the formation of piperidine derivatives via cyclization of protected δ-amino allenes (Table 1, entries 5−10). *N*-Allenyl carbamates **6**, **8**, and **12**, which possessed an axially chiral allenyl moiety, underwent Au-catalyzed cyclization to form heterocycles **7**, **9**, and **13**, respectively, with selective (≥50:1) formation of the *E*-alkene (Table 1, entries 6, 7, and 10). Noteworthy was that the Au-catalyzed intramolecular hydroamination of **10** to form pyrrolidine **11** was run under ambient atmosphere without any apparent decrease in rate or efficiency (Table 1, entry 8).

Although relatively high catalyst loadings (5 mol %) were employed in the preparative-scale reactions described above, efficient hydroamination was realized with significantly lower catalyst loading. In one experiment, a concentrated solution of *N*-allenyl carbamate **10** (0.64 mmol, 1.3 M) in dioxane was treated with a catalytic 1:1 mixture of **2** and AgOTf (1 mol %) and stirred for 25 min at room temperature. GC analysis revealed complete consumption of **10** to form **11** as the exclusive product. A second portion of **10** (0.64 mmol) was added, the reaction mixture was stirred for 25 min at room temperature, and subsequent GC analysis again revealed complete consumption of **10** with formation of **11** as the exclusive product. Chromatography of the reaction mixture gave **11** in 96% isolated yield. Likewise, reaction of **10** (0.5 M) with a catalytic 1:1 mixture of **2** and AgOTf (0.5 mol %) at room temperature for 14 h led to isolation of **11** in 96% yield.

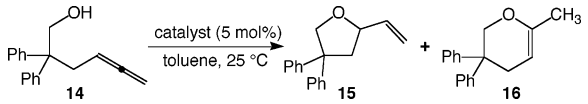
***exo*-Hydroalkoxylation of Allenyl Alcohols.** In contrast to the hydroamination of 4,5-hexadienyl carbamates, the hydroalkoxylation of 4,5-hexadienyl alcohols catalyzed by **2**/AgOTf occurred rapidly but with poor regioselectivity. For example, reaction of 2,2-diphenyl-4,5-hexadienol (**14**) catalyzed by a 1:1 mixture of **2** and AgOTf at room temperature for 5 min led to complete consumption of **14** to form a 1.3:1 mixture of tetrahydrofuran **15** and dihydropyran **16** in 85% combined yield by GC (Table 2, entry 1). However, subsequent experimentation revealed that the regioselectivity of Au-catalyzed hydroalkoxylation depended strongly on the nature of the

Table 1. Intramolecular Hydroamination of *N*-Allenyl Carbamates Catalyzed by a 1:1 Mixture of Au[P(*t*-Bu)$_2$(*o*-biphenyl)]Cl (**2**) and AgOTf in Dioxane at 25 °C for 5−180 min

entry	allenyl carbamate	heterocycle	yield (%)[a]
1	R = Boc		94
2	R = Fmoc		88
3			80 (16:1)
4			90 (4:1)
5			97
6	R = Me (**6**)	**7**	92 (≥50:1)
7	R = *n*-Pr (**8**)	**9**	98 (≥50:1)
8			96
9			92 (7.0:1)[b]
10			96 (≥50:1)

[a] Isolated material of >95% purity. [b] Reaction run at 25 °C for 22 h.

Table 2. Intramolecular Hydroalkoxylation of 14 as a Function of Catalyst



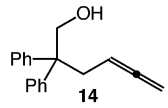
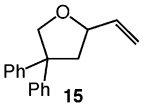
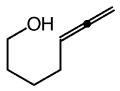
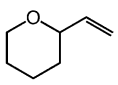
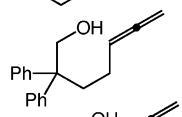
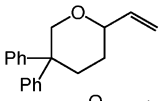
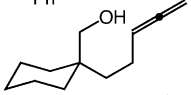
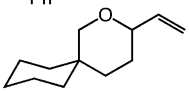
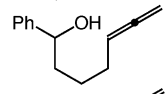
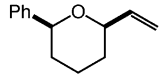
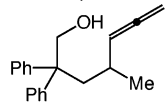
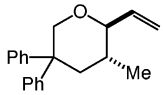
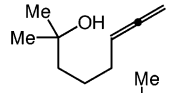
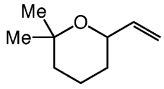
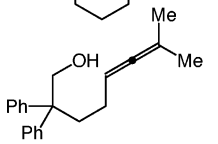
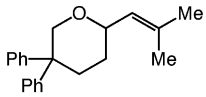
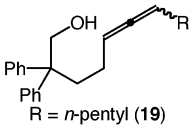
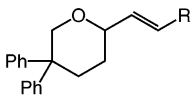
entry	catalyst	time	conv.	yield **15**[a]	yield **16**[a]
1	**2**/AgOTf	5 min	>99%	48%	37%
2	**2**/AgOTs	3 min	>99%	96%	≤1%
3	$AgNO_3$	16 h	17%	14%	0%
4	AgOTs	48 h	0%		
5	$[PtCl(H_2C{=}CH_2)]_2$/$P(C_6H_5CF_3)_3$	5 min	>99%	0%	49%

[a] Yield determined by GC analysis vs internal standard.

(33) For recent examples of the Au(I)-catalyzed cyclization of enynes and related substrates see: (a) Nieto-Oberhuber, C.; Lopez, S.; Echavarren, A. M. *J. Am. Chem. Soc.* **2005**, *127*, 6178. (b) Luzung, M. R.; Markham, J. P.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 10858. (c) Mamane, V.; Gress, T.; Krause, H.; Furstner, A. *J. Am. Chem. Soc.* **2004**, *126*, 8654. (d) Nieto-Oberhuber, C.; Munoz, M. P.; Bunuel, E.; Nevado, C.; Cardenas, D. J.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2004**, *43*, 2402. (e) Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 15978. (f) Faza, O. N.; Lopez, C. S.; Alvarez, R.; de Lera, A. R. *J. Am. Chem. Soc.* **2006**, *128*, 2434. (g) Mezailles, N.; Ricard, L.; Gagosz, F. *Org. Lett.* **2005**, *7*, 4133. (h) Gagosz, F. *Org. Lett.* **2005**, *7*, 4129. (i) Suhre, M. H.; Reif, M.; Kirsch, S. F. *Org. Lett.* **2005**, *7*, 3925. (j) Shi, X.; Gorin, D. J.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 5802. (k) Zhang, L.; Wang, S. *J. Am. Chem. Soc.* **2006**, *128*, 1442. (l) Ma, S.; Yu, S.; Gu, Z. *Angew. Chem. Int. Ed.* **2006**, *45*, 200.

(34) The presence of significant acid-catalyzed background reactions in the Au-catalyzed *exo*-hydrofunctionalization of allenes was ruled out by the following control experiments: Treatment of **10** with a catalytic amount of HOTf (5 mol %) in dioxane at room temperature for 2 h led to no detectable formation of **11.** Treatment of **14** with a catalytic amount of HOTs (10 mol %) in toluene at room temperature for 1 h led to no detectable formation of **15.** Treatment of **21** with a catalytic amount of HOTf (10 mol %) in dioxane at room temperature for 2 h led to no detectable formation of **22.**

Table 3. Intramolecular Hydroalkoxylation of Allenyl Alcohols Catalyzed by a 1:1 Mixture of Au[P(*t*-Bu)$_2$(*o*-biphenyl)]Cl (**2**) and AgOTs in Toluene at 25 °C for 5−75 min

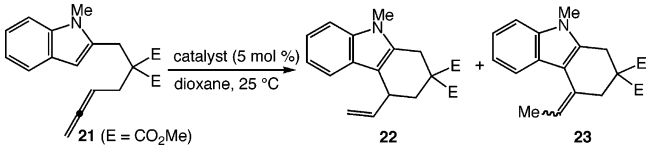
entry	allenyl alcohol	heterocycle	yield (%)[a]
1	 **14**	 **15**	91
2			98[b]
3			98
4			75
5			96 (7.2:1)
6			96 (5.6:1)
7			97[b]
8			96
9	R^1 = H, R^2 = *n*-Pr (**17a**)	**18a**	97 (5.3:1)[b]
10	R^1 = Ph, R^2 = *n*-pentyl (**17b**)	**18b**	90 (5.5:1)
11	R^1 = Ph, R^2 = Me (**17c**)	**18c**	93 (6.1:1)
12	 R = *n*-pentyl (**19**)	 **20**	99 (20:1)

[a] Isolated material of >95% purity. [b] H NMR yield; reaction run in dioxane-d_8.

counterion. In an optimized procedure, reaction of **14** with a catalytic 1:1 mixture of **2** and AgOTs in toluene at room temperature for 3 min led to complete consumption of **14** to form **15** in 96% yield (GC) without formation of significant amounts (≤1%) of **16** (Table 2, entry 2). Subsequent chromatography gave **15** in 91% isolated yield (Table 3, entry 1).

In contrast to mixtures of **2** and AgOTs, Ag(I) salts alone displayed little activity for the *exo*-hydroalkoxylation of **14**. Reaction of **14** with a catalytic amount of $AgNO_3$ at room temperature led to only 17% conversion after 16 h to form **15** in 14% yield (Table 2, entry 3). Treatment of **14** with a catalytic amount of AgOTs led to no detectable consumption of **14** after 48 h at room temperature (Table 2, entry 4). Reaction of **14** with a catalytic 1:1 mixture of $[PtCl(H_2C{=}CH_2)]_2$ and $P(C_6H_5\text{-}CF_3)_3$, previously employed as a catalyst for the intramolecular hydroalkoxylation of alkenyl alcohols,[11] led to rapid consumption of **14** to form **16** in 49% yield without formation of detectable amounts of **15** (Table 2, entry 5).[34]

Table 4. Intramolecular Hydroarylation of **21** as a Function of Catalyst



21 (E = CO_2Me) **22** **23**

entry	catalyst	time (h)	conversion (%)[a]	yield **22** (%)[a]	yield **23** (%)[a]
1	**2**/AgOTf	0.25	>99	>99	0
2	$AgBF_4$	2	0	0	0
3	$PdCl_2(MeCN)_2$	2	19	0	0
4	$Pd(OAc)_2$	2	15	0	0
5	$Pd(OAc)_2$/dppb	2	17	0	0
6	$[Pd(allyl)Cl]_2$/dppf	2	14	0	0
7	$PtCl_2$	2	20	10	14
8	$PtCl_4$	2	92	44	26
9	$AuCl_3$/AgOTf	2	68	40	15
10	AuCl/AgOTf	2	>99	25	56

[a] Conversion and yield determined by GC analysis vs internal standard.

5,6-Heptadien-1-ols also underwent efficient *exo*-hydroalkoxylation within minutes at room temperature in the presence of catalytic amount of **2**/AgOTs to form the corresponding 2-alkenyl tetrahydropyran derivatives in good yield (Table 3, entries 2−12). Gold-catalyzed hydroalkoxylation tolerated substitution at the C(1), C(2), or C(4) position of the 5,6-heptadienyl chain and was effective for the cyclization of unsubstituted 5,6-heptadienol (Table 3, entries 2−7). 5,6-Heptadien-1-ols that possessed a single substituent at either the C(1) or C(4) position underwent Au-catalyzed hydroalkoxylation with good diastereoselectivity (Table 3, entries 5 and 6). Furthermore, both the 5-*exo* hydroalkoxylation of γ-hydroxy allenes and the 6-*exo* hydroalkoxylation of δ-hydroxy allenes tolerated substitution at the terminal allenyl carbon atom (Table 3, entries 8−12). Noteworthy was that the gold-catalyzed hydroalkoxylation of the axially chiral γ-hydroxy allenes **17a**−**c** formed tetrahydrofurans **18a**−**c**, respectively, in ≥90% yield with ≥5.3:1 *E*:*Z* selectivity (Table 3, entries 9−11). Likewise, gold-catalyzed hydroalkoxylation of the axially chiral δ-hydroxy allene **19** formed tetrahydropyran **20** in 99% yield with 20:1 *E*:*Z* selectivity (Table 3, entry 12).

***exo*-Hydroarylation of Allenyl Indoles.** Mixtures of **2** and AgOTf catalyzed the room-temperature intramolecular *exo*-hydroarylation of 2-allenyl indoles to form functionalized tetrahydrocarbazoles. As an example, treatment of the 2-(4,5-hexadienyl)indole **21** with a catalytic 1:1 mixture of **2** and AgOTf in dioxane at 25 °C for 15 min led to complete consumption of **21** to form tetrahydrocarbazole **22** in >99% yield by GC analysis of the crude reaction mixture (Table 4, entry 1). A number of complexes were screened as catalysts for the conversion of **21** to **22**, but none proved as active or as selective as was the catalyst generated from **2** and AgOTf (Table 4). Silver(I) and Pd(II) complexes displayed no catalytic activity with respect to the conversion of **21** to **22** (Table 4, entries 2−6). Platinum dichloride, which catalyzes the hydroarylation of 2- and 3-alkenyl indoles,[5b] displayed little catalytic activity for the intramolecular hydroarylation of **21** (Table 4, entry 7). Neutral Pt(IV) complexes and cationic, "ligandless" Au(III) and Au(I)

complexes displayed considerably greater catalytic activity than did $PtCl_2$ but also displayed poor regioselectivity for hydroarylation (Table 4, entries 8−10).[34]

Gold-catalyzed hydroarylation was effective for allenyl indoles that possessed either an electron-donating or an electron-withdrawing group on the indole moiety and the protocol tolerated substitution at either the internal or terminal allenyl carbon atom (Table 5, entries 2−6). From this group of examples, several points are worth noting. First, the axially chiral 2-allenylindole **24** underwent Au-catalyzed cyclization to form tetrahydrocarbazole **25** with exclusive (≥ 50:1) formation of the *E*-alkene (Table 5, entry 5). Second, allenyl indole **26**, which possessed a single carbomethoxy group at the C(2) position of the 4,5-hexadienyl chain, cyclized in good yield to form tetrahydrocarbazole **27** as a 5:1 mixture of cis:trans diastereomers (Table 5, entry 7). Third, reaction of the bis(hydroxymethyl) substituted indole **28** with a catalytic 1:1 mixture of **2**/AgOTf led to formation of tetrahydrocarbazole **29** via 6-*exo* hydroarylation without formation of detectable amounts of the corresponding tetrahydrofuran via 5-*exo* hydroalkoxylation (Table 5, entry 8). The 2-(5,6-heptadienyl) indole **30** underwent Au-catalyzed cyclization at room temperature to form the seven-membered ring derivative **31** in good yield, although longer reaction time was required (Table 5, entry 9). In comparison, allenyl carboxamide **32** underwent gold-catalyzed hydroarylation at 60 °C to form a ∼1:1 mixture of dihydro-β-carbolinone **33** and dihydroazepinoindolone **34** in 72% combined yield (Table 5, entry 10).

Axial to Tetrahedral Chirality Transfer. Transfer of chirality from an axially chiral allenyl moiety to a tetrahedral stereogenic carbon atom has been observed for a number of catalytic and noncatalytic reactions including the intramolecular [4+2] cycloaddition of allenyl propargyl alcohols,[35] the intermolecular [4+2] cycloaddition of allene-1,3-dicarboxylates,[36] the [2+2] cycloaddition of allenylsilanes,[37] the Nazarov-type cyclization of allenyl alkenes,[38] the Mo- and Zr-mediated carbonylative bicyclization of ynallenes,[39] the Ni-catalyzed coupling of an allene, aldehyde, and a silane,[40] the Rh(I)-catalyzed cycloisomerization of allenyl cyclopropylalkenes,[41] the iodohydroxylation of allenylsulfoxides,[42] and the methoxymercuration and halogenation of 1,3-dimethylallenes.[43] Because the Au-catalyzed hydroamination of axially chiral *N*-allenyl carbamates **6**, **8**, and **12** occurred with exclusive formation of the *E*-alkene, we considered that the Au-catalyzed hydroamination of *N*-allenyl carbamates might also occur with transfer of chirality from the allenyl moiety to the newly formed stereogenic carbon atom. Indeed, treatment of the enantiomerically enriched *N*-allenyl carbamate (*S*)-**8** (≤84% ee)[44] with a catalytic 1:1 mixture of **2** and AgOTf led to isolation of (*R*)-**9** in 96% yield with 74% ee (eq 3). Gold-catalyzed hydroarylation of axially chiral allenyl indoles also occurred with transfer of chirality from the allenyl moiety to the newly formed stereogenic carbon atom. For example, reaction of enantiomerically enriched

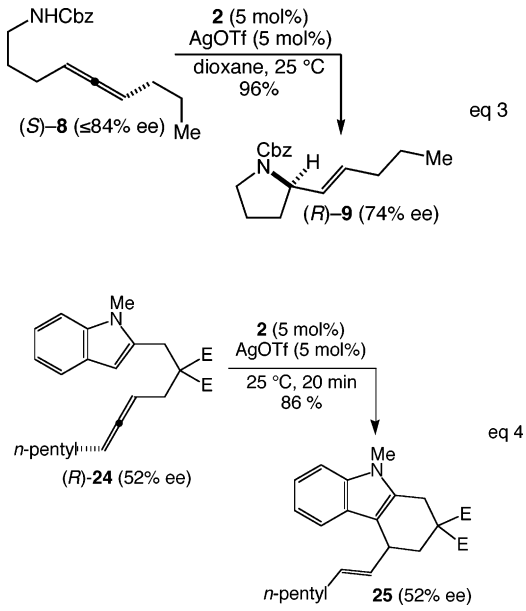
Table 5. Intramolecular Hydroarylation of 2-Allenyl Indoles Catalyzed by a 1:1 Mixture of Au[P(*t*-Bu)$_2$(*o*-biphenyl)]Cl (**2**) and AgOTf in Dioxane at 25 °C for 30 min

entry	allenyl indole[a]	product	yield (%)[b]
1	R = H (**21**)	**22**	87
2	R = OMe		89
3	R = F		91
4			71
5			82 (≥50:1)
6			92
7	**26**	**27**	94 (5:1)
8	**28**	**29**	82
9[c]	**30**	**31**	70[c]
10[d]	**32**	**33** + **34**	37 + 35

[a] E = CO_2Me. [b] Isolated material of >95% purity. [c] Reaction run for 22 h. [d] Reaction run at 60 °C for 1 h.

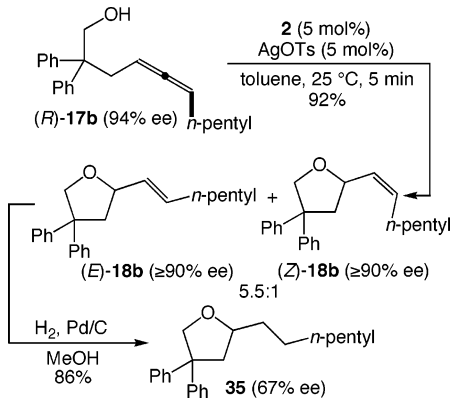
(35) Gibbs, R. A.; Bartels, K.; Lee, R. W. K.; Okamura, W. H. *J. Am. Chem. Soc.* **1989**, *111*, 3717.
(36) Ikeda, I.; Honda, K.; Osawa, E.; Shiro, M.; Aso, M.; Kanematsu, K. *J. Org. Chem.* **1996**, *61*, 2031.
(37) Shepard, M. S.; Carreira, E. M. *J. Am. Chem. Soc.* **1997**, *119*, 2597.
(38) Hu, H.; Smith, D.; Cramer, R. E.; Tius, M. A. *J. Am. Chem. Soc.* **1999**, *121*, 9895.
(39) Brummond, K. M.; Kerekes, A. D.; Wan, H. *J. Org. Chem.* **2002**, *67*, 5156.
(40) (a) Ng, S.-S.; Jamison, T. F. *J. Am. Chem. Soc.* **2005**, *127*, 7320. (b) Ng, S.-S.; Jamison, T. F. *Tetrahedron* **2005**, *61*, 11405.
(41) Wender, P. A.; Glorius, F.; Husfeld, C. O.; Langkopf, E.; Love, J. A. *J. Am. Chem. Soc.* **1999**, *121*, 5348.
(42) Ma, S.; Ren, H.; Wei, Q. *J. Am. Chem. Soc.* **2003**, *125*, 4817.
(43) Waters, W. L.; Linn, W. S.; Caserio, M. C. *J. Am. Chem. Soc.* **1968**, *90*, 6741.

(*R*)-**24** (52% ee) with a catalytic 1:1 mixture of **2** and AgOTf led to isolation of **25** in 86% yield with 52% ee (eq 4).



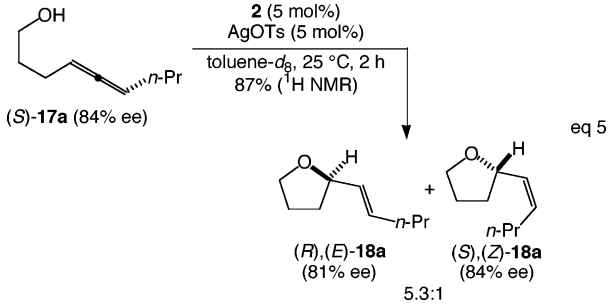
In contrast to Au-catalyzed hydroarylation and hydroamination, the Au-catalyzed hydroalkoxylation of axially chiral allenyl alcohols **17** formed mixtures of *E* and *Z*-alkenes (Table 3, entries 9−11). Nevertheless, the Au-catalyzed hydroalkoxylation of axially chiral allenyl alcohols also occurred with transfer of chirality from the allenyl moiety to the newly formed stereogenic carbon atom. For example, treatment of the enantiomerically enriched allenyl alcohol (*R*)-**17b** (94% ± 3% ee) with a catalytic 1:1 mixture of **2** and AgOTs led to isolation of a 5.5:1 mixture of (*E*)-**18b** (≥90% ee) and (*Z*)-**18b** (≥90% ee) in 92% combined yield (Scheme 1).[45] Noteworthy was that (*E*)-**18b** and (*Z*)-**18b**

Scheme 1



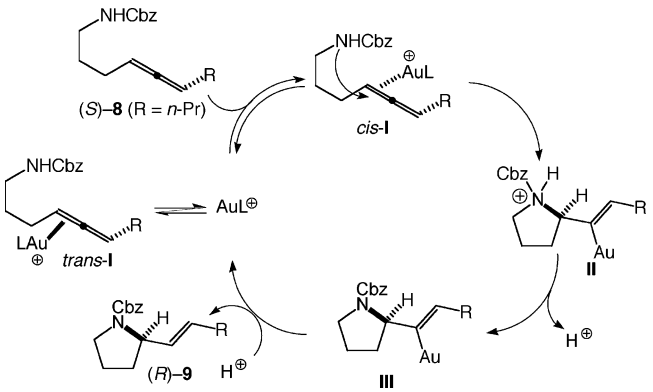
possessed opposite stereochemistry at the stereogenic C(2) carbon atom. Catalytic hydrogenation of the aforementioned mixture of enantiomerically enriched (*E*)-**18b** and (*Z*)-**18b** formed 2-*n*-heptyl-4,4-diphenyltetrahydrofuran (**35**) in 86% yield with 67% ee (er = 5.1:1).

An additional experiment was performed to assign the absolute stereochemistry to the *E* and *Z*-isomers formed via the gold-catalyzed hydroalkoxylation of an axially chrial allenyl alcohol. To this end, reaction of the enantiomerically enriched allenyl alcohol (*S*)-**17a** (84% ee) with a catalytic 1:1 mixture of **2** and AgOTs led to formation of a 5.3:1 mixture of (*R*),(*E*)-**18a** (81% ee) and (*S*),(*Z*)-**18a** (84% ee) in 87% combined yield by ^{1}H NMR analysis (eq 5). The absolute stereochemistry of (*R*),(*E*)-**18a** and (*S*),(*Z*)-**18a** was assigned by comparison to an authentic sample of a 25:1 mixture of (*R*),(*Z*)-**18a** and (*R*),(*E*)-**18a** synthesized in two steps from commercially available (*R*)-2-hydroxymethyltetrahydrofuran.[46]



Mechanism. Both inner-sphere[47] and outer-sphere[7,16a,28,32] mechanisms have been suggested for the gold-catalyzed addition of C-, N-, and O-nucleophiles to alkenes and alkynes. However, stereochemical analysis of the Au(I)-catalyzed hydroalkylation of 4-pentynyl β-keto esters,[28] the hydroamination of 4-pentenyl sulfonamides,[7] and the hydroalkoxylation of (*Z*)-2-en-4-yne-1-ols[32] in each case established the anti-addition of the nucleophile and Au atom across the C−C multiple bond, consistent with outer-sphere C−X bond formation. Similarly, the stereospecific conversion of (*S*)-**8** to (*R*)-**9** (eq 3) directly implicates a mechanism involving nucleophilic anti-attack of the carbamate nitrogen atom on the Au-complexed allene of intermediate *cis*-**I** to form the ammonium intermediate **II** (Scheme 2). Deprotonation of **II** followed by protonolysis of the Au−C bond[48] of the neutral gold alkenyl complex **III** with retention of stereo-

Scheme 2



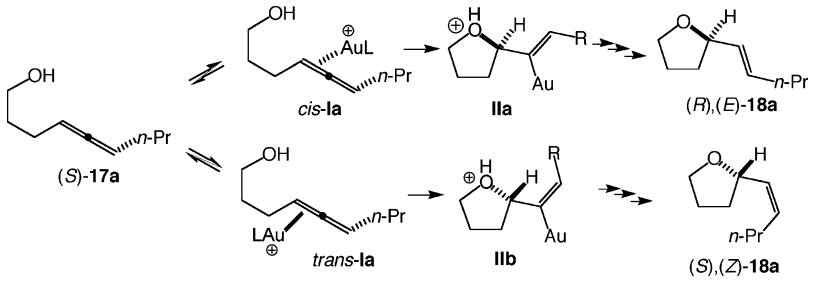
(44) (a) We were unable to determine directly the enantiomeric purity of (*S*)-**8.** Rather, the enantiomeric purity of (*S*)-9-(tetrahydropyran-2-yloxy)-5-nonyn-4-ol [(*S*)-**36**] was determined (84% ee) by ^{19}F NMR analysis of the corresponding Mosher ester. Compound (*S*)-**36** was deprotected to give (*S*)-**17a**, which was then converted to (*S*)-2-(3,4-octadienyloxy)tetrahydropyran employing the method of Myers[44b] and subsequently converted to (*S*)-**8** without further manipulation of the chiral allenyl moiety (See Supporting Information). (b) Myers, A. G.; Zheng, B. *J. Am. Chem. Soc.* **1996**, *118*, 4492.

(45) Determination of the enantiomeric purity of (*E*)-**18b** and (*Z*)-**18b** was complicated by coelution of one enantiomer of (*E*)-**18b** with one enantiomer of (*Z*)-**18b** on HPLC (see Supporting Information).

(46) (a) Bianchi, P.; Roda, G.; Riva, S.; Danieli, B.; Zabelinskaja-Mackova, A.; Griengl, H. *Tetrahedron* **2001**, *57*, 2213. (b) Cominetti, F.; Deagostino, A.; Prandi, C.; Venturello, P. *Tetrahedron* **1998**, *54*, 14603.

(47) Teles, J. H.; Brode, S.; Chabanas, M. *Angew. Chem. Int. Ed.* **1998**, *37*, 1415.

Scheme 3



chemistry[49] would release (*R*)-**9** with regeneration of the catalytically active cationic gold phosphine complex.[50]

Formation of the *E*-alkene moiety of (*R*)-**9** requires selective cyclization of gold-allene intermediate *cis*-**I**, in which the gold atom is cis to the proximal *n*-propyl group, in preference to cyclization of *trans*-**I**, in which the gold atom is trans to the proximal *n*-propyl group (Scheme 2). Because it appears likely that *cis*-**I** is less stable than is *trans*-**I**, Au-catalyzed conversion of (*S*)-**8** to (*R*)-**9** presumably involves rapid and reversible formation of *trans*-**I** followed by irreversible cyclization of *cis*-**I** to form **II** (Scheme 2). It follows that the transition state for C−N bond formation is destabilized to a greater extent by a cis arrangement of the carbamate moiety and *n*-propyl group (*trans*-**I** → **II**) than by a cis arrangement of the Au[P(*t*-Bu)$_2$(*o*-biphenyl)] moiety and the *n*-propyl group (*cis*-**I** → **II**).

The high selectivity for transfer of chirality and the high diastereoselectivity of the Au-catalyzed hydroarylation of allenyl indole (*R*)-**24** strongly suggest that conversion of (*R*)-**24** to **25** also occurs via outer-sphere attack of the indole moiety on a cis Au-allene complex. In comparison, Au-catalyzed hydroalkoxylation of the axially chiral allenyl alcohol (*S*)-**17a** formed a 5.3:1 mixture of (*R*),(*E*)-**18a** and (*S*),(*Z*)-**18a**. This result is in accord with a mechanism involving competitive outer-sphere attack of the hydroxyl group on the diastereomeric gold allene complexes *cis*-**Ia** and *trans*-**Ia** to form **IIa** and **IIb**, respectively (Scheme 3). Deprotonation/protonolysis of **IIa** and **IIb** would then form tetrahydrofurans (*R*),(*E*)-**18a** and (*S*),(*Z*)-**18a**, respectively (Scheme 3). Destabilization of the transition state for conversion of *trans*-**Ia** → **IIb** is presumably attenuated relative to the corresponding processes involving C−N or C−C bond formation due to the smaller size of the hydroxyl group relative to a carbamate or indole group.

Conclusions

We have found that Au[P(*t*-Bu)$_2$(*o*-biphenyl)]Cl (**2**) activated by either AgOTf or AgOTs is a highly active and highly selective precatalyst for the intramolecular *exo*-hydroamination of *N*-allenyl carbamates, the intramolecular *exo*-hydroalkoxylation of allenyl alcohols, and the intramolecular *exo*-hydroarylation of 2-allenyl indoles. *N*-Allenyl carbamates, allenyl alcohols, and allenyl indoles that possessed an axially chiral allenyl moiety underwent cyclization with transfer of chirality from the allene to the newly formed stereogenic carbon atom with selective formation of the *E*-alkene. The selective conversion of (*S*)-**8** to (*R*)-**9** supported a mechanism for the gold-catalyzed hydroamination of *N*-allenyl carbamates involving outer-sphere, anti-attack of the carbamate nitrogen atom on the allenyl group of a gold allene complex in which the gold atom is complexed to the allene π-face cis to the proximal allenyl substituent.

Experimental Section

Benzyl 4,4-diphenyl-2-vinylpyrrolidine-1-carboxylate (5). A suspension of **4** (96 mg, 0.25 mmol), **2** (6.9 mg, 1.3×10^{-2} mmol), and AgOTf (3.3 mg, 1.3×10^{-2} mmol) in dioxane (2.00 mL) was stirred at 25 °C for 45 min. The crude reaction mixture was chromatographed (SiO_2; hexanes−EtOAc = 4:1) to give **5** (91 mg, 95%) as a viscous, colorless oil. TLC (SiO_2; hexanes−EtOAc = 4:1): $R_f = 0.34$. ^{1}H NMR (1:1 ratio of rotamers): δ 7.46−7.11 (m, 15 H), 5.87−5.70 (m, 1 H), 5.37−4.99 (m, 4 H), [4.77 (d, J = 11.6 Hz), 4.61 (d, J = 11.3 Hz), 1:1, 1 H], 4.24−4.02 (m, 1 H), 3.71 (dd, J = 7.3, 11.5 Hz, 1 H), 2.90−2.79 (m, 1 H), 2.51−2.38 (m, 1 H). ^{13}C{^{1}H} NMR (1:1 ratio of rotamers): δ 155.6, 154.8, 145.4, 144.8, 139.2, 138.5, 137.1, 136.9, 128.7, 128.6, 128.4, 128.2, 128.1, 127.8, 127.6, 126.9, 126.7, 126.5, 115.8, 115.2, 66.9, 59.5, 59.1, 56.2, 53.1, 52.8, 45.7, 44.7. IR (neat, cm^{-1}): 3060, 3030, 2976, 2881, 1698, 1598, 1493, 1446, 1408, 1353, 1313, 1202, 1105, 979, 918, 750, 697. Anal. calcd. (found) for $C_{26}H_{25}NO_2$: C, 81.43 (81.18); H, 6.57 (6.54); N, 3.65 (3.66).

The remaining nitrogen heterocycles derivatives depicted in Table 1 were synthesized employing a procedure similar to that used to synthesize **5**.

4,4-Diphenyl-2-vinyltetrahydrofuran (15). A mixture of **2** (3.3 mg, 6.25×10^{-3} mmol) and AgOTs (1.7 mg, 6.25×10^{-3} mmol) in toluene (0.4 mL) was stirred at room temperature for 10 min and then treated with a solution of **14** (31.3 mg, 0.125 mmol) in toluene (0.6 mL). The resulting suspension was stirred at room temperature for 3 min and then chromatographed (SiO_2; hexanes−EtOAc = 50:1 → 20:1) to give **15** (28.4 mg, 91%) as a colorless oil. TLC (hexanes−EtOAc = 5:1): $R_f = 0.57$. ^{1}H NMR: δ 7.34−7.17 (m, 10 H), 5.90 (ddd, J = 6.8, 10.0, 17.2 Hz, 1 H), 5.24 (d, J = 16.8 Hz, 1 H), 5.10 (d, J = 10.0 Hz, 1 H), 4.67 (d, J = 8.4 Hz, 1 H), 4.43 (td, J = 6.4, 10.0 Hz, 1 H), 4.15 (d, J = 8.4 Hz, 1 H), 2.66 (ddd, J = 0.8, 6.0, 12.4 Hz, 1 H), 2.44 (dd, J = 9.6, 12.0 Hz, 1 H). ^{13}C{^{1}H} NMR: δ 146.2, 145.8, 139.0, 128.7, 128.6, 127.4, 127.3, 126.7, 126.5, 116.1, 79.9, 56.4, 45.3. IR (neat, cm^{-1}): 3056, 2973, 2866, 1650, 1499, 1445, 1056, 926, 757, 699. Anal. Calcd (found) for $C_{18}H_{18}NO_4$: C, 86.53 (86.36); H, 7.18 (7.25).

The remaining oxygen heterocycles depicted in Table 3 were synthesized employing a procedure similar to that used to synthesize **15**.

2,2-Dicarbomethoxy-9-methyl-4-vinyl-2,3,4,9-tetrahydrocarbazole (22). A mixture of **2** (6.6 mg, 1.3×10^{-2} mmol) and AgOTf (3.2 mg, 1.3×10^{-2} mmol) in dioxane (0.1 mL) was stirred for 10 min at room temperature. To this, a solution of **21** (82 mg, 0.25 mmol) in dioxane (0.4 mL) was added and the resulting solution was stirred for 30 min. Column chromatography of the reaction mixture (SiO_2; hexanes−EtOAc = 10:1 → 5:1) gave **22** (71 mg, 87%) as a pale yellow oil. TLC (SiO_2; hexanes−EtOAc = 2:1): $R_f = 0.56$. ^{1}H NMR: δ 7.53

(48) (a) Mitchell, C. M.; Stone, F. G. A. *J. Chem. Soc. Dalton Trans.* **1972**, 102. (b) Johnson, A.; Pudephatt, R. J. *J. Chem. Soc. Dalton Trans.* **1977**, 1384.
(49) Johnson, A.; Pudephatt, R. J. *J. Chem. Soc. Dalton Trans.* **1978**, 980.
(50) An analogous mechanism involving intermolecular protonolysis of a Pt−C bond has been established for the Pt-catalyzed hydroamination of alkenylamines.[8a]

(d, $J = 8.0$ Hz, 1 H), 7.24 (d, $J = 8.0$ Hz, 1 H), 7.14 (t, $J = 7.6$ Hz, 1 H), 7.00 (t, $J = 7.2$ Hz, 1 H), 5.83 (ddd, $J = 8.0$, 9.6, 17.6 Hz, 1 H), 5.30−5.14 (m, 2 H), 3.76 (s, 3 H), 3.71−3.69 (m, 1 H), 3.69 (s, 3 H), 3.66 (s, 3 H), 3.45 (d, $J = 8.0$ Hz, 1 H), 3.15 (dd, $J = 2.0$, 8.0 Hz, 1 H), 2.65 (ddd, $J = 0.8$, 6.0, 13.2 Hz, 1 H), 2.05 (dd, $J = 10.0$, 13.2 Hz, 1 H). $^{13}C\{^1H\}$ NMR: δ 172.2, 171.1, 141.8, 137.8, 133.0, 126.9, 121.2, 119.9, 119.1, 115.8, 109.2, 109.0, 54.5, 53.3, 36.7, 36.3, 29.6, 28.3. IR (neat, cm^{-1}): 2952, 1731, 1469, 1373, 1319, 1289, 1250, 1083, 916, 743. Anal. Calcd. (found) for $C_{18}H_{21}NO_4$: C, 69.71 (69.50); H, 6.47 (6.55).

The remaining tricyclic indoles depicted in Table 5 were synthesized employing a procedure similar to that used to synthesize **22**.

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Supporting Information Available: Experimental procedures, analytical and spectroscopic data for new compounds, and copies of pertinent spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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