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Gold(I)-catalyzed enantioselective bromocyclization reactions of allenes†

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The enantioselective bromocyclization of allenes is accomplished through the use of a chiral dinuclear gold complex and/or chiral phosphate anions in the presence of an *N*-bromolactam as an electrophilic bromine source. This method provides access to heterocyclic vinyl bromides with an allylic stereocenter in excellent yield and enantioselectivity. These enantioenriched vinyl bromides may serve as a handle for further derivatization *via* cross-coupling reactions.

The formation of halogenated molecules has been an area of continuous interest in synthetic chemistry; numerous applications exist in the production of both pharmaceuticals and agrochemicals. In recent times, the asymmetric halofunctionalization of alkenes has emerged as an intense area of research,[1] mainly through the use of chiral organocatalysts such as phosphoric acids, alkaloids, and ureas.[2] Although employed less often, chiral transition metal complexes have also proven to be competent catalysts.[3] Surprisingly, the corresponding halofunctionalization of allenes is relatively unexplored, considering the potential utility of the vinyl halide products to partake in further cross-coupling reactions. Fluoro-, bromo-, and iodocyclization reactions of allenes with alcohol, acid, amide, and carbamate nucleophiles yielding racemic products with fair to excellent diastereoselectivities have been reported;[4] however no enantioselective variants have been described to date. In contrast, the corresponding gold-catalyzed enantioselective hydroamination and hydroalkoxylation reactions of allenes have been developed.[5] These reactions are proposed to proceed through a vinylgold intermediate **A** that forms upon gold-promoted nucleophilic addition of the heteroatom nucleophile to the allene.[6] Although protodeauration[7] is the usual fate of this intermediate, we envisioned an *in situ* intermolecular halodeauration with an electrophilic halogen source (eqn (1)) to yield a vinyl halide containing an allylic stereocenter.

hydrofunctionalization: X = H *this work:* X = Br

On the basis of previous reports[8] of faster reaction rates and improved yields of the desired halogenated product compared to control reactions without gold catalyst, we selected *N*-iodosuccinimide (NIS) and *N*-bromosuccinimide (NBS) as convenient and air-stable halogen sources. We initiated our studies using the bisphosphinegold(I) 4-nitrobenzoate complexes previously employed in the gold-catalyzed enantioselective hydroamination of allenes.[5h] Unfortunately, the DM-BINAP(AuPNB)$_2$-catalyzed reactions of **1a** in the presence NIS and NBS afforded racemic **2a** and **3a** in modest yield as a result of the fast uncatalyzed background reaction (Table 1, entries 1 and 2).[9] In contrast, when *N*-chlorosuccinimide (NCS) was employed as the halogenating reagent (Table 1, entry 3), moderate enantioselectivity was observed, suggesting the majority of product was formed through a gold-catalyzed processes; however, the decreased reactivity of NCS allowed for competitive protodeauration and a significant amount of side-product **5a** was also produced.

While use of NCS as a halogen source was moderately successful, uncatalyzed background reaction and competitive protodeauration persisted as problems in subsequent optimizations. For example, in attempts to decrease the amount of **5a** produced, we explored addition of an external base, such as Na_2CO_3. Although the amount of **5a** did decrease, incomplete conversion was observed (Table 1, entry 4). Similarly, the presence of additional succinimide was also found to be detrimental to the reaction, dramatically lowering both the yield and ee (Table 1, entry 5).

Therefore, we refocused our attention on finding a more suitable electrophilic halogen source.[10] We envisioned a reagent that would generate a stronger internal base than the succinimide anion, hopefully suppressing the protodeauration pathway (Fig. 1a).[11] To this end, we settled upon the *N*-halolactams, a class of relatively unexplored compounds. Unfortunately, the use of *N*-chlorocaprolactam[12] gave exclusively **5a**, while *N*-iodopyrrolidinone[2i] yielded the desired product but with no significant enantioenrichment (Table 1, entries 6 and 7).[13] In contrast, we were delighted to find that use of 1.1 eq. of

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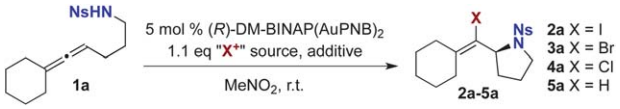
Table 1 Optimization of gold-catalyzed enantioselective aminohalogenation of allenes[a]



Entry	"X^+" source	Additive	Product	% Yield[b] (% ee[c])	% Yield **5a**[b]
1	NIS	None	**2a**	63 (<5)	0
2	NBS	None	**3a**	35 (<5)	0
3	NCS	None	**4a**	57 (76)	16
4	NCS	2 eq. Na_2CO_3	**4a**	52 (83)	10
5[d]	NCS	1 eq. succimide	**4a**	27 (15)	0
6[d]		None	**4a**	0 (n.d.)	89
7[e]		None	**2a**	67 (<5)	0
8	**6a**	None	**3a**	83 (97)	7
9[d]	**6a**	None	**3a**	88[f] (99)	0

[a] Ns: 4-nitrobenzenesulfonyl; PNB: 4-nitrobenzoate; 0.2 M in $MeNO_2$. [b] Determined by ^1H NMR using 1,3-dinitrobenzene as an internal standard. [c] Determined by chiral HPLC. [d] 2 eq. "X^+" used. [e] 1.5 eq. "X^+" used. [f] Isolated yield after column chromatography.

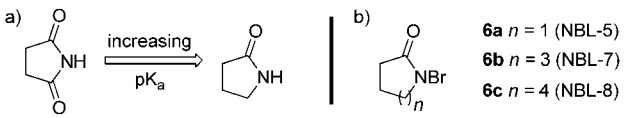
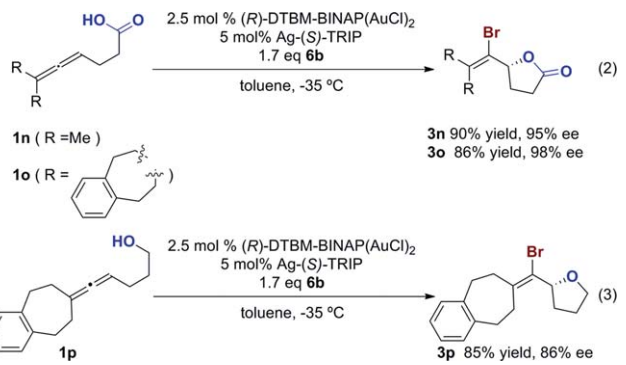


Fig. 1 *N*-Bromolactams as electrophilic halogen sources.

N-bromopyrrolidinone[14] (**6a**) in the gold-catalyzed bromocyclization of **1a** afforded **3a** in excellent yield and ee, although accompanied by a small amount of **5a** (Table 1, entry 8). By increasing the loading of **6a** to 2 eq., the desired product was obtained in pure form with no trace of the product derived from competing protodeauration (Table 1, entry 9). Moreover, in sharp contrast to the detrimental effect of succinimide (Table 1 entry 5), a reaction with 5 mol% (*R*)-DM-BINAP(AuPNB)$_2$, 2 eq. **6a**, and 1 eq. 2-pyrrolidone added initially to the $MeNO_2$ solution gave **3a** in nearly identical yield and enantioselectivity (89% yield and 98% ee).

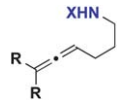
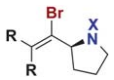
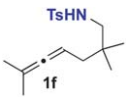
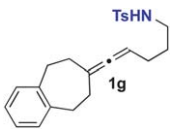
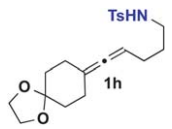
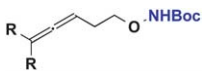
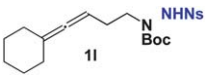
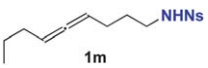
With the optimized conditions in hand, we explored the scope of our bromofunctionalization reaction (Table 2). A range of tosyl- (**3d–h**) or nosyl-protected (**3a–c**) amines gave excellent enantioselectivities in the chiral bisphosphinegold(I) 4-nitrobenzoate-catalyzed bromoamination reaction employing **6a** as the bromine source. Moreover, the reaction tolerated variation in the allene substituents (entries 7 and 8) and tether substitution (entry 6). We then focused our efforts on substrates containing different types of nucleophiles. To this end, (*R*)-DM-BINAP(AuPNB)$_2$-catalyzed reaction of **1i**, under the same conditions employed to form pyrrolidines **3a–h**, afforded the desired isoxazolidine **3i** in only 61% ee. Attempts to enhance the enantioselectivity of this transformation by changing the chiral phosphine ligand did not result in significant improvements.[15]

Given the observed dependence of enantioselectivity on the identity of the halogenating reagent, we next explored modification of the *N*-bromolactam. Fortunately, varying the ring size of the *N*-bromolactam allowed better enantioselectivity to be achieved, with **6b** and **6c** giving **3i** in 84% and 91% ee (entry 9), respectively.[16] This dependence of ee on lactam ring size highlights the tunability as a useful feature of *N*-bromolactam reagents. Variation of the lactam again proved useful in gold-catalyzed amino bromination of hydrazine **1l**, where the use of **6b** gave the desired product in 80% yield and 96% ee (entry 12). Moreover, the catalyst system could be applied to the bromoamination of a racemic 1,3-disubstituted allene giving a 2.6 : 1 mixture of *Z* : *E*-alkenes in 26% and 96% ee, respectively (entry 13).[17,5i]



In contrast, under the standard conditions ($MeNO_2$, r.t., 2 eq. **6a**) the DM-BINAP(AuPNB)$_2$-catalyzed reaction of carboxylic acid **1n** gave racemic lactone **3n**. We have previously observed that the use of chiral phosphate counterions[18] in nonpolar solvents dramatically improved enantioselectivity in gold catalyzed

Table 2 Gold-catalyzed enantioselective aminobromination[a]

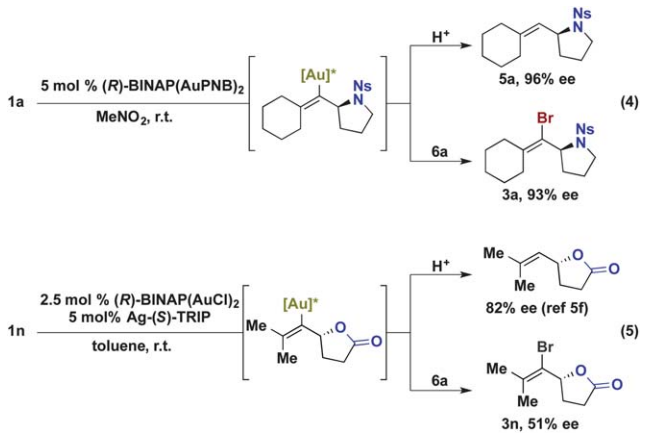
Entry	Substrate	NBL	Product	% Yield	% ee
					
1	**1a** R = $-CH_2(CH_2)_3CH_2-$; X = Ns	**6a** (2 eq.)	**3a**	88	99
2[b]	**1b** R = Me; X = Ns	**6a** (2 eq.)	**3b**	89	98
3[b]	**1c** R = $-CH_2(CH_2)_4CH_2-$; X = Ns	**6a** (2 eq.)	**3c**	93	99
4	**1d** R = $-CH_2(CH_2)_3CH_2-$; X = Ts	**6a** (2 eq.)	**3d**	93	98
5	**1e** R = Me; X = Ts	**6a** (2 eq.)	**3e**	89	99
6[b]		**6a** (2 eq.)	**3f**	89	99
7[b]		**6a** (2 eq.)	**3g**	86	95
8[c]		**6a** (2 eq.)	**3h**	74	93
					
9	**1i** R = $-CH_2(CH_2)_3CH_2-$	**6c** (1.5 eq.)	**3i**	75	91
10	**1j** R = Me	**6c** (1.5 eq.)	**3j**	83	88
11	**1k** R = $-CH_2(CH_2)_4CH_2-$	**6c** (1.5 eq.)	**3k**	88	91
12		**6b** (1.5 eq.)		80	96
13		**6a** (2 eq.)		74 2.6 : 1 (Z : E)	26(Z) 91(E)

[a] 5 mol% (*R*)-DM-BINAP(AuPNB)$_2$, 0.2 M $MeNO_2$, r.t., 12–14 h. [b] (*R*)-Cl-MeO-BIPHEP(AuPNB)$_2$. [c] (*S*)-BINAP(AuPNB)$_2$.

lactonization reactions of allenes.[5f] Gratifyingly, these findings translated to the bromolactonization reaction of **1n** catalyzed by (*R*)-DTBM-BINAP(AuCl)$_2$/Ag-(*S*)-TRIP in toluene and **6a** as the bromine source, which furnished **3n** in 48% yield and 88% ee. By changing to *N*-bromolactam **6b**, the yield and enantioselectivity were improved to 90% and 95% ee, respectively (eqn (2)). The impact of the phosphate chiral anion on the selectivity is supported by the observation that **3n** was formed with lower enantioselectivity when the anion was changed from (*S*)-TRIP (95% ee) to either (*R*)-TRIP (81% ee) or *p*-nitrobenzoate (85% ee) under otherwise identical conditions. Similarly, the bromoetherification of alcohol **1p** with 5 mol% (*R*)-DTBM-BINAP(AuCl)$_2$/10 mol% Ag-(*S*)-TRIP produced tetrahydrofuran **3p** in 86% ee (eqn (3)) compared to the 25% ee generated using DTBM-BINAP(AuPNB)$_2$ as the catalyst.

In order to examine our initial premise (eqn (1)) that the gold-catalyzed hydroamination and aminobromination reactions were proceeding through vinylgold intermediate **A**, we examined both reactions under identical reaction conditions. In accord with this hypothesis, the BINAP(AuPNB)$_2$-catalyzed hydroamination and aminobromination reaction of **1a** afforded pyrrolidines **5a** and **3a** in 96% and 93% ee, respectively (eqn (4)).[19,20] Similarly, the DM-BINAP(AuPNB)$_2$-catalyzed cyclization and bromocyclization reactions of **1a** produced the corresponding adducts with nearly identical enantioselectivity (88 and 93% ee). The similarity in enantioselectivity is most consistent with an enantiodetermining cyclization to form a vinylgold intermediate; therefore the enantioselectivity is independent of whether this intermediate undergoes either proto- or bromodeauration. In contrast, when the gold-catalyzed bromolactonization was performed under conditions we previously reported to give the lactone in 82% ee,[5f] bromolactone **3n** was obtained in substantially lower enantioselectivity (51% ee, eqn (5)). This result lends support to a recent study from Gagné and Widenhoefer that concludes that cyclization is reversible and protodeauration is likely the

enantiodetermining step in gold-catalyzed hydroalkoxylation reactions;[6c] therefore the nature of the electrophile and its interaction with the catalyst and its counterion in the deauration step is critical to the enantioselectivity.[21] Nevertheless, the enantioselectivity for the bromolactonization to give **3n** could be improved to 95% ee (eqn (2)). Moreover, while the two limiting scenarios of nucelophile influence on enantiodetermining cyclization and deauration are discussed above, its is likely that cases exists where the relative rates of these two steps are similar. Taken together, these results suggest a delicate balance between the relative rates of cycloreversion[22] and electrophilic deauration of vinylgold intermediates in gold-catalyzed cyclization reactions; thus tuning the electrophilic species is critical to achieving high enantioselectivity.



In summary, we have explored *in situ* electrophilic deauration of vinylgold intermediates to achieve the first asymmetric bromofunctionalization of allenes. The use of relatively underexplored *N*-bromolactams **6** as tunable electrophiles enabled wide substrate tolerance to furnish enantioenriched pyrrolidine, isoxazolidine, pyrazolidine, lactone, and furan products. The resulting vinyl halides can readily be employed in subsequent cross-coupling reactions, further demonstrating the orthogonal reactivity of gold(I)- and palladium(0)-based catalysts.[23] The broad scope of amine, hydroxylamine, hydrazine, acid, and alcohol nucleophiles highlights the robust nature of this strategy and the usefulness of *N*-bromolactams as a source of electrophilic bromine.

Acknowledgements

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Notes and references

1 (*a*) S. E. Denmark, W. E. Kuester and M. T. Burk, *Angew. Chem., Int. Ed.*, 2012, **51**, 10938; (*b*) U. Hennecke, *Chem.–Asian J.*, 2012, **7**, 456; (*c*) C. K. Tan, L. Zhou and Y.-Y. Yeung, *Synlett*, 2011, 1335; (*d*) A. Castellanos and S. P. Fletcher, *Chem.–Eur. J.*, 2011, **17**, 5766.

2 (*a*) K. Ikeuchi, S. Ido, S. Yoshimura, T. Asakawa, M. Inai, Y. Hamashima and T. Kan, *Org. Lett.*, 2012, **14**, 6016; (*b*) M. C. Dobish and J. N. Johnston, *J. Am. Chem. Soc.*, 2012, **134**, 6068; (*c*) X. Jiang, C. K. Tan, L. Zhou and Y.-Y. Yeung, *Angew. Chem., Int. Ed.*, 2012, **51**, 7771; (*d*) S. E. Denmark and M. T. Burk, *Org. Lett.*, 2012, **14**, 256; (*e*) D. H. Paull, C. Fang, J. R. Donald, A. D. Pansick and S. F. Martin, *J. Am. Chem. Soc.*, 2012, **134**, 11128; (*f*) Y.-M. Wang, J. Wu, C. Hoong, V. Rauniyar and F. D. Toste, *J. Am. Chem. Soc.*, 2012, **134**, 12928; (*g*) V. Rauniyar, A. D. Lackner, G. L. Hamilton and F. D. Toste, *Science*, 2011, **334**, 1681; (*h*) D. Huang, H. Wang, F. Xue, H. Guan, L. Li, X. Peng and Y. Shi, *Org. Lett.*, 2011, **13**, 6350; (*i*) U. Hennecke, C. H. Müller and R. Fröhlich, *Org. Lett.*, 2011, **13**, 860; (*j*) O. Lozano, G. Blessley, T. M. del Campo, A. L. Thompson, G. T. Giuffredi, M. Bettati, M. Walker, R. Borman and V. Gouverneur, *Angew. Chem., Int. Ed.*, 2011, **50**, 8105; (*k*) G. E. Veitch and E. N. Jacobsen, *Angew. Chem., Int. Ed.*, 2010, **49**, 7332; (*l*) L. Zhou, C. K. Tan, X. Jiang, F. Chen and Y.-Y. Yeung, *J. Am. Chem. Soc.*, 2010, **132**, 15474; (*m*) W. Zhang, S. Zheng, N. Liu, J. B. Werness, I. A. Guzei and W. J. Tang, *J. Am. Chem. Soc.*, 2010, **132**, 3664; (*n*) D. C. Whitehead, R. Yousefi, A. Jaganathan and B. Borhan, *J. Am. Chem. Soc.*, 2010, **132**, 3298.

3 (*a*) N. A. Cochrane, H. Nguyen and M. R. Gagné, *J. Am. Chem. Soc.*, 2013, **135**, 628; (*b*) M. T. Bovino and S. R. Chemler, *Angew. Chem., Int. Ed.*, 2012, **51**, 3923; (*c*) H. J. Lee and D. Y. Kim, *Tetrahedron Lett.*, 2012, **53**, 6984; (*d*) Y. Cai, X. Liu, Y. Hui, J. Jiang, W. Wang, W. Chen, L. Lin and X. Feng, *Angew. Chem., Int. Ed.*, 2010, **49**, 6160; (*e*) S. H. Kang, C. M. Park, S. B. Lee and M. Kim, *Synlett*, 2004, 1279; (*f*) S. H. Kang, S. B. Lee and C. M. Park, *J. Am. Chem. Soc.*, 2003, **125**, 15748; (*g*) O. Kitagawa, T. Hanano, K. Tanabe, M. Shiro and T. Taguchi, *J. Chem. Soc., Chem. Commun.*, 1992, 1005.

4 (*a*) H. Cui, Z. Chai, G. Zhao and S. Zhu, *Chin. J. Chem.*, 2009, **27**, 189; (*b*) C. Jonasson, A. Horváth and J.-E. Bäckvall, *J. Am. Chem. Soc.*, 2000, **122**, 9600; (*c*) X. Zhang, C. Fu, Y. Yu and S. Ma, *Chem.–Eur. J.*, 2012, **18**, 13501; (*d*) B. Lü, X. Jiang, C. Fu and C. Ma, *J. Org. Chem.*, 2009, **74**, 438; (*e*) B. Gockel and N. Krause, *Eur. J. Org. Chem.*, 2010, 311.

5 (*a*) K. L. Butler, M. Tragni and R. A. Widenhoefer, *Angew. Chem., Int. Ed.*, 2012, **51**, 5175; (*b*) L.-I. Rodríguez, T. Roth, J. Lloret Fillol, H. Wadepohl and L. H. Gade, *Chem.–Eur. J.*, 2012, **18**, 3721; (*c*) K. Aikawa, M. Kojima and K. Mikami, *Adv. Synth. Catal.*, 2010, **352**, 3131; (*d*) R. L. LaLonde, Z. J. Wang, M. Mba, A. D. Lackner and F. D. Toste, *Angew. Chem., Int. Ed.*, 2010, **49**, 598; (*e*) K. Aikawa, M. Kojima and K. Mikami, *Angew. Chem., Int. Ed.*, 2009, **48**, 6073; (*f*) G. L. Hamilton, E. J. Kang, M. Mba and F. D. Toste, *Science*, 2007, **317**, 496; (*g*) Z. Zhang and R. A. Widenhoefer, *Angew. Chem., Int. Ed.*, 2007, **46**, 283; (*h*) R. L. LaLonde, B. D. Sherry, E. J. Kang and F. D. Toste, *J. Am. Chem. Soc.*, 2007, **129**, 2452; (*i*) Z. Zhang, C. F. Bender and R. A. Widenhoefer, *J. Am. Chem. Soc.*, 2007, **129**, 14148.

6 (*a*) L.-P. Liu and G. B. Hammond, *Chem. Soc. Rev.*, 2012, **41**, 3129; (*b*) D. Weber, T. D. Jones, L. L. Adduci and M. R. Gagné,

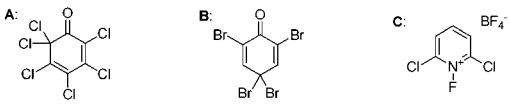
Angew. Chem., Int. Ed., 2012, **51**, 2452; (*c*) T. J. Brown, D. Weber, M. R. Gagné and R. A. Widenhoefer, *J. Am. Chem. Soc.*, 2012, **134**, 9134; (*d*) Z. J. Wang, D. Benitez, E. Tkatchouk, W. A. Goddard III and F. D. Toste, *J. Am. Chem. Soc.*, 2010, **132**, 13064. See also: (*e*) M. W. Johnson, S. L. Shevick, F. D. Toste and R. G. Bergman, *Chem. Sci.*, 2013, **4**, 1023.

7 K. E. Roth and S. A. Blum, *Organometallics*, 2010, **29**, 1712.

8 (*a*) R. B. Dateer, K. Pati and R.-S. Liu, *Chem. Commun.*, 2012, **48**, 7200; (*b*) S. G. Sethofer, T. Mayer and F. D. Toste, *J. Am. Chem. Soc.*, 2010, **132**, 8276; (*c*) A. S. K. Hashmi, T. D. Ramamurthi, M. H. Todd, A. S.-K. Tsang and K. Graf, *Aust. J. Chem.*, 2010, **63**, 1619; (*d*) A. S. K. Hashmi, T. D. Ramamurthi and F. Rominger, *J. Organomet. Chem.*, 2009, **694**, 592; (*e*) B. Crone and S. F. Kirsch, *J. Org. Chem.*, 2007, **72**, 5435; (*f*) M. Yu, G. Zhang and L. Zhang, *Org. Lett.*, 2007, **9**, 2147; (*g*) S. F. Kirsch, J. T. Binder, B. Crone, A. Duschek, T. T. Haug, C. Liébert and H. Menz, *Angew. Chem., Int. Ed.*, 2007, **46**, 2310; (*h*) A. Buzas and F. Gagosz, *Org. Lett.*, 2006, **8**, 515.

9 Reaction of **1a** with NIS and NBS for 30 min, in the absence of gold catalyst, afforded **2a** and **3a** in 81% and 43% yields, respectively. Full consumption of **1a** was observed in both cases.

10 Use of other electrophilic halogen sources A, B, and C with added base gave low yields and no ee.



11 An alternative explanation is that the *N*-bromolactams are better H-bond acceptors and, as a result, stabilize the transition state for the bromo-deauration event. We thank a reviewer for this suggestion. For a relevant discussion contrasting pK_a and H-bonding ability see: P. Gill, L. Pretto, V. Bertolasi and G. Gill, *Acc. Chem. Res.*, 2009, **42**, 33.

12 (*a*) Y.-L. Zhong, H. Zhou, D. R. Gauthier, J. Lee, D. Askin, U. H. Dolling and R. P. Volante, *Tetrahedron Lett.*, 2005, **46**, 1099; (*b*) O. V. Larionov, S. I. Kozhushkov and A. D. Meijere, *Synthesis*, 2003, 1916.

13 The low enantioselectivity is presumably a result of the uncatalyzed background reaction between **1a** and *N*-iodopyrrolidinone. A mixture of **1a** and *N*-iodopyrrolidinone without catalyst afforded **2a** in 71% yield after 30 min with full consumption of **1a**.

14 S. Fujisaki, S. Hamura, H. Eguchi and A. Nishida, *Bull. Chem. Soc. Jpn.*, 1993, **66**, 2426.

15 The following catalysts were examined in the formation of **3i**: (*R*)-DTBM-BINAP(AuPNB)$_2$ (20% ee); (*R*)-Cl-MeO-BIPHEP-(AuPNB)$_2$ (65% ee); (*R*)-BINAP(AuPNB)$_2$ (68% ee).

16 Reaction of **1i** with **6a** and **6c**, in the absence of gold catalyst, produced **3i** in 45% and 39% conversion, respectively, after 1 h. This observation suggests that the change in enantioselectivity is not only due to a difference in the relative rate of the non-catalyzed background reaction.

17 Z. Zhang, C. Liu, R. E. Kinder, X. Han, H. Qian and R. A. Widenhoefer, *J. Am. Chem. Soc.*, 2006, **128**, 9066.

18 For reviews on chiral anions in asymmetric catalysis, see: (*a*) R. J. Phipps, G. L. Hamilton and F. D. Toste, *Nat. Chem.*, 2012, **4**, 603; (*b*) K. Brak and E. N. Jacobsen, *Angew. Chem., Int. Ed.*, 2013, **52**, 534; (*c*) M. Mahlau and B. List, *Angew. Chem., Int. Ed.*, 2013, **52**, 518.

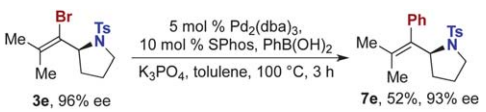
19 The absolute stereochemistry of **3b**, as determined by X-ray crystallography, is consistent with that produced in the bisphosphinegold(I) 4-nitrobenzoate catalyzed hydroamination reactions in ref. 5*h*.

20 The slightly lower ee in the aminobromination may come from the background reaction: at the point when the catalyzed reaction was substantially complete (2.75 h), **3a** was produced in 5% yield in the absence of the catalyst.

21 While this paper was under review, Lalic and coworkers reported the observation of a vinylgold intermediate as the resting state in gold-catalyzed hydroaloxylation of allenes, further supporting this hypothesis. N. Cox, M. R. Uehling, K. T. Haelsig and G. Lalic, *Angew. Chem., Int. Ed.*, 2013, **52**, 4878.

22 For examples of cycloreversion of isolated gold complexes see: (*a*) R. L. LaLonde, W. E. Brenzovich, D. Benitez, E. Tkatchouk, K. Kelley, W. A. Goddard and F. D. Toste, *Chem. Sci.*, 2010, **1**, 226; (*b*) Y. Shi, K. E. Roth, S. D. Ramgren and S. A. Blum, *J. Am. Chem. Soc.*, 2008, **131**, 18022 and ref. 6*c*.

23 For example, palladium-catalyzed reaction of **3e** (prepared by (*R*)-BINAP(AuPNB)$_2$-catalyzed aminobromination) with phenylboronic acid afforded **7e** in moderate yield with only a slight decrease in enantiopurity.



3e, 96% ee **7e**, 52%, 93% ee