Efficient gold(I)/silver(I)-cocatalyzed cascade inter-molecular N-Michael addition/intramolecular hydroalkylation of unactivated alkenes with α-ketones

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Full Research Paper

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Abstract

The gold(I)/silver(I)-cocatalyzed cascade intermolecular N-Michael addition/intramolecular hydroalkylation reaction offers a simple and efficient method for the synthesis of pyrrolidine derivatives in moderate to excellent product yields and with moderate to good diastereoselectivities. The reaction conditions and the substrate scope of this reaction are examined, and a possible mechanism involving $AgClO_4$ catalyzed intermolecular N-Michael addition and the subsequent gold(I)-catalyzed hydroalkylation is proposed.

Introduction

Gold complexes are presently receiving a surge of interest in the field of metal-catalyzed organic reactions. They have been shown to be versatile and efficient catalysts for the promotion of a large number of organic transformations, most of which are based on the propensity of gold ion to act as a soft and carbophilic Lewis acid to activate unsaturated C–C bonds towards nucleophilic attack [1-10] (for selected reviews on gold-catalyzed reactions see [1-9]). Based on this mode of acti-

vation, several methods for the gold-catalyzed inter- and intramolecular addition of oxygen- [11-15], nitrogen- [10,16-18] (for recent reviews on gold-catalyzed hydroamination see [16-18]), or carbon-nucleophiles [19-24] to unactivated alkenes [21-25] have been developed. On the other hand, in recent years, considerable efforts have been devoted to the development of dual-metal-catalyzed reactions as new strategies for the synthesis of organic compounds with intriguing diversity and selectivity [26-29] (for reviews on cooperative catalysis see [26,27] and for a general review on cocatalysis see [28]). This type of reaction could have the advantages of the combined characteristic features of two metals, often displaying unique reactivity, have a shortened synthetic route and generate less chemical waste. All of these features are of significant economic and environmental benefit. In this context, extensive studies have been conducted on the design and utilization of dual-metal catalyst systems in organic synthesis [26-40] (for recent examples of Au/Pd-cocatalysis see [30-33]; for Au/Mo-cocatalysis see [31,35]; for Au/Ag-cocatalysis see [36-38]; for Au/Yb-cocatalysis see [39] and for Au/Rh-cocatalysis see [40]). However, the use of homogeneous gold catalysts in cooperation with other metal catalysts has been reported only in a few cases [30-40]. In this work, we describe a highly efficient gold(I)/silver(I)-cocatalyzed cascade intermolecular N-Michael addition/intramolecular hydroalkylation process. A variety of pyrrolidine compounds were conveniently prepared in moderate to excellent yields and with moderate to good diastereoselectivities from the simple starting materials.

More recently, we have reported that gold(I) complexes can efficiently catalyze direct intramolecular hydroalkylation of unactivated alkenes with α-ketones, via the exo-trig cyclization, to build a variety of new five- and six-membered rings [24]. However, all of the substrates examined in this gold(I)-catalyzed reaction were prepared and isolated prior to use, and this is not desirable as the synthesis of these substrates could be tedious and time-consuming. The increasing demand for environmentally benign and economical synthetic processes calls for the development of cascade reactions for the efficient construction of cyclic compounds from simple starting materials [41]. We initially envisioned that the gold(I)-catalyzed cascade process could be established starting from the intermolecular N-Michael reaction of α,β-unsaturated ketone **1** and substituted allylamine **2** to furnish an α-ketone intermediate **I** [42-44] (for gold-catalyzed intramolecular N-Michael reaction see [42,43]), which further undergoes a subsequent gold(I)-catalyzed hydroalkylation to give pyrrolidine compounds **3** (Scheme 1); these compounds are versatile synthetic building blocks for organic synthesis and are important structural elements of many therapeutic drug molecules. Disappointingly, no conversion was observed when (*t*-Bu)$_2$(*o*-diphenyl)PAuOTf
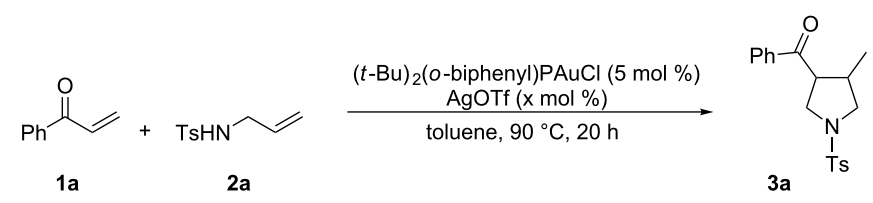
only was used as the catalyst. Since dual-metal-catalysis is of interest from the perspective of unique reactivity [26-40], we explored a new cascade reaction involving intermolecular N-Michael addition catalyzed by an appropriate transition metal salt and subsequent intramolecular hydroalkylation catalyzed by a gold complex (Scheme 1).
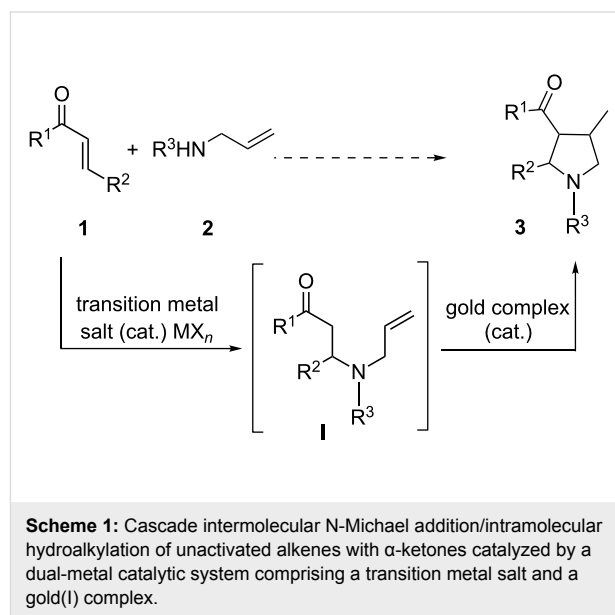
Scheme 1: Cascade intermolecular N-Michael addition/intramolecular hydroalkylation of unactivated alkenes with α-ketones catalyzed by a dual-metal catalytic system comprising a transition metal salt and a gold(I) complex.

Results and Discussion

The optimization of the reaction conditions was performed using the reaction of phenyl vinyl ketone (**1a**) with N-tosylallylamine (**2a**) in the presence of 5 mol % of (*t*-Bu)$_2$(*o*-diphenyl)PAuOTf. However, no desired product **3a** was observed (Table 1, entry 1). When using a combination of 5 mol % of (*t*-Bu)$_2$(*o*-diphenyl)PAuCl and AgOTf as catalyst, the corresponding product **3a** was obtained in 25% yield (Table 1, entry 2) (a small amount of silver salt may have remained in the reaction system when the mol ratio of silver salt to gold complex was 1:1, see [45]). Upon further increase of the AgOTf loading to 10 mol %, the corresponding product **3a** was formed in 58% yield with a diastereomeric ratio of 5.4:1 (Table 1, entry 3) [46]. Using a combination of 5 mol % of (*t*-Bu)$_2$(*o*-diphenyl)PAuCl and 15 mol % of AgOTf as a dual-metal catalyst system lead to the formation of pyrrolidine derivative **3a** as a 5.3:1 mixture of two diastereomers in 67% yield (Table 1, entry 4). The yield increased from 58% to 67% as the mol ratio of **2a** to **1a** was increased from 1.2/1 to 1.5/1 (Table 1, entries 4 and 5). However, the yield did not increase remarkably when the mol ratio of **2a** to **1a** was raised from 1.5/1 to 2.5/1 (Table 1, entries 4–7). As depicted in Table 1, varying the method of the addition of phenyl vinyl ketone (**1a**) to the reaction mixture did not have a noticeable effect on the yield of **3a** (Table 1, entries 8–11).
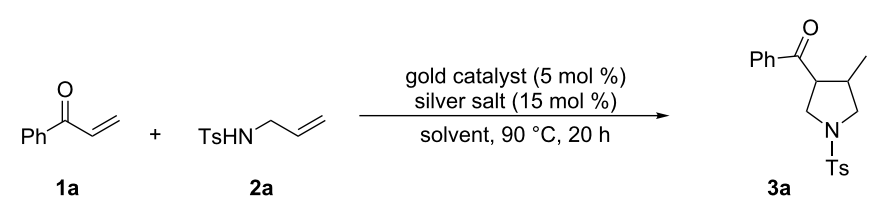
Table 1: The optimization of the reaction conditions.

entry[a]	x (mol %)	mol ratio (**2a**/**1a**)	*trans/cis*[b]	yield (%)[b]
1[c]	5	1.5/1	–	–[d]
2	5	1.5/1	1.4:1	25
3	10	1.5/1	5.4:1	58
4	15	1.5/1	5.3:1	67
5	15	1.2/1	5.7:1	58
6	15	2.0/1	5.9:1	66
7	15	2.5/1	5.5:1	64
8	15	1/1.5	5.5:1	64
9[e]	15	1/1.5	5.2:1	60
10[f]	15	1/1.5	5.5:1	65
11[g]	15	1/1.5	5.5:1	64

[a]Reactions were carried out in toluene (0.5 mL) at 0.25 mmol scale based on **1a** or **2a**, **1a** was added in one portion. [b]Yield and selectivity were determined by ^{1}H NMR spectroscopy (internal standard: trimethyl(phenyl)silane). [c]5 mol % of (*t*-Bu)$_2$(*o*-diphenyl)PAuOTf was used as catalyst. [d]no desired product **3a** was detected. [e]**1a** (dissolved in 0.3 mL of toluene) was added dropwise over 6 h. [f]**1a** was added in two portions every 3 h. [g]**1a** was added in three portions every 2 h.

To identify further the optimal reaction conditions for the gold(I)/silver(I)-cocatalyzed cascade reaction, a number of dual-metal catalyst systems, composed of 15 mol % of silver salt with 5 mol % of gold(I) complex in different organic solvents, were tested in the reaction of phenyl vinyl ketone (**1a**) with 1.5 equiv of *N*-tosylallylamine (**2a**) (Table 2). AgClO$_4$ was found to be the best silver salt for this reaction (Table 2, entries 1–5). A panel of Au(I) complexes with different ancillary ligands was also screened for activity and diastereo-induction in this cascade reaction (Table 2, entries 5–9). Among the

complexes examined, (*t*-Bu)$_2$(*o*-biphenyl)PAuCl gave the best result (Table 2, entry 5). Further screening of solvents revealed that toluene gave the best result, while the other solvents, dioxane, nitromethane, 1,2-dichloroethane, tetrahydrofuran, benzene, and acetonitrile, gave low product yields and low diastereoselectivity (Table 2, entries 5 and 10–15). After optimization of the reaction conditions, the protocol with the combination of 5 mol % of (*t*-Bu)$_2$(*o*-biphenyl)PAuCl and 15 mol % of AgClO$_4$ as a dual-metal catalyst system at 90 °C in toluene for 20 h gave the product **3a** in 76% yield.

Table 2: Screening catalysts and solvents.

entry[a]	gold catalyst/silver salt	solvent	*trans/cis*[b]	yield (%)[b]
1	(*t*-Bu)$_2$(*o*-biphenyl)PAuCl/AgOTf	toluene	5.3:1	67
2	(*t*-Bu)$_2$(*o*-biphenyl)PAuCl/AgSbF$_6$	toluene	2.2:1	35
3	(*t*-Bu)$_2$(*o*-biphenyl)PAuCl/AgPF$_6$	toluene	2.6:1	62
4	(*t*-Bu)$_2$(*o*-biphenyl)PAuCl /AgBF$_4$	toluene	–	<5

Table 2: Screening catalysts and solvents. (continued)

5	**(t-Bu)₂(o-biphenyl)PAuCl/AgClO₄**	**toluene**	**4.1:1**	**76**
6	Ph₃PAuCl/AgClO₄	toluene	–	<5
7	Cy₃PAuCl/AgClO₄	toluene	–	<5
8	IPrAuCl/AgClO₄[c]	toluene	4.4:1	63
9	L¹AuCl/AgClO₄[d]	toluene	3.1:1	50
10	(t-Bu)₂(o-biphenyl)PAuCl/AgClO₄	dioxane	4.0:1	63
11	(t-Bu)₂(o-biphenyl)PAuCl/AgClO₄	CH₃NO₂	2.8:1	47
12[e]	(t-Bu)₂(o-biphenyl)PAuCl/AgClO₄	DCE	1.8:1	34
13[e]	(t-Bu)₂(o-biphenyl)PAuCl/AgClO₄	THF	1.8:1	76
14[e]	(t-Bu)₂(o-biphenyl)PAuCl/AgClO₄	benzene	3.2:1	60
15[e]	(t-Bu)₂(o-biphenyl)PAuCl/AgClO₄	CH₃CN	–	<5

[a]Reactions were carried out in toluene (0.5 mL) at 0.25 mmol scale, **1a** (0.25 mmol) and **2a** (0.375 mmol) were added in one portion. [b]Yield and selectivity were determined by ¹H NMR spectroscopy (internal standard: trimethyl(phenyl)silane). [c]IPr= *N,N'*-bis(2,6-diisopropylphenyl)imidazol-2-ylidene. [d]L¹ = (Cy)₂(2',4',6'-triisopropyl-*o*-biphenyl)P. [e]Reactions were carried out under reflux.

With the optimal reaction conditions, we next explored the substrate scope with the protocol for the Au(I)/Ag(I)-cocatalytic system (Table 3). For example, treatment of substrate **1b**, which has an electron-donating *para*-methoxy group on the phenyl ring, with **2a** under the optimized reaction conditions gave the expected product **3b** in 92% yield, albeit with no diastereoselectivity (Table 3, entry 2). In addition to substrate **1b**, α,β-unsaturated ketone **1c**, with electron-withdrawing substituent on the phenyl ring, underwent this cascade reaction to afford the corresponding product **3c** in 58% yield with a diastereomeric ratio of 1.7:1 (Table 3, entry 3). Reaction of alkyl α,β-unsaturated ketone **1d** in the presence of 5 mol % of (*t*-Bu)₂(*o*-

Table 3: Cascade synthesis of pyrrolidine catalyzed by a dual-metal catalytic system comprising of gold(I) and silver(I) catalysts.
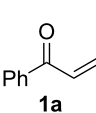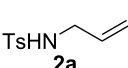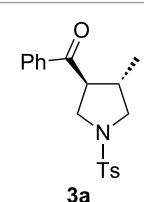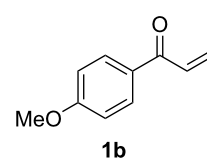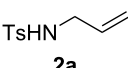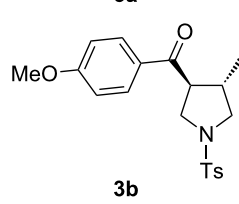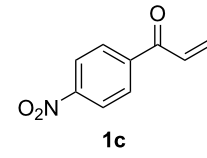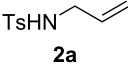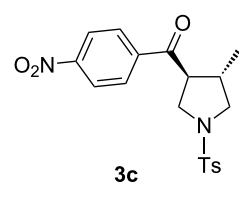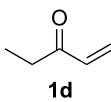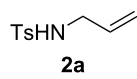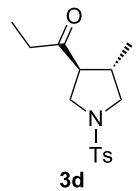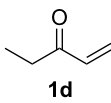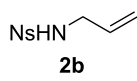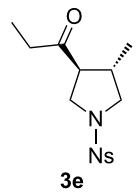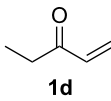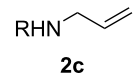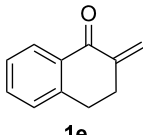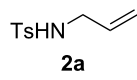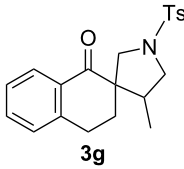
entry[a]	α,β-unsaturated ketone	substituted allylamine	major product	dr[b]	yield (%)[b]
1	**1a**	**2a**	**3a**	4.1:1	76
2	**1b**	**2a**	**3b**	1.0:1	92
3	**1c**	**2a**	**3c**	1.7:1	58

Table 3: Cascade synthesis of pyrrolidine catalyzed by a dual-metal catalytic system comprising of gold(I) and silver(I) catalysts. (continued)

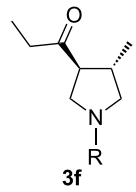| 4 | 1d | 2a | 3d | 5.5:1 | 92 |
5	1d	2b	3e	5.3:1	76
6[c]	1d	2c	3f	5.2:1	91
7	1e	2a	3g	1.8:1	52

[a]Reactions were carried out in toluene (0.5 mL) at 0.25 mmol scale. The α,β-unsaturated ketone (0.25 mmol) and the substituted allyl amine (0.375 mmol) were added in one portion. [b]Yield and selectivity were determined by ^{1}H NMR spectroscopy (internal standard: trimethyl(phenyl)silane). [c]R = 2,4,6-triisopropylbenzenesulfonyl.

biphenyl)PAuCl and 15 mol % of AgClO$_4$ also gave the desired product **3d** in 92% yield with a diastereomeric ratio of 5.5:1 (Table 3, entry 4). Other substituted allylamines were also examined. A series of substituted allylamines with 4-nitrobenzenesulfonyl group and 2,4,6-triisopropylbenzenesulfonyl group were similarly treated with alkyl α,β-unsaturated ketone **1d**, and the corresponding products **3e** and **3f** were obtained in moderate to excellent yields with similar diastereomeric ratios of around 5.2:1 (Table 3, entries 4–6). Notably, the gold(I)/silver(I)-cocatalyzed cascade reaction was also successfully applied to furnish spirocyclic pyrrolidine derivative **3g** in 52% yield starting from the readily available precursor 2-methylene-3,4-dihydronaphthalen-1(2*H*)-one (**1e**) and *N*-tosylallylamine (**2a**) (Table 3, entry 7).

To gain insight into the mechanism of the gold(I)/silver(I)-cocatalyzed cascade reaction, we first examined the reaction of phenyl vinyl ketone (**1a**) with 1.5 equiv of *N*-tosylallylamine (**2a**) in the presence of 5 mol % of (*t*-Bu)$_2$(*o*-biphenyl)PAuClO$_4$ at 90 °C in toluene for 20 h, however, no desired product **3a** or α-ketone intermediate **4** was observed by ^{1}H NMR analysis of the reaction mixture (Scheme 2, reaction 1). This finding

revealed that the gold(I) complex is ineffective in the catalysis of the intermolecular N-Michael reaction. Upon subsequent treatment of phenyl vinyl ketone (**1a**) with *N*-tosylallylamine (**2a**) in the presence of 10 mol % of AgClO$_4$ at 90 °C for 3 h, the α-ketone intermediate **4** was formed in 85% yield, however, no product **3a** was observed. Even after a longer reaction time (20 h) under the same reaction conditions, **3a** was also not detected, and α-ketone intermediate **4** was isolated in lower yield (66%) (Scheme 2, reaction 2), which may be due to the *retro*-N-Michael reaction [47]. On the other hand, product **3a** and α-ketone intermediate **4** were not observed in the presence of 10 mol % of AgCl under the same reaction conditions (Scheme 2, reaction 3), revealing that the newly formed AgCl from the reaction of (*t*-Bu)$_2$(*o*-biphenyl)PAuCl and AgClO$_4$ did not affect the reaction. All the results demonstrated the dual roles of the silver salt that serves firstly to abstract the coordinated Cl$^-$ ligand, to give a reactive gold catalyst, and secondly to act as an efficient catalyst for the intermolecular N-Michael addition.

On the basis of these observations and our previous work on gold(I)-catalyzed intramolecular hydroalkylation of unactivated
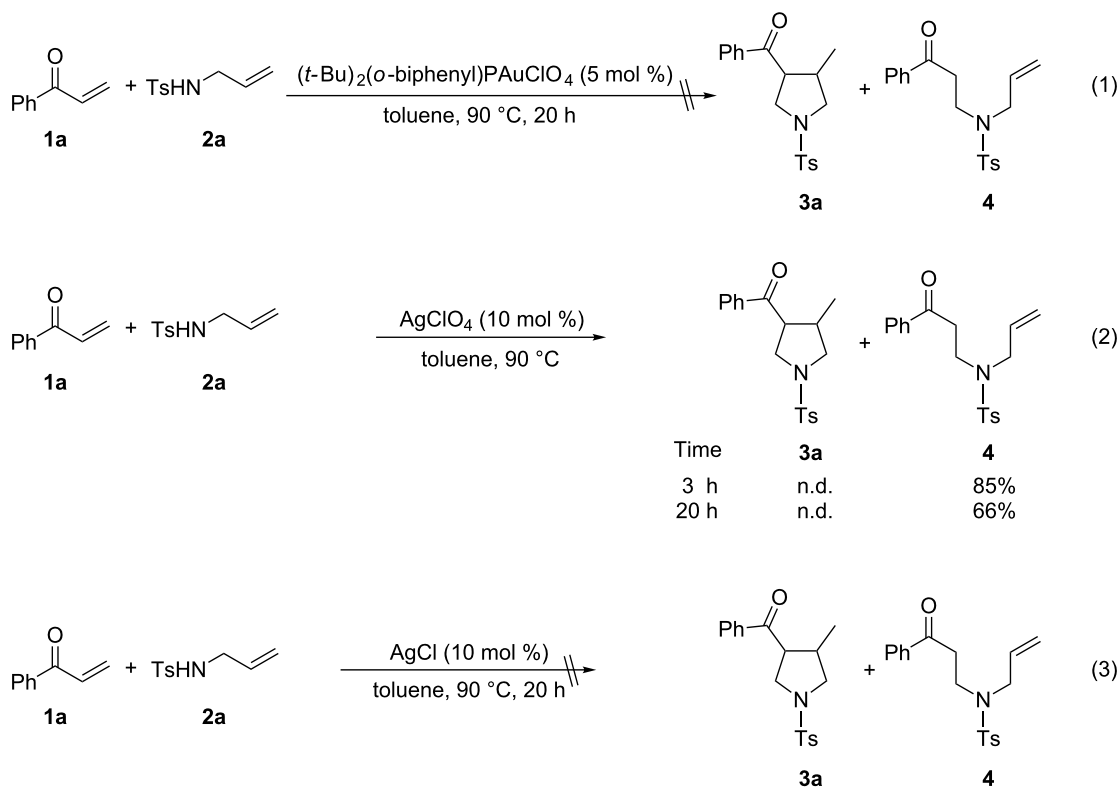
Scheme 2: Some control experiments.

alkenes with α-ketones [24], a reaction mechanism for the formation of pyrrolidine **3** from the reaction of α,β-unsaturated ketone **1** with substituted allylamine **2** is proposed (Scheme 3), which involves silver-catalyzed intermolecular N-Michael addition of substituted allylamine **2** to α,β-unsaturated ketone **1** to generate the α-ketone intermediate **I** and subsequent gold(I)-catalyzed intramolecular hydroalkylation of the α-ketone intermediate **I** to form the cyclic compound **3** (Scheme 3).
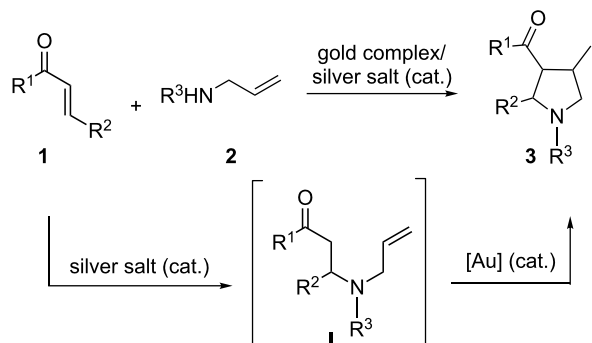
Scheme 3: The reaction pathway.

Conclusion

In summary, we have developed a simple and efficient gold(I)/silver(I)-cocatalyzed cascade intermolecular N-Michael addition/intramolecular hydroalkylation reaction. The present protocol with a dual-metal catalytic system provides a highly efficient method for the synthesis of a variety of pyrrolidine compounds in moderate to excellent product yields and with moderate to good diastereoselectivities from α,β-unsaturated ketones and substituted allylamines. Further studies to expand the substrate scope are currently in progress.

Supporting Information

Supporting Information File 1

Experimental section and spectra of compounds.
[http://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-7-126-S1.pdf]

Acknowledgements

References

1. Gorin, D. J.; Toste, F. D. *Nature* **2007,** *446,* 395–403. doi:10.1038/nature05592

2. Hashmi, A. S. K. *Chem. Rev.* **2007,** *107,* 3180–3211. doi:10.1021/cr000436x

3. Li, Z.; Brouwer, C.; He, C. *Chem. Rev.* **2008,** *108,* 3239–3265. doi:10.1021/cr068434l

4. Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008,** *108,* 3326–3350. doi:10.1021/cr0684319

5. Gorin, D. J.; Sherry, B. D.; Toste, F. D. *Chem. Rev.* **2008,** *108,* 3351–3378. doi:10.1021/cr068430g

6. Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2010,** *49,* 5232–5241. doi:10.1002/anie.200907078

7. Corma, A.; Leyva-Perez, A.; Sabater, M. J. *Chem. Rev.* **2011,** *111,* 1657–1712. doi:10.1021/cr100414u

8. Krause, N.; Winter, C. *Chem. Rev.* **2011,** *111,* 1994–2009. doi:10.1021/cr1004088

9. Bandini, M. *Chem. Soc. Rev.* **2011,** *40,* 1358–1367. doi:10.1039/c0cs00041h

10. LaLonde, R. L.; Brenzovich, J. W. E.; Benitez, D.; Tkatchouk, E.; Kelley, K.; Goddard, W. A., III; Toste, F. D. *Chem. Sci.* **2010,** *1,* 226–233. doi:10.1039/c0sc00255k

11. Yang, C.-G.; He, C. *J. Am. Chem. Soc.* **2005,** *127,* 6966–6967. doi:10.1021/ja050392f

12. Nguyen, R.-V.; Yao, X.; Li, C.-J. *Org. Lett.* **2006,** *8,* 2397–2399. doi:10.1021/ol0607692

13. Hashmi, A. S. K.; Schäfer, S.; Wölfle, M.; Diez Gil, C.; Fischer, P.; Laguna, A.; Blanco, M. C.; Gimeno, M. C. *Angew. Chem., Int. Ed.* **2007,** *46,* 6184–6187. doi:10.1002/anie.200701521

14. Zhang, X.; Corma, A. *Chem. Commun.* **2007,** 3080–3082. doi:10.1039/b706961h

15. Aponick, A.; Li, C.-Y.; Biannic, B. *Org. Lett.* **2008,** *10,* 669–671. doi:10.1021/ol703002p

16. Widenhoefer, R. A.; Han, X. *Eur. J. Org. Chem.* **2006,** 4555–4563. doi:10.1002/ejoc.200600399

17. Widenhoefer, R. A. *Chem.–Eur. J.* **2008,** *14,* 5382–5391. doi:10.1002/chem.200800219

18. Krause, N.; Belting, V.; Deutsch, C.; Erdsack, J.; Fan, H. T.; Gockel, B.; Hoffmann-Röder, A.; Morita, N.; Volz, F. *Pure Appl. Chem.* **2008,** *80,* 1063–1069. doi:10.1351/pac200880051063

19. Yao, X.; Li, C.-J. *J. Am. Chem. Soc.* **2004,** *126,* 6884–6885. doi:10.1021/ja0482637

20. Nguyen, R.-V.; Yao, X.-Q.; Bohle, D. S.; Li, C.-J. *Org. Lett.* **2005,** *7,* 673–675. doi:10.1021/ol047543o

21. Zhou, C.-Y.; Che, C.-M. *J. Am. Chem. Soc.* **2007,** *129,* 5828–5829. doi:10.1021/ja070027j

22. Wang, M.-Z.; Wong, M.-K.; Che, C.-M. *Chem.–Eur. J.* **2008,** *14,* 8353–8364. doi:10.1002/chem.200800040

23. Xiao, Y.-P.; Liu, X.-Y.; Che, C.-M. *J. Organomet. Chem.* **2009,** *694,* 494–501. doi:10.1016/j.jorganchem.2008.07.035

24. Xiao, Y.-P.; Liu, X.-Y.; Che, C.-M. *Angew. Chem., Int. Ed.* **2011,** *50,* 4937–4941. doi:10.1002/anie.201100044

25. Liu, X.-Y.; Li, C.-H.; Che, C.-M. *Org. Lett.* **2006,** *8,* 2707–2710. doi:10.1021/ol060719x

26. Van den Beuken, E. K.; Feringa, B. L. *Tetrahedron* **1998,** *54,* 12985–13011. doi:10.1016/S0040-4020(98)00319-6

27. Park, Y. J.; Park, J.-W.; Jun, C.-H. *Acc. Chem. Res.* **2008,** *41,* 222–234. doi:10.1021/ar700133y

28. Lee, J. M.; Na, Y.; Han, H.; Chang, S. *Chem. Soc. Rev.* **2004,** *33,* 302–312. doi:10.1039/b309033g

29. Wasilke, J.-C.; Obrey, S. J.; Baker, R. T.; Bazan, G. C. *Chem. Rev.* **2005,** *105,* 1001–1020. doi:10.1021/cr020018n

30. Shi, Y.; Peterson, S. M.; Haberaecker, W. W., III; Blum, S. A. *J. Am. Chem. Soc.* **2008,** *130,* 2168–2169. doi:10.1021/ja710648b

31. Shi, Y.; Ramgren, S. D.; Blum, S. A. *Organometallics* **2009,** *28,* 1275–1277. doi:10.1021/om801206g

32. Hashmi, A. S. K.; Lothschütz, C.; Döpp, R.; Rudolph, M.; Ramamurthi, T. D.; Rominger, F. *Angew. Chem., Int. Ed.* **2009,** *48,* 8243–8246. doi:10.1002/anie.200902942

33. Shi, Y.; Roth, K. E.; Ramgren, S. D.; Blum, S. A. *J. Am. Chem. Soc.* **2009,** *131,* 18022–18023. doi:10.1021/ja9068497

34. Egi, M.; Yamaguchi, Y.; Fujiwara, N.; Akai, S. *Org. Lett.* **2008,** *10,* 1867–1870. doi:10.1021/ol800596c

35. Ye, L.; Zhang, L. *Org. Lett.* **2009,** *11,* 3646–3649. doi:10.1021/ol901346k

36. Weber, D.; Tarselli, M. A.; Gagné, M. R. *Angew. Chem., Int. Ed.* **2009,** *48,* 5733–5736. doi:10.1002/anie.200902049

37. Weber, D.; Gagne, M. R. *Org. Lett.* **2009,** *11,* 4962–4965. doi:10.1021/ol902116b

38. Ramon, R. S.; Bosson, J.; Diez-Gonzalez, S.; Marion, N.; Nolan, S. P. *J. Org. Chem.* **2010,** *75,* 1197–1202. doi:10.1021/jo902461a

39. Dai, L.-Z.; Shi, M. *Chem.–Eur. J.* **2010,** *16,* 2496–2502. doi:10.1002/chem.200902321

40. Aksın-Artok, Ö.; Krause, N. *Adv. Synth. Catal.* **2011,** *353,* 385–391. doi:10.1002/adsc.201000903

41. Tietze, L. F.; Gordon, B.; Kersten, G. M., Eds. *Domino Reactions in Organic Synthesis;* Wiley-VCH: Weinheim, Germany, 2006.

42. Jung, H. H.; Floreancig, P. E. *J. Org. Chem.* **2007,** *72,* 7359–7366. doi:10.1021/jo071225w

43. Huang, J.; Huang, X.; Liu, B. *Org. Biomol. Chem.* **2010,** *8,* 2697–2699. doi:10.1039/c003734f

44. Kobayashi, S.; Kakumoto, K.; Sugiura, M. *Org. Lett.* **2002,** *4,* 1319–1322. doi:10.1021/ol0256163

45. Lin, G.-Y.; Li, C.-W.; Hung, S.-H.; Liu, R.-S. *Org. Lett.* **2008,** *10,* 5059–5062. doi:10.1021/ol802047g

46. The control experiment was suggested by one reviewer. We used the product **3a** with a diastereomeric ratio of 1.5:1 heated with 5 mol % of (*t*-Bu)$_2$(*o*-diphenyl)PAuCl and 10 mol % of AgOTf in toluene at 90 °C, indeed, we could get a 5.2:1 mixture of two diastereomers after 20 h. The effect of catalyst loading on diastereoselectivity may be due to the silver salt acting as a lewis acid promoting the isomerisation of *cis*-configuration to *trans*-configuration.

47. Gaunt, M. J.; Spencer, J. B. *Org. Lett.* **2001,** *3,* 25–28. doi:10.1021/ol0066882