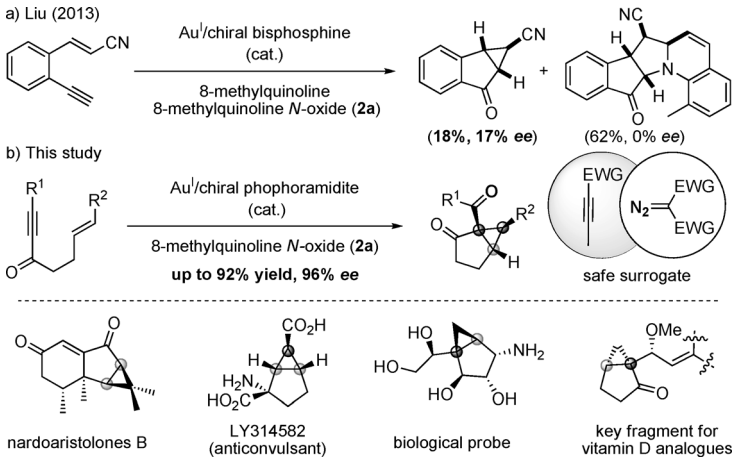
Asymmetric Catalysis

DOI: 10.1002/anie.201407717

Gold(I)-Catalyzed Highly Diastereo- and Enantioselective Alkyne Oxidation/Cyclopropanation of 1,6-Enynes**

*Deyun Qian, Haoxiang Hu, Feng Liu, Bin Tang, Weimin Ye, Yidong Wang, and Junliang Zhang**

Abstract: *A highly enantioselective oxidative cyclopropanation of 1,6-enynes catalyzed by cationic Au^I/chiral phophoramidite complexes is presented. The new method provides convenient access to densely functionalized bicyclo[3.1.0]hexanes bearing three contiguous quaternary and tertiary stereogenic centers with high enantioselectivity (up to e.r. 98:2). Control experiments suggest that the quinoline moiety of the β-gold vinyloxyquinolinium intermediate in the reaction plays an important role in promoting good enantioselectivity through a transitional auxiliary effect in the transition state.*



Scheme 1. Intramolecular cyclopropanation of enynes by gold(I)-catalyzed alkyne oxidation for the asymmetric synthesis of bicyclo[3.1.0]hexanes, and examples of compounds containing a bicyclo[3.1.0]hexane ring system. EWG = electron-withdrawing group.

Asymmetric cyclopropanation (ACP) of olefins with metallocarbenes serves as a bedrock for synthetic chemistry.[1] In this context, the intramolecular ACP reaction of linear unsaturated diazo precursors for the stereoselective construction of [*n*.1.0]bicyclic ring systems has recently attracted renewed attention owing to its fundamental scientific interest and daunting challenge.[1–6] Over the years, remarkable progress has been described in the formation of optically active 3-oxa- and 3-azabicyclo[3.1.0]hexane derivatives.[1,2] More recently, P. Zhang and co-workers successfully developed an intramolecular ACP reaction leading to 3-oxabicyclo[3.1.0]hexanes with diverse substituents by the application of chiral cobalt(II)–porphyrin complexes as metalloradical catalysts.[3] In contrast, highly catalytic ACP reactions with metal carbenoids for the synthesis of bicyclo-[3.1.0]hexanes, in particular those containing a challenging all-carbon quaternary stereocenter,[4] remain comparatively rare,[5] although such enantiomerically enriched skeletons are tremendously important because of their wide occurrence in bioactive natural products, pharmaceuticals, and conformationally restricted biological probes as well as their versatility in organic synthesis as chiral building blocks (Scheme 1, bottom).[5e,6] Thus, a new and complementary approach that enables fast access to such architectures with multifunctionalized stereocenters is still in great demand.

Gold carbenoids, that is, gold carbenes and/or gold-stabilized carbocations, are promising candidates for the ACP reaction and provide complementarity and orthogonality to other traditional-metal carbenoids (e.g., Rh) in that they display increased electrophilicity and are less sterically demanding than their counterparts.[7–9] In 2005, Toste and co-workers reported the first example of an intermolecular ACP reaction exploiting propargyl esters as gold(I)–carbene precursors.[8a] Recently, Briones and Davies[9a] and Zhou and co-workers[9b] presented highly enantioselective cyclopropenation and cyclopropanation, respectively, with donor/acceptor-substituted diazo reagents.

The functionalization of alkynes via α-oxo metal carbenoids generated by alkyne oxidation with pyridine/quinoline *N*-oxides, as pioneered by L. Zhang and co-workers,[10] is considered to be a notable breakthrough in gold catalysis. Moreover, the research groups of Liu,[11a] Li,[11b] and L. Zhang,[11c] as well as our own,[11d] have independently demonstrated oxidative intramolecular cyclopropanations of various 1,*n*-enynes with high efficiency.[12] Such transformations provide a safe alternative to the use of diazo compounds as carbene precursors. Despite significant achievements in the functionalization of alkynes by this novel strategy,[13] there was no catalytic enantioselective version of the reaction[14] until Liu and co-workers[15] disclosed a single example of the asymmetric intramolecular cyclopropanation of a 1,5-enyne, although unfortunately to afford the cyclopropane as a by-

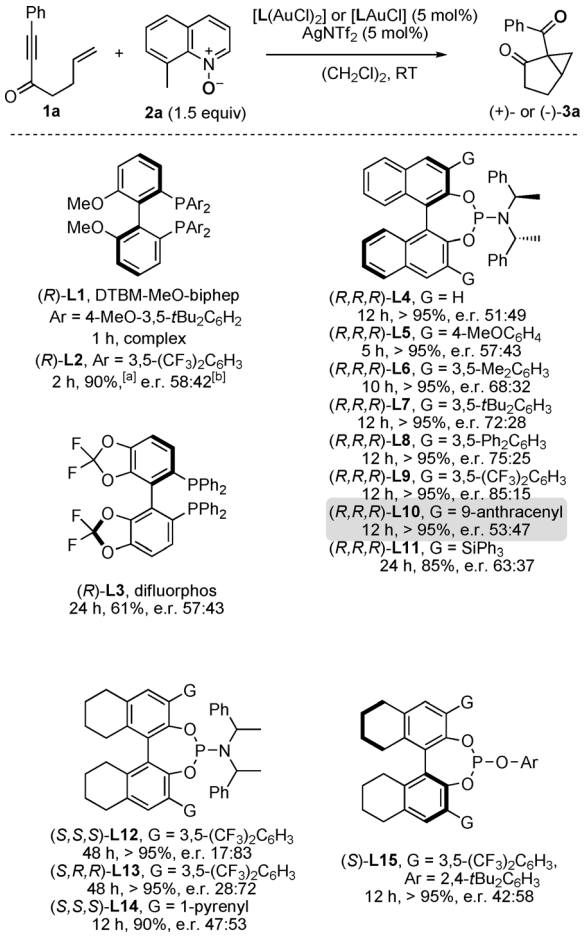
[*] D. Qian, H. Hu, F. Liu, B. Tang, W. Ye, Y. Wang, Prof. J. Zhang
Shanghai Key Laboratory of Green Chemistry and Chemical Processes
Department of Chemistry, East China Normal University
Shanghai 200062 (P.R. China)
E-mail: jlzhang@chem.ecnu.edu.cn

[**] We are grateful to the 973 Programs (2011CB808600), the National Natural Science Foundation of China (21372084), the STCSM (12XD1402300), and the ECNU "Scholarship Award for Excellent Doctoral Students" (xrzz2013022) for financial support.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201407717.

product with only 17% *ee* (Scheme 1a). Herein, we describe a highly diastereo- and enantioselective intramolecular cyclopropanation of 1,6-enynes through gold(I)-catalyzed alkyne oxidation with a chiral phophoramidite ligand.[16] The reaction leads to optically active bicyclo[3.1.0]hexane-2-ones containing three contiguous quaternary and tertiary stereogenic centers (Scheme 1b).[4] Control experiments revealed that the β-gold vinyloxyquinolinium intermediate rather than the generally proposed gold carbene is involved in the enantiodetermining step. Furthermore, the new method features a practical one-pot protocol without the slow addition of substrates;[2] that is, ynones can be visualized as safe and reliable surrogates for acceptor/acceptor diazo compounds.

Our initial study began with 1,6-enyne **1a** as a model substrate and 8-methylquinoline *N*-oxide (**2a**) as the external oxidant.[11d] Gold(I) complexes derived from chiral phosphoramidite ligands were tested, and satisfactory control of the enantioselectivity was observed. Selected representative reaction conditions are summarized in Scheme 2. Interestingly, the privileged chiral bisphosphine ligands (*R*)-2,2′-bis(diphenylphosphanyl)-1,1′-binaphthyl ((*R*)-binap) and **L1**–**3** used in previous gold(I)-catalyzed asymmetric cyclopropanation reactions[8,9] did not induce high enantioselectivity. The introduction of substituents at the 3- and 3′-positions of the binaphthol moiety increased the enantiomeric ratio of the product: Ligand (*R*,*R*,*R*)-**L9** with two electron-deficient aryl substituents afforded (+)-**3a** with up to e.r. 85:15. The use of H_8-binol analogues **L12**–**L15** did not improve the result. We explored other chiral-ligand backbones and found that the spirobiindane phosphoramidite ligand (*R*)-siphos-PE produced (+)-**3a** in 92% yield, but with a low enantiomeric ratio (e.r. 56:44). Further optimization of the reaction conditions (see the Supporting Information) revealed that the *N*-oxide species **2** had an influence on conversion and enantioselectivity (Table 1, entries 1–3), thus indicating that the oxidant



Scheme 2. Investigation of chiral ligands. Reaction conditions: chiral gold complex (5 mol%), $AgNTf_2$ (5 mol%), **1a** (0.20 mmol), **2a** (0.30 mmol), $(CH_2Cl)_2$ (4.0 mL), room temperature. [a] The yield was determined by ^1H NMR spectroscopy. [b] The enantiomeric ratio was determined by HPLC on a chiral stationary phase. Tf = trifluoromethanesulfonyl.

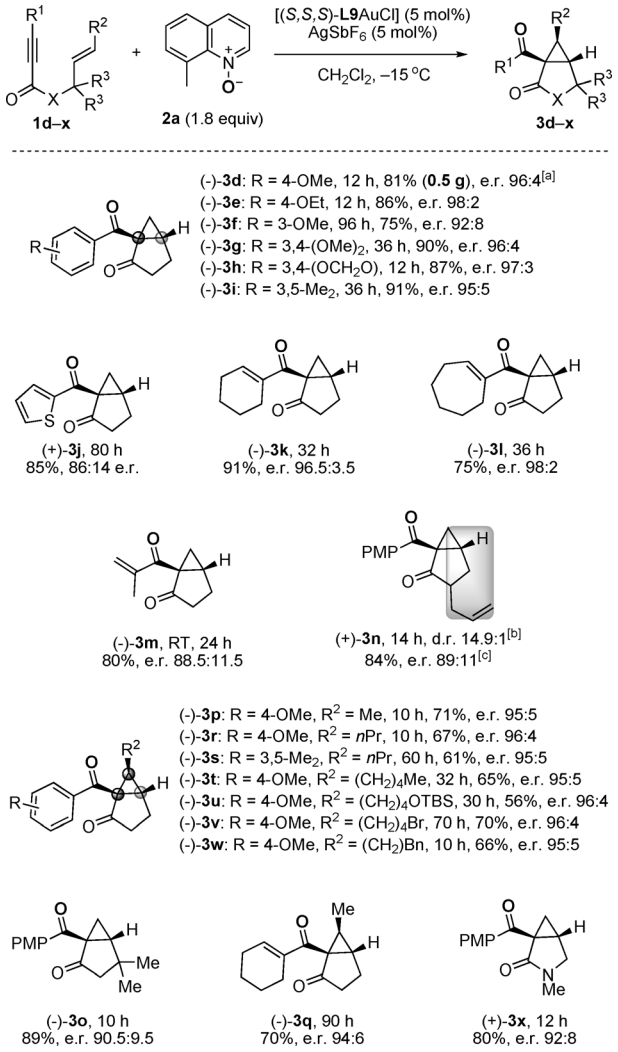
Table 1: Optimization of the reaction conditions.[a]

Entry	R^1, **1**	R	*T* [°C]	*t* [h]	Yield [%][b]	e.r.[c]
1	Ph, **1a**	H	25	70	30	90:10
2	Ph, **1a**	Me	25	10	91	88:12
3	Ph, **1a**	*i*Pr	25	18	90	84:16
4	Ph, **1a**	Me	0	23	91	89:11
5[d]	Ph, **1a**	Me	−15	96	85	93:7
6[d]	4-FC_6H_4, **1b**	Me	−15	96	55	91:9
7[d]	4-MeC_6H_4, **1c**	Me	−15	96	86	94:6
8[d]	4-$MeOC_6H_4$, **1d**	Me	−15	10	92	97:3

[a] Reaction conditions: [(*S*,*S*,*S*)-**L9**AuCl] (5 mol%), $AgSbF_6$ (5 mol%), **1** (0.20 mmol), **2** (0.30 mmol), dichloromethane (4.0 mL). [b] Yield of the isolated product. [c] The enantiomeric ratio was determined by HPLC analysis. [d] The reaction was carried out with **2a** (0.36 mmol) in the presence of 4 Å molecular sieves.

may play a key role in the enantiodetermining step. When the reaction was conducted at −15 °C with 1.8 equivalents of **2a**, the enantiomeric ratio was improved further (Table 1, entry 5). Finally, the enantioselectivity increased with the electron-donating character of the substituent R^1; thus, (−)-**3d** was isolated with e.r. 97:3 in 92% yield (Table 1, entry 8).

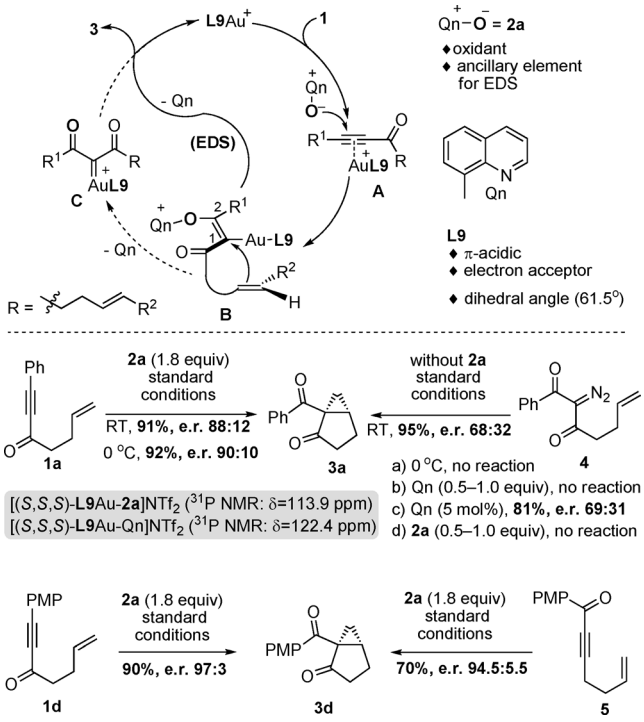
We examined the scope and generality of this asymmetric oxidative cyclopropanation with various 1,6-enynes (Scheme 3). The transformation generally afforded bicyclo-[3.1.0]hexanes with good to excellent enantioselectivity (up to e.r. 98:2). With respect to the substituent at the alkyne terminus (R^1), not only substituted phenyl but also thienyl and vinyl-substituted enynes (substrates **1e**–**i**, **1j**–**m**) were converted into the desired cyclopropanation products with high yields and e.r. values, although a higher reaction temperature (25 °C) was required for vinyl derivative **1m** for the reaction to reach completion. Notably, the reaction of allyl-substituted substrate **1n** gave **3n** with high diastereoselectivity and enantioselectivity by the strategy of desymmetrization. More importantly, alkyl-substituted alkenes (R^2 = alkyl) that are often unreactive in rhodium-catalyzed cyclo-



Scheme 3. Generality of the reaction. [a] The reaction was carried out with **1d** (2.71 mmol) and [(*S*,*S*,*S*)-**L9**AuCl]/$AgSbF_6$ (4 mol%). [b] The diastereomeric ratio was determined by ^{1}H NMR spectroscopic and HPLC analysis. [c] The minor diastereomer was obtained with e.r. 85.5 : 14.5. PMP = 4-methoxyphenyl. Bn = benzyl, TBS = *tert*-butyldimethylsilyl.

propanation reactions of acceptor/acceptor diazo reagents were successfully transformed into the corresponding cyclopropanes in moderate yields with good to excellent selectivity (substrates **1p**–**w**).[2c] Furthermore, the *N*-methylamide-linked 1,6-enyne **1x** also underwent asymmetric cyclopropanation to form 3-azabicyclo[3.1.0]hexan-2-one **3x** in high yield with high stereoselectivity. All of the above catalytic reactions generated the bicyclo[3.1.0]hexan-2-one products as a single diastereomers. To test the practicality of the methodology, we carried out a large-scale synthesis of chiral bicyclic **3d**. The treatment of **1d** on a 2.7 mmol scale gave the desired product (−)-**3d** in 81% yield with e.r. 96:4.

Two plausible pathways that account for this asymmetric oxidative cyclopropanantion are depicted in Scheme 4 (top). In one mechanism, a chiral gold(I)-derived carbene **C** generated from **B** by back donation from the gold to the C1 center with loss of the quinoline moiety (Qn) is a key

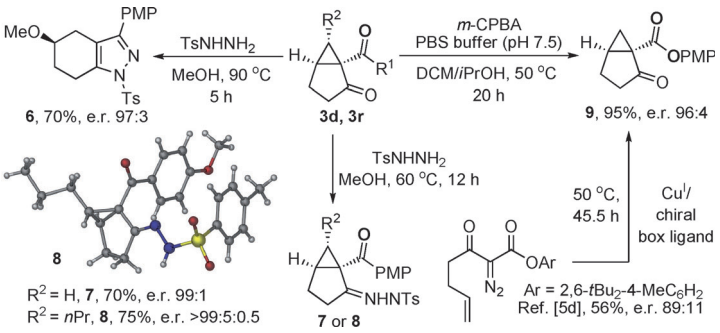


Scheme 4. Possible mechanistic pathway and control experiment. Qn = 8-methylquinoline.

intermediate.[10,11,13] On the other hand, it is possible that species **B** is sufficiently long-lived to undergo enantioselective cyclopropanation through a stepwise or concerted process.[17] To distinguish between these two plausible mechanisms, we examined the gold-catalyzed reactions of the authentic diazo carbonyl species **4** and 1,5-enyne **5**. These reactions led to products **3a** and **3d** with lower enantiomeric ratios (see Table S3 and Schemes S4 and S5 for details). Furthermore, the coordination of the *N*-oxide or quinoline to the gold complex was revealed by a series of NMR spectroscopic experiments (see Scheme S6 and Figures S2 and S3).[13f,h] Consequently, the reaction of diazo compound **4** would be seriously suppressed by **2a**/Qn, thus indicating that the alkyne might be a better ligand for gold than the weakly nucleophilic acceptor/acceptor-substituted diazo compound.[18] These control experiments imply that the pure α-oxo gold carbene **C** may not be the true reactive intermediate in the enantiodetermining step (EDS) and that the quinoline moiety of species **B** is required for this process. The quinoline moiety (Qn) most likely acts as a transient ancillary group in **B** to facilitate both conversion and enantioselectivity through a intramolecular cyclopropanation process. Additionally, the large dihedral angle of **L9** (61.5°) may provide sufficient steric protection to the gold center (see Figure S1), thereby placing the Au center more effectively in a chiral environment.[7,16] Alternatively to what has been generally proposed,[10,11,13] and to take into account the effect of the substituent, the ligand, and the gold fragment in the limiting form **C** and gold-stabilized carbocation,[19] we propose that the reactive intermediate is better pictured as a β-gold vinyloxyquinolinium intermediate **B**. In fact, the mechanistic aspects that determine the outcome of

gold-catalyzed alkyne oxidation are still under debate (gold carbene versus β-gold vinyloxyquinolinium intermediate).[10,11,13] Herein, we offer strong evidence in support of the β-gold vinyloxyquinolinium species rather than the simple gold carbene in the cyclopropanation step.[20]

To further demonstrate synthetic applications of our method, we carried out several transformations of the bicyclo[3.1.0]hexan-2-one derivatives. The reactions proceeded smoothly with no decrease in the enantiomeric ratio (Scheme 5). Furthermore, the relative and absolute configuration of **8** was unambiguously determined to be 1*S*,5*S*,6*S* by X-ray crystal-structure analysis (see Figure S4). The PMP group on the ketone directs the regioselectivity of a subsequent Baeyer–Villiger oxidation to form an ester (e.g., **9**) of the type used as a starting material for the total synthesis of natural products, such as vitamin D_3, carbocyclic nucleosides (e.g. carbovir), and (+)-coronafacic acid.[6a–c] Notably, only modest enantioselectivities have been observed so far for the synthesis of carboxylic acid esters via metal carbenes derived from diazo compounds (up to 78% *ee*), despite the versatility of the use of such carboxylic acid esters.[5d,e]



Scheme 5. Transformation of the product. box = bisoxazoline, *m*-CPBA = *m*-chloroperbenzoic acid, PBS = phosphate-buffered saline, Ts = *p*-toluenesulfonyl.

In summary, we have demonstrated a highly efficient and selective synthesis of enantiomerically enriched bicyclo-[3.1.0]hexan-2-ones through gold(I)-catalyzed asymmetric alkyne oxidation/cyclopropanation. With the readily available chiral phosphoramidite ligand **L9**, a variety of bicyclo-[3.1.0]hexane derivatives containing three contiguous stereocenters with multiple functionalities were obtained with up to e.r. 98:2 under mild conditions. Moreover, the efficiency of ynones as safe surrogates of acceptor/acceptor diazo reagents was recognized. Mechanistic studies suggest that the β-gold vinyloxyquinolinium species contributes to the enantioselectivity of the cyclopropanation. This demonstration of gold(I)-catalyzed alkyne oxidation for asymmetric intramolecular cyclopropanation may open the door for the discovery of other reactions for the enantioselective functionalization of alkynes by oxidation with pyridine/quinoline *N*-oxides.

Received: July 29, 2014
Published online: September 24, 2014

Keywords: alkyne oxidation · carbenoids · cyclopropanation · enantioselectivity · gold

[1] a) M. P. Doyle, D. C. Forbes, *Chem. Rev.* **1998**, *98*, 911; b) H. M. L. Davies, E. G. Antoulinakis, *Org. React.* **2001**, *57*, 1; c) H. Lebel, J. F. Marcoux, C. Molinaro, A. B. Charette, *Chem. Rev.* **2003**, *103*, 977; d) H. Pellissier, *Tetrahedron* **2008**, *64*, 7041; e) *Contemporary Carbene Chemistry* (Eds.: R. A. Moss, M. P. Doyle), Wiley, New York, **2014**.

[2] For seminal studies, see: a) M. P. Doyle, R. J. Pieters, S. F. Martin, R. E. Austin, C. J. Oalmann, P. Müller, *J. Am. Chem. Soc.* **1991**, *113*, 1423; b) M. P. Doyle, R. E. Austin, A. S. Bailey, M. P. Dwyer, A. B. Dyatkin, A. V. Kalinin, M. M. Y. Kwan, S. Liras, C. J. Oalmann, R. J. Pieters, M. N. Protopopova, C. E. Raab, G. H. P. Roos, Q. L. Zhou, S. F. Martin, *J. Am. Chem. Soc.* **1995**, *117*, 5763; c) W. Lin, A. B. Charette, *Adv. Synth. Catal.* **2005**, *347*, 1547.

[3] X. Xu, H. J. Lu, J. V. Ruppel, X. Cui, S. L. de Mesa, L. Wojtas, X. P. Zhang, *J. Am. Chem. Soc.* **2011**, *133*, 15292.

[4] For the construction of stereogenic quaternary centers, see: C. J. Douglas, L. E. Overman, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5363.

[5] a) W. G. Dauben, R. T. Hendricks, M. Luzzio, H. P. Ng, *Tetrahedron Lett.* **1990**, *31*, 6969; b) C. Piqué, B. Fahndrich, A. Pfaltz, *Synlett* **1995**, 491; c) M. Honma, T. Sawada, Y. Fujisawa, M. Utsugi, H. Watanabe, A. Umino, T. Matsumura, T. Hagihara, M. Takano, M. Nakada, *J. Am. Chem. Soc.* **2003**, *125*, 2860; d) H. Takeda, M. Honma, R. Ida, T. Sawada, M. Nakada, *Synlett* **2007**, 579; e) M. Honma, H. Takeda, M. Takano, M. Nakada, *Synlett* **2009**, 1695.

[6] For selected examples, see: a) H. Nemoto, X. M. Wu, H. Kurobei, K. Minemura, M. Ihara, K. Fukumoto, T. Kametani, *J. Chem. Soc. Perkin Trans. 1* **1985**, 1185; b) S. Tanimori, M. Tsubota, M. He, M. Nakayama, *Synth. Commun.* **1997**, *27*, 2371; c) D. F. Taber, R. B. Sheth, W. Tian, *J. Org. Chem.* **2009**, *74*, 2433; d) M.-L. Liu, Y.-H. Duan, Y.-L. Hou, C. Li, H. Gao, Y. Dai, X.-S. Yao, *Org. Lett.* **2013**, *15*, 1000; e) M. J. Marino, L. J. S. Knutsen, M. Williams, *J. Med. Chem.* **2008**, *51*, 1077; f) J. Li, T. L. Lowary, *Org. Lett.* **2008**, *10*, 881; g) A. Toyoda, H. Nagai, T. Yamada, Y. Moriguchi, J. Abe, T. Tsuchida, K. Nagasawa, *Tetrahedron* **2009**, *65*, 10002.

[7] For reviews of enantioselective gold catalysis, see: a) D. J. Gorin, B. D. Sherry, F. D. Toste, *Chem. Rev.* **2008**, *108*, 3351; b) R. A. Widenhoefer, *Chem. Eur. J.* **2008**, *14*, 5382; c) S. Sengupta, X. Shi, *ChemCatChem* **2010**, *2*, 609; d) A. Pradal, P. Y. Toullec, V. Michelet, *Synthesis* **2011**, 1501; e) Y.-M. Wang, A. D. Lackner, F. D. Toste, *Acc. Chem. Res.* **2014**, *47*, 889.

[8] a) M. J. Johansson, D. J. Gorin, S. T. Staben, F. D. Toste, *J. Am. Chem. Soc.* **2005**, *127*, 18002; b) I. D. G. Watson, S. Ritter, F. D. Toste, *J. Am. Chem. Soc.* **2009**, *131*, 2056.

[9] a) J. F. Briones, H. M. L. Davies, *J. Am. Chem. Soc.* **2012**, *134*, 11916; b) Z.-Y. Cao, X. Wang, C. Tan, X.-L. Zhao, J. Zhou, K. Ding, *J. Am. Chem. Soc.* **2013**, *135*, 8197.

[10] a) L. Ye, L. Cui, G. Zhang, L. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 3258; b) B. Lu, C. Li, L. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 14070; c) W. He, C. Li, L. Zhang, *J. Am. Chem. Soc.* **2011**, *133*, 8482.

[11] a) D. Vasu, H.-H. Hung, S. Bhunia, S. A. Gawade, A. Das, R.-S. Liu, *Angew. Chem. Int. Ed.* **2011**, *50*, 6911; *Angew. Chem.* **2011**, *123*, 7043; b) K.-B. Wang, R.-Q. Ran, S.-D. Xiu, C.-Y. Li, *Org. Lett.* **2013**, *15*, 2374; c) K. Ji, L. Zhang, *Org. Chem. Front.* **2014**, *1*, 34; d) D. Qian, J. Zhang, *Chem. Commun.* **2011**, *47*, 11152.

[12] For gold-catalyzed enyne cycloisomerization, see: a) E. Jiménez-Núñez, A. M. Echavarren, *Chem. Rev.* **2008**, *108*, 3326; b) C. Obradors, A. M. Echavarren, *Acc. Chem. Res.* **2014**, *47*, 902.

[13] For selected reviews, see: a) J. Xiao, X. Li, *Angew. Chem. Int. Ed.* **2011**, *50*, 7226; *Angew. Chem.* **2011**, *123*, 7364; b) *Modern Gold Catalyzed Synthesis* (Eds.: A. S. K. Hashmi, F. D. Toste), Wiley-VCH, Weinheim, **2012**; c) L. Zhang, *Acc. Chem. Res.* **2014**, *47*, 877; for other representative examples, see: d) P. W. Davies, A. Cremonesi, N. Martin, *Chem. Commun.* **2011**, *47*, 379; e) D. Qian, J. Zhang, *Chem. Commun.* **2012**, *48*, 7082; f) A. S. K. Hashmi, T. Wang, S. Shi, M. Rudolph, *J. Org. Chem.* **2012**, *77*, 7761; g) S. Ghorpade, M.-D. Su, R.-S. Liu, *Angew. Chem. Int. Ed.* **2013**, *52*, 4229; *Angew. Chem.* **2013**, *125*, 4323; h) G. Henrion, T. E. J. Chavas, X. L. Goff, F. Gagosz, *Angew. Chem. Int. Ed.* **2013**, *52*, 6277; *Angew. Chem.* **2013**, *125*, 6397; i) L. Wang, X. Xie, Y. Liu, *Angew. Chem. Int. Ed.* **2013**, *52*, 13302; *Angew. Chem.* **2013**, *125*, 13544.

[14] For previous endeavors with enantiomerically enriched substrates, see: a) L. Ye, W. He, L. Zhang, *Angew. Chem. Int. Ed.* **2011**, *50*, 3236; *Angew. Chem.* **2011**, *123*, 3294; b) C. Shu, M.-Q. Liu, S.-S. Wang, L. Li, L.-W. Ye, *J. Org. Chem.* **2013**, *78*, 3292; c) C. Shu, L. Li, Y.-F. Yu, S. Jiang, L.-W. Ye, *Chem. Commun.* **2014**, *50*, 2522.

[15] D. B. Huple, S. Ghorpade, R.-S. Liu, *Chem. Eur. J.* **2013**, *19*, 12965.

[16] For reviews on phosphoramidite ligands in asymmetric catalysis, see: a) J. F. Teichert, B. L. Feringa, *Angew. Chem. Int. Ed.* **2010**, *49*, 2486; *Angew. Chem.* **2010**, *122*, 2538; for pioneering studies in gold chemistry, see: b) I. Alonso, B. Trillo, F. López, S. Montserrat, G. Ujaque, L. Castedo, A. Lledós, J. L. Mascareñas, *J. Am. Chem. Soc.* **2009**, *131*, 13020; c) A. Z. Gonzáles, F. D. Toste, *Org. Lett.* **2010**, *12*, 200; d) H. Teller, S. Flügge, R. Goddard, A. Fürstner, *Angew. Chem. Int. Ed.* **2010**, *49*, 1949; *Angew. Chem.* **2010**, *122*, 1993.

[17] An alternative pathway involving sequential enyne cycloisomerization and oxidation of the gold carbenoid intermediate is difficult (see Ref. [11]). For a related theoretical study on stereoselective cyclopropanation by gold carbenoids, see: a) L. Batiste, A. Fedorov, P. Chen, *Chem. Commun.* **2010**, *46*, 3899; b) P. Pérez-Galán, E. Herrero-Gómez, D. T. Hog, N. J. A. Martin, F. Maseras, A. M. Echavarren, *Chem. Sci.* **2011**, *2*, 141.

[18] Diazo compounds bearing two electron-withdrawing groups typically display both low reactivity and poor stereoselectivity in transition-metal-catalyzed carbene-transfer reactions (see Ref. [1–3, 5]).

[19] a) Ref. [13h]; b) D. Benitez, N. D. Shapiro, E. Tkatchouk, Y. Wang, W. A. Goddard III, F. D. Toste, *Nat. Chem.* **2009**, *1*, 482; c) A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2010**, *49*, 5232; *Angew. Chem.* **2010**, *122*, 5360.

[20] For examples of gold-catalyzed alkyne oxidation that do not proceed via gold carbene intermediates (amine *N*-oxides or sulfoxides as oxidants), see: a) E. L. Noey, Y. Luo, L. Zhang, K. N. Houk, *J. Am. Chem. Soc.* **2012**, *134*, 1078; b) B. Lu, Y. Li, Y. Wang, D. H. Aue, Y. Luo, L. Zhang, *J. Am. Chem. Soc.* **2013**, *135*, 8512.

