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Enantioselective Ir^I-Catalyzed Carbocyclization of 1,6-Enynes by the Chiral Counterion Strategy

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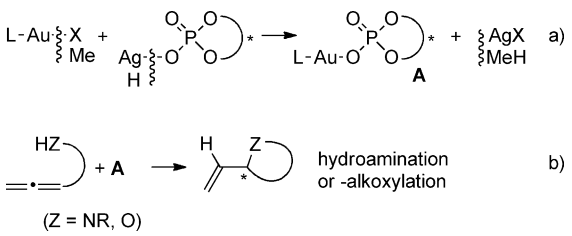
Abstract: Enantioenriched bicyclo-[4.1.0]hept-2-enes were synthesized by Ir^I-catalyzed carbocyclization of 1,6-enynes. No chiral ligands were used, CO and PPh_3 were the only ligands bound to iridium. Instead, the stereochemical information was localized on the counterion of the catalyst, generated in situ by reaction of Vaska's complex (*trans*-$[IrCl(CO)(PPh_3)_2]$) with a chiral silver phosphate. Enantiomeric excesses up to 93% were obtained when this catalytic mixture was used. ^{31}P NMR and IR spectroscopy suggest that formation of the *trans*-$[Ir(CO)(PPh_3)_2]^+$ moiety occurs by chlorine abstraction. Moreover, density functional theory calculations support a 6-*endo*-dig cyclization promoted by this cationic moiety. The chiral phosphate anion (O–P*) controls the enantioselectivity through formation of a loose ion pair with the metal center and establishes a C–H···O–P* hydrogen bond with the substrate. This is a rare example of asymmetric counterion-directed transition-metal catalysis and represents the first application of such a strategy to a C–C bond-forming reaction.

Keywords: chirality · enynes · homogeneous catalysis · ion pairs · iridium

Introduction

Asymmetric counterion-directed transition-metal catalysis is an emergent strategy in organic synthesis.[1] Whether the chiral anion acts as an organocatalyst[2] (for example, by assisting proton transfers) or remains a spectator but generates an asymmetric environment,[3] this new approach has proven to be a powerful tool. Interest in this concept has been notably illustrated by Toste et al. in the field of gold-catalyzed allene cyclizations.[3b,e] Because gold forms linear cationic intermediates of type $[L^*–Au^+···Y][A^-]$, in which L* is an L-type chiral ligand, Y is the substrate, and $[A^-]$ is the counterion, the stereochemical information at L* is remote from Y.[4] Provided the anion can establish a binding interaction with Au^+ or Y, the use of a chiral anion, as in $[L–Au^+···Y][A^{*-}]$, can bring this information closer to the substrate and give rise to highly enantioselective processes.[5] Chiral silver phosphates or phosphoric acids were used for this purpose, which led to gold phosphates of type A after halide abstraction or methane elimination (Scheme 1a).[3b,d,e,h] Such species catalyze enantioselective intramolecular hydroamination or hydroalkoxylation of allenes (Scheme 1b).[3b,e] To the best of our knowledge, the chiral anion strategy has been limited to heterocyclizations. We decided to explore the vast area of carbocyclizations, starting from the typical cycloisomerization of 1,6-enynes.[6]

A large array of products can be obtained from 1,6-enyne substrates, which include chiral members of the bicyclo-[4.1.0]hept-2-ene family (Scheme 2). The success of this transformation, which can be performed by using various metal salts of platinum,[7] gold,[8] rhodium,[9] or iridium,[10] is often critically dependent on the presence of a nitrogen or an oxygen atom in the tether. Asymmetric versions have been reported with chiral platinum–monophosphine,[7k–l]



Scheme 1. Chiral-phosphate-directed gold-catalyzed allene cyclization.

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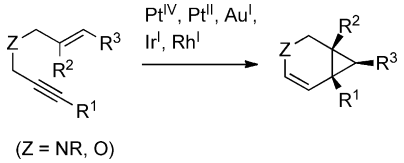
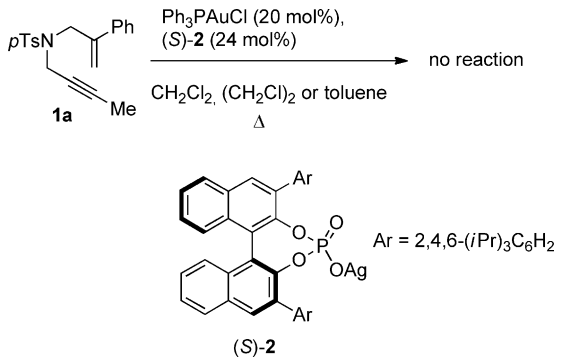


Scheme 2. Cycloisomerization of nitrogen- and oxygen-tethered 1,6-enynes.

gold–bisphosphine,[8e,g] gold–phosphoramidite,[8f] iridium–bisphosphine (under a CO atmosphere),[10] rhodium–tetrafluorobenzobarrelene,[9b] and rhodium–diene–phosphine complexes.[9d]

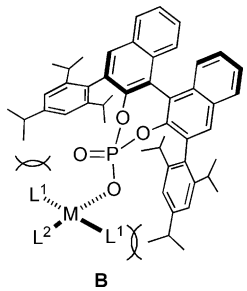
Results and Discussion

Whereas the $Ph_3PAuCl/Ag[SbF_6]$ catalytic mixture promotes the cycloisomerization of nitrogen-bridged enynes,[8a,c] our initial attempts to carry out enantioselective carbocyclizations by using the chiral silver phosphate (*S*)-**2**[3b] were unsuccessful (Scheme 3). No reaction occurred, even after prolonged heating.



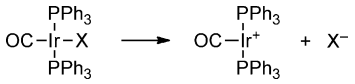
Scheme 3. Attempted chiral-phosphate-directed gold-catalyzed carbocyclization of **1a**.

We hypothesized that, in contrast to the successful heterocyclization process, the impossible formation of a strong O/N–H···O hydrogen bond between the phosphate and a ZH group might go against the dissociation of species **A** (Scheme 1).[11,12] We reasoned that this step would be easier with a square planar active species, such as **B**, because of steric hindrance between the ligands *cis* to the bulky phosphate.


B

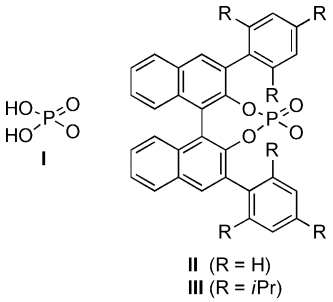
Our hypothesis was corroborated by DFT calculations[13] carried out on species of type **B**, which arise from Vaska's-type complexes, *trans*-$[IrX(CO)(PPh_3)_2]$ (X = phosphate **I**, **II**, or **III**). Estimated gas-phase dissociation energies (ΔE) actually decreased with the steric demand (Table 1).[14]

Table 1. Computed dissociation energies [kcal mol^{-1}].



X	ΔE	ΔH	ΔG
I	113.08	111.62	97.79
II	73.90	_[a]	_[a]
III	48.05	_[a]	_[a]

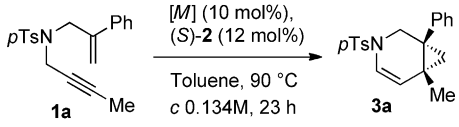
[a] The frequency calculation could not be carried out due to the size of the system.


I

II (R = H)
III (R = *i*Pr)

Thus, we turned our attention to iridium and rhodium catalysts, initially the relatively cheap Vaska's complex.[15] To the best of our knowledge, this compound has only been used once as precatalyst, in racemic experiments for enyne cycloisomerization by Shibata and co-workers.[10] Reaction of substrate **1a** with Vaska's complex (10 mol%) and silver salt (*S*)-**2** (12 mol%) in toluene ($c = 0.134$ M) at 90 °C led to the expected bicyclic product **3a** in 80% yield and 81% *ee* (see Table 2, entry 1 and Table S1 in the Supporting Information for a full screening of conditions).[16] At a higher concentration ($c = 0.250$ M), although the same enantioselectivity was detected, the yield was lower (Table 2, entry 2). Vaska's complex was found to be more efficient in terms of yield and enantioselectivity than either $[IrBr(CO)(dppe)]$[17] (Table 2, entry 3; dppe = 1,2-bis(diphenylphosphino)ethane) or $[RhCl(CO)(PPh_3)_2]$ (Table 2, entry 4).

Table 2. Optimization of the reaction conditions.



Entry	[*M*]	Yield [%][a]	*ee* [%][b]
1	**$[IrCl(CO)(PPh_3)_2]$**	**80**	**81**
2	$[IrCl(CO)(PPh_3)_2]$	74[c]	80
3	$[IrBr(CO)(dppe)]$	10[d]	43
4	$[RhCl(CO)(PPh_3)_2]$	69[d]	48

[a] Isolated yield. [b] HPLC, AS-H column. [c] $c = 0.250$ M. [d] [*M*] (20 mol%), (*S*)-**2** (24 mol%).

The scope and limitations of the reaction were investigated next (Table 3). In addition to the *p*-toluenesulfonyl (*p*-Ts) derivative **1a**, several protecting groups at the nitrogen

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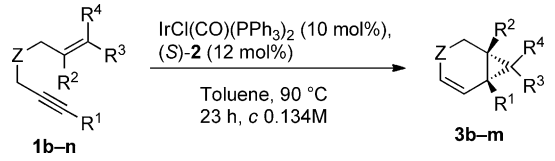
Table 3. Scope and limitations of the reaction.



Entry	Enyne	Z	R^1	R^2	R^3	R^4	Yield [%][a]	*ee* [%][b]
1	**1b**	*o*-TsN	Me	Ph	H	H	74	87
2	**1c**	MesN[c]	Me	Ph	H	H	77	93
3	**1d**	*p*-NsN[d]	Me	Ph	H	H	79	82
4	**1e**	*o*-NsN	Me	Ph	H	H	73	72
5	**1f**	BocN[e]	Me	Ph	H	H	38[f]	80
6	**1g**	*p*-TsN	Me	PMP[g]	H	H	76	86
7	**1h**	*p*-TsN	Me	4-ClPh	H	H	79	89
8	**1i**	*p*-TsN	Me	Me	H	H	61	86
9[h]	**1j**	*p*-TsN	Me	H	Ph	H	47	43
10	**1k**	*p*-TsN	Me	H	Me	Me	16	17
11	**1l**	O	Me	Ph	H	H	16	n.d.[i]
12	**1m**	O	PMP	H	Ph	H	73	88[j]
13	**1n**	$C(CO_2Et)_2$	Me	Ph	H	H	0	–

[a] Isolated yields. [b] HPLC, AS-H or AD-H column. [c] Mes = $(2,4,6\text{-}Me_3)C_6H_2SO_2$. [d] Ns = $O_2N\text{–}C_6H_4SO_2$. [e] Boc = *tert*-butoxycarbonyl. [f] 59% brsm. [g] PMP = 4-$MeOC_6H_4$. [h] 110 °C for 40 h. [i] None detected. [j] Opposite absolute configuration.

atom were tested (Table 3, entries 1–4). Whereas the *o*-Ts and mesityl (Mes) groups significantly improved the stereoselectivity (Table 3, entries 1 and 2), *o*-nosyl (*o*-Ns) provoked a decrease in the enantioselectivity to 72% *ee* (Table 3, entry 4). On the other hand, *p*-Ns substrate **1d** (Table 3, entry 3) gave similar results to **1a**. *N-tert*-butoxycarbonyl (*N*-Boc) enyne **1f** led cleanly to the desired vinylcyclopropane **3f** with a satisfying 80% *ee*, albeit in moderate yield due to a low conversion [38%, 59% based on recovered starting material (brsm)]. Within the family of *p*-TsN-bridged enynes, we noticed that the introduction of either an electron-donating or electron-withdrawing substituent at the *para* position of the phenyl group located at the internal double-bond carbon atom resulted in an increase of the *ee* value (Table 3, entries 6 and 7).

The presence of a *para*-methyl group, as in **1i** (Table 3, entry 8), rather than an aryl group did not alter the *ee*, but decreased the yield by 15–18% due to the formation of other unidentified products. In the absence of any substitution at R^2, as in **1j** and **1k** (Table 3, entries 9 and 10), both the yields and *ee* values dramatically decreased.[18] The replacement of the *p*-TsN framework of **1a** with an oxygen atom (**1l**) seriously impeded the reaction (Table 3, entry 11). Nevertheless, the oxygen-bridged enyne **1m**, which displays no substitution at R^2 and a phenyl group at R^3, transformed efficiently into the desired product with 88% *ee* (Table 3, entry 12). The absolute configuration of product **3m** was found to be opposite to that observed for the nitrogen-bridged products.[19] Lastly, the carbon-tethered enyne **1n** transformed into a complex mixture of products from which **3n** could not be detected.

Overall, in terms of stereoselectivity, the use of a chiral counterion provided products **3** with better *ee* values than reaction in the presence of chiral diphosphine ligands.[10] Additionally, because the starting iridium complex already bears a π-acceptor CO ligand, the use of a CO atmosphere could be avoided. To gain insight into the structure of the active species, the following control experiment was carried out (Figure 1): Vaska's complex was mixed with (*S*)-**2** in [D_8]toluene and the yellow suspension was stirred at room temperature. Although virtually no change in the chemical shift of the PPh_3 signal in the ^{31}P NMR spectra was observed at 92 °C, the peak of the phosphate was significantly shifted upfield: *trans*-[IrCl(CO)(PPh_3)$_2$]: $\delta = 25.6$ ppm (PPh_3); (*S*)-**2**: $\delta = 14.8$ ppm (silver phosphate); **4**: $\delta = 25.5$ (PPh_3) and 3.4 ppm (iridium phosphate).[20] More-

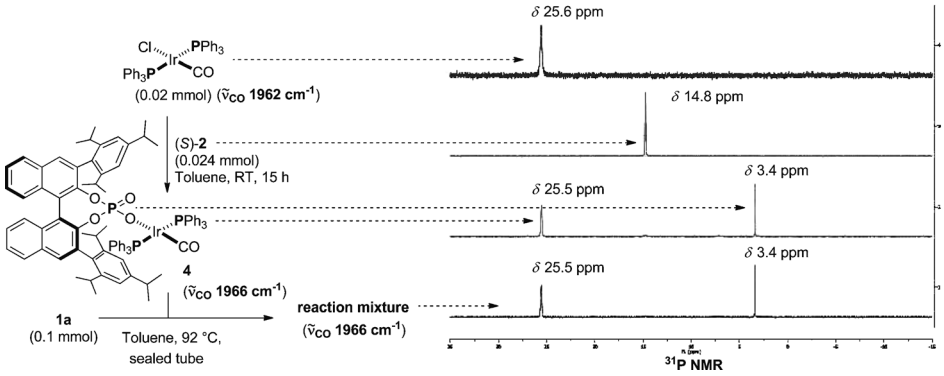


Figure 1. IR and ^{31}P NMR spectroscopic monitoring (242 MHz, 92 °C).

over, the IR spectra remained similar. After completion of the reaction (15 h), the white precipitate of AgCl was filtered off and the solution transferred to an NMR tube that contained a solution of enyne **1a** in [D_8]toluene. The tube was sealed and heated to 92 °C. No change in the ^{31}P NMR spectra could be detected during the course of the reaction;[21] likewise, the IR spectra after the reaction was similar to that recorded before the reaction ($\tilde{\nu}_{CO} = 1966\ cm^{-1}$). In particular, no loss of CO or PPh_3 could be observed. These results suggest that chloride metathesis takes place and that the *trans* geometry of Vaska's complex is conserved (the two phosphine groups remain magnetically equivalent).

All attempts to isolate suitable crystals for an X-ray study of the iridium–chiral phosphate adduct have so far been unsuccessful. Moreover, because of the narrow range of the chemical shifts, even when a 600 MHz spectrometer was used, it was not possible to identify any reaction intermediate.[22] Thus, density functional theory (DFT) calculations were carried out to shed light on some mechanistic issues.

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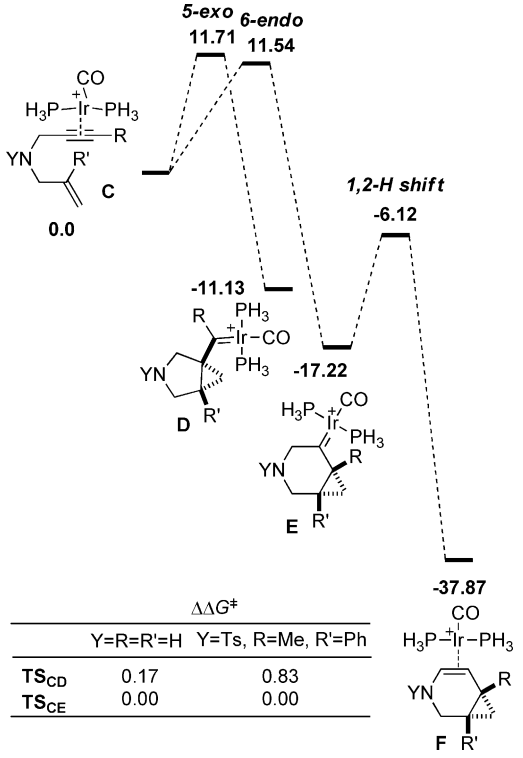
An initial set of results was rapidly generated for PH_3 and a model enyne with an NH tether and no substituent (Figure 2, Y = R = R′ = H). Both the 5-*exo*-dig and 6-*endo*-dig cyclization pathways were modeled.[23,24] From **C**, in which the alkyne moiety of the enyne coordinates iridium, the direct cyclization pathways were found to proceed to give **D** and **E** with very close free energies of activation ($\Delta G^{\neq}$) of 11.71 and 11.54 kcal mol^{-1}, respectively. The *endo* pathway is appreciably more exergonic than the *exo* pathway. The final product **F** is obtained by a 1,2-hydride shift to the carbenic center of **E**. A *p*-Ts group at nitrogen, a phenyl group at the internal alkene carbon atom, and a methyl group at the alkyne terminus (as in **1a**) were then introduced in the computations (Y = *p*-Ts, R = Me, R′ = Ph). The transition states were reoptimized. The 6-*endo* transition state ($\mathbf{TS_{CE}}$) was again the lowest lying, followed by the 5-*exo* analogue ($\mathbf{TS_{CD}}$) at $\Delta\Delta G^{\neq} = 0.83$ kcal mol^{-1}.



ΔΔG‡	Y=R=R'=H	Y=Ts, R=Me, R'=Ph
$\mathbf{TS_{CD}}$	0.17	0.83
$\mathbf{TS_{CE}}$	0.00	0.00

Figure 2. Calculated energy profile (ΔG, kcal mol^{-1}) for the cyclization of enynes mediated by $[Ir(CO)(PH_3)_2]^+$ (values in bold correspond to Y = R = R′ = H).

The model phosphate HPO_4^- was next considered and the two transition states $\mathbf{TS_{CD}}$ and $\mathbf{TS_{CE}}$ were reoptimized. Trying to bring the phosphate close to the iridium center resulted in its systematic repulsion from the coordination sphere. Other 5- and 6-coordinate geometries were attempted, yet it was not possible to keep all of the ligands together.

The best option we could find was to put the phosphate in such a way that it could establish hydrogen bonds with the CH_2 α to the nitrogen atom[25] and with one *ortho*-hydrogen atom of the tolyl group (Figure 3). The distances are typical for strong C–H···O hydrogen bonds that involve phosphates (although N–H···O and O–H···O hydrogen bonds remain the strongest type).[11] It is noteworthy that NC(sp^3)–H···O hydrogen bonds may participate in the control of the stereoselectivity in some organocatalyzed reactions.[26] Again, transition state $\mathbf{TS_{CE}}$ was found to be the lowest lying, although close to $\mathbf{TS_{CD}}$ ($\Delta\Delta G^{\neq} = 0.81$ kcal mol^{-1}).

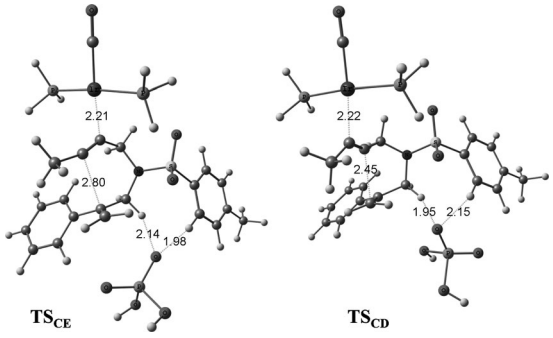


Figure 3. Optimized 6-*endo* and 5-*exo* transition states.

Thus, these calculations support a 6-*endo*-dig cyclization pathway and corroborate our hypothesis that the chiral phosphate controls the enantioselectivity through the formation of a loose ion pair with the metal center.[27]

Conclusion

The first asymmetric chiral-anion-directed transition-metal-catalyzed carbocyclizations have been achieved. Although the chiral counterion strategy proved to be successful in the field of gold-catalyzed heterocyclizations, the choice of iridium as catalyst was adequate in the case of nitrogen- and oxygen-bridged 1,6-enynes.[29] Of particular interest, the combination of Vaska's complex with a chiral silver phosphate provided better enantioselectivities than the classical approach, which involves an Ir^+/chiral diphosphine mixture. Our results suggest the formation of a loose ion pair, in which the organometallic fragment and the chiral phosphate are separated by the substrate. The Ir^+ moiety coordinates the triple bond and the phosphate can establish strong C–H···O hydrogen bonds, even with less acidic C(sp^3)–H donors.[28] Extension of this concept to other types of cycloisomerizations is underway in our laboratory.

Experimental Section

Typical experimental procedure when the enyne is a solid: In a glovebox, $[IrCl(CO)(PPh_3)_2]$ (7.8 mg, 0.010 mmol, 0.10 equiv), **2** (10.3 mg, 0.012 mmol, 0.12 equiv), and enyne **1** (0.1 mmol, 1 equiv) were added to a vial equipped with a magnetic stirring bar. The vial was sealed, taken out of the glovebox, and freshly distilled toluene (0.75 mL, $c = 0.134$ M) was added through the cap. The vial was immersed in a preheated oil bath at 90 °C. After 23 h, the reactor was cooled to RT and the vial was

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opened. The reaction mixture was filtered through a short pad of silica (Et_2O), then concentrated under reduced pressure. Subsequent purification by flash chromatography on silica gel afforded cyclized product **3**.

Typical experimental procedure when the enyne is an oil: In a glovebox, $[IrCl(CO)(PPh_3)_2]$ (7.8 mg, 0.010 mmol, 0.10 equiv) and **2** (10.3 mg, 0.012 mmol, 0.12 equiv) were added to a vial equipped with a magnetic stirring bar. The vial was sealed, then taken out of the glovebox. A solution of enyne **1** (0.1 mmol, 1 equiv) in freshly distilled toluene (0.75 mL, $c = 0.134$ M) was added through the cap and the vial was immersed in a preheated oil bath (90 °C). After 23 h, the reactor was cooled to RT and the vial was opened. The reaction mixture was filtered through a short pad of silica (Et_2O) and the volatile substances were removed in vacuo. Subsequent purification by flash chromatography on silica gel afforded cyclized product **3**.

Acknowledgements

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[1] a) M. Rueping, R. M. Koenigs, I. Atodiresei, *Chem. Eur. J.* **2010**, *16*, 9350; b) J. Lacour, D. Moraleda, *Chem. Commun.* **2009**, 7073; c) M. Klussmann, *Angew. Chem.* **2009**, *121*, 7260; *Angew. Chem. Int. Ed.* **2009**, *48*, 7124; d) A. S. K. Hashmi, C. Hubbert, *Angew. Chem.* **2010**, *122*, 5360; *Angew. Chem. Int. Ed.* **2010**, *49*, 1010; e) C. Zhong, X. Shi, *Eur. J. Org. Chem.* **2010**, 2999; f) J. Lacour, D. Linder, *Science* **2007**, *317*, 462.

[2] a) M. Rueping, A. P. Antonchick, C. Brinkmann, *Angew. Chem.* **2007**, *119*, 7027; *Angew. Chem. Int. Ed.* **2007**, *46*, 6903; b) S. Mukherjee, B. List, *J. Am. Chem. Soc.* **2007**, *129*, 11336; c) C. Li, C. Wang, B. Villa-Marcos, J. Xiao, *J. Am. Chem. Soc.* **2008**, *130*, 14450; d) G. L. Hamilton, T. Kanai, F. D. Toste, *J. Am. Chem. Soc.* **2008**, *130*, 14984; e) X.-Y. Liu, C.-M. Che, *Org. Lett.* **2009**, *11*, 4204; f) P. de Armas, D. Tejedor, F. García-Tellado, *Angew. Chem.* **2010**, *122*, 1029; *Angew. Chem. Int. Ed.* **2010**, *49*, 1013; g) R. Yazaki, N. Kumagai, M. Shibasaki, *J. Am. Chem. Soc.* **2010**, *132*, 10275; h) J. Lv, X. Li, L. Zhong, S. Luo, J.-P. Cheng, *Org. Lett.* **2010**, *12*, 1096; i) F. Drouet, C. Lalli, H. Liu, G. Masson, J. Zhu, *Org. Lett.* **2011**, *13*, 94; j) U. Hennecke, C. H. Müller, R. Fröhlich, *Org. Lett.* **2011**, *13*, 860; k) G. K. Ingle, Y. Liang, M. G. Mormino, G. Li, F. R. Fronczek, J. C. Antilla, *Org. Lett.* **2011**, *13*, 2054.

[3] a) D. B. Llewellyn, D. Adamson, B. A. Arndsten, *Org. Lett.* **2000**, *2*, 4165; b) G. L. Hamilton, E. J. Kang, M. Mba, F. D. Toste, *Science* **2007**, *317*, 496; c) B. Zhao, H. Du, Y. Shi, *J. Org. Chem.* **2009**, *74*, 8392; d) K. Aikawa, M. Kojima, K. Mikami, *Angew. Chem.* **2009**, *121*, 6189; *Angew. Chem. Int. Ed.* **2009**, *48*, 6073; e) R. L. LaLonde, Z. J. Wang, M. Mba, A. D. Lackner, F. D. Toste, *Angew. Chem.* **2010**, *122*, 608; *Angew. Chem. Int. Ed.* **2010**, *49*, 598; f) D. Chen, B. Sundararaju, R. Krause, J. Klankermayer, P. H. Dixneuf, W. Leitner, *ChemCatChem* **2010**, *2*, 55; g) C. Wang, Z.-Y. Han, H.-W. Luo, L.-Z. Gong, *Org. Lett.* **2010**, *12*, 2266 (for the hydroamination step); h) K. Aikawa, M. Kojima, K. Mikami, *Adv. Synth. Catal.* **2010**, *352*, 3131; i) S. Liao, B. List, *Angew. Chem.* **2010**, *122*, 638; *Angew. Chem. Int. Ed.* **2010**, *49*, 4409; j) V. Rauniyar, Z. J. Wang, H. E. Burks, F. D. Toste, *J. Am. Chem. Soc.* **2011**, *133*, 8486.

[4] a) N. Bongers, N. Krause, *Angew. Chem.* **2008**, *120*, 2208; *Angew. Chem. Int. Ed.* **2008**, *47*, 2178; b) H. Amouri, M. Gruselle, *Chirality in Transition Metal Chemistry: Molecules, Supramolecular Assemblies and Materials*, John Wiley & Sons, Chichester, **2008**.

[5] D. Zuccaccia, L. Belpassi, F. Tarantelli, A. Macchioni, *J. Am. Chem. Soc.* **2009**, *131*, 3170.

[6] a) G. C. Lloyd-Jones, *Org. Biomol. Chem.* **2003**, *1*, 215; b) C. Bruneau, *Angew. Chem.* **2005**, *117*, 2380; *Angew. Chem. Int. Ed.* **2005**, *44*, 2328; c) L. Zhang, J. Sun, S. A. Kozmin, *Adv. Synth. Catal.* **2006**, *348*, 2271; d) V. Michelet, P. Y. Toullec, J.-P. Genêt, *Angew. Chem.* **2008**, *120*, 4338; *Angew. Chem. Int. Ed.* **2008**, *47*, 4268; e) E. Jiménez-Núñez, A. M. Echavarren, *Chem. Rev.* **2008**, *108*, 3326; f) S. I. Lee, N. Chatani, *Chem. Commun.* **2009**, 371.

[7] a) J. Blum, H. Beer-Kraft, Y. Badrieh, *J. Org. Chem.* **1995**, *60*, 5567; b) A. Fürstner, H. Szillat, F. Stelzer, *J. Am. Chem. Soc.* **2000**, *122*, 6785; c) M. Méndez, M. P. Muñoz, C. Nevado, D. J. Cárdenas, A. M. Echavarren, *J. Am. Chem. Soc.* **2001**, *123*, 10511; d) A. Fürstner, F. Stelzer, H. Szillat, *J. Am. Chem. Soc.* **2001**, *123*, 11863; e) C. Nevado, C. Ferrer, A. M. Echavarren, *Org. Lett.* **2004**, *6*, 3191; f) A. Fürstner, P. W. Davies, T. Gress, *J. Am. Chem. Soc.* **2005**, *127*, 8244; g) E. J. Cho, M. Kim, D. Lee, *Org. Lett.* **2006**, *8*, 5413; h) A. Hercouet, F. Berrée, C. H. Lin, L. Toupet, B. Carboni, *Org. Lett.* **2007**, *9*, 1717; i) C. Ferrer, M. Raducan, C. Nevado, C. K. Claverie, A. M. Echavarren, *Tetrahedron* **2007**, *63*, 6306; j) D. Brissy, M. Skander, P. Retailleau, A. Marinetti, *Organometallics* **2007**, *26*, 5782; k) D. Brissy, M. Skander, P. Retailleau, G. Frison, A. Marinetti, *Organometallics* **2009**, *28*, 140; l) D. Brissy, M. Skander, H. Jullien, P. Retailleau, A. Marinetti, *Org. Lett.* **2009**, *11*, 2137; m) J.-B. Xia, W.-B. Liu, T.-M. Wang, S.-L. You, *Chem. Eur. J.* **2010**, *16*, 6442.

[8] a) C. Nieto-Oberhuber, M. P. Muñoz, E. Buñuel, C. Nevado, D. J. Cárdenas, A. M. Echavarren, *Angew. Chem.* **2004**, *116*, 2456; *Angew. Chem. Int. Ed.* **2004**, *43*, 2402; b) S. I. Lee, S. M. Kim, S. Y. Kim, Y. K. Chung, *Synlett* **2006**, 2256; c) S. I. Lee, S. M. Kim, M. R. Choi, S. Y. Kim, Y. K. Chung, *J. Org. Chem.* **2006**, *71*, 9366; d) S. M. Kim, J. H. Park, S. Y. Choi, Y. K. Chung, *Angew. Chem.* **2007**, *119*, 6284; *Angew. Chem. Int. Ed.* **2007**, *46*, 6172; e) C.-M. Chao, D. Beltrami, P. Y. Toullec, V. Michelet, *Chem. Commun.* **2009**, 6988; f) H. Teller, A. Fürstner, *Chem. Eur. J.* **2011**, *17*, 7764; g) A. Pradal, C.-M. Chao, P. Y. Toullec, V. Michelet, *Beilstein J. Org. Chem.* **2011**, *7*, 1021.

[9] a) P. Costes, J. Weckesser, O. Dechy-Cabaret, M. Urrutigoïty, P. Kalck, *Appl. Organomet. Chem.* **2008**, *22*, 211; b) T. Nishimura, T. Kawamoto, M. Nagaosa, H. Kumamoto, T. Hayashi, *Angew. Chem.* **2010**, *122*, 1682; *Angew. Chem. Int. Ed.* **2010**, *49*, 1638; c) S. Y. Kim, Y. K. Chung, *J. Org. Chem.* **2010**, *75*, 1281; d) T. Nishimura, Y. Maeda, T. Hayashi, *Org. Lett.* **2011**, *13*, 3674.

[10] T. Shibata, Y. Kobayashi, S. Maekawa, N. Toshida, K. Takagi, *Tetrahedron* **2005**, *61*, 9018.

[11] Phosphates tend to form very strong N−H···O and O−H···O hydrogen bonds, and strong C−H···O hydrogen bonds, see: a) T. Dorn, A.-C. Chamayou, C. Janiak, *New J. Chem.* **2006**, *30*, 156; b) K. C. Kumara Swamy, S. Kumaraswamy, P. Kommana, *J. Am. Chem. Soc.* **2001**, *123*, 12642; c) F. M. Raymo, M. D. Bartberger, K. N. Houk, J. F. Stoddart, *J. Am. Chem. Soc.* **2001**, *123*, 9264, and the references therein.

[12] Despite the so-called "weakly coordinating" nature of the phosphate, the Au−O bond is expected to be strong. Crystal structure analysis of $[(o\text{-Tol})P]_3AuOTf$ showed a short Au···O contact of 2.110(3) Å, indicative of a strong covalent bonding: M. Preisenberger, A. Schier, H. Schmidbaur *J. Chem. Soc. Dalton Trans.* **1999**, 1645. Even shorter Au···O contacts around 2.06 Å have been reported in a phosphine–gold phosphate complex, see ref. [3d] (X-ray).

[13] All geometries of intermediates and transition states were optimized fully without symmetry constraints by using the Gaussian 09 program. The iridium atom was described by a double-ζ basis set (LANL2DZ), and the 6–31G(d,p) basis set was used for the other elements. See the Supporting Information for details.

[14] ΔH and ΔG values could not be computed because of the size of the system. However, ΔE is close to ΔH with $H_2PO_4^-$ (Table 1, X = **I**).

[15] Approximately 95 € per gram.

[16] Lowering the load of iridium to 5 mol% resulted in a much longer reaction time of 71 h. The best *ee* value (75%) was obtained at $c = 0.268$ M (77% yield).

[17] B. J. Fisher, R. Eisenberg, *Inorg. Chem.* **1984**, *23*, 3216.

[18] The dimethyl group in **1k** presumably renders the double bond more nucleophilic, which would alter the reactivity of the system. For examples of diverted cycloisomerization reactivity with a prenyl

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unit, see: Y. Harrak, A. Simonneau, M. Malacria, V. Gandon, L. Fensterbank, *Chem. Commun.* **2010**, *46*, 865 and references therein.
[19] See ref. [8e] and P. J. Stephens, D. M. McCann, E. Butkus, S. Stončius, J. R. Cheeseman, M. J. Frisch, *J. Org. Chem.* **2004**, *69*, 1948.
[20] Modest shifts in $\tilde{\nu}_{CO}$ and $\delta^{31}P$ have been reported for *trans*-[Ir(OCF$_3$SO$_2$)(CO)(PPh$_3$)$_2$] relative to *trans*-[IrCl(CO)(PPh$_3$)$_2$], see: a) D. J. Liston, Y. J. Lee, W. R. Scheidt, C. A. Reed, *J. Am. Chem. Soc.* **1989**, *111*, 6643; b) D. P. Paterniti, L. W. Francisco, J. D. Atwood, *Organometallics* **1999**, *18*, 123.
[21] In this NMR spectroscopic monitoring, the anion metathesis was complete before introduction of the enyne, in contrast with the protocol used for the results in Tables 2 and 3. Nevertheless, **3a** was obtained as in Table 2, entry 8, which suggests that the presence of the enyne from the beginning of the reaction is inconsequential to the *ee*.
[22] The absence of detection of any intermediate could also be due to transient character on the NMR spectroscopic timescale.
[23] For related calculations in the gold and platinum series, see ref. [8a] and a) E. Soriano, P. Ballesteros, J. Marco-Contelles, *J. Org. Chem.* **2004**, *69*, 8018; b) N. Cabello, E. Jiménez-Núñez, E. Buñuel, D. J. Cárdenas, A. M. Echavarren, *Eur. J. Org. Chem.* **2007**, 4217.
[24] The direct 1,2-hydrogen shift originally proposed by Shibata (see ref. [10]) was also modeled but proved to be energetically disfavored compared with these two (see the Supporting Information).
[25] For representative examples of such XC(sp^3)–H···O hydrogen bonds in crystallographic structures, see: a) S. Sarkhel, G. R. Desiraju, *Proteins Struct. Funct. Bioinf. Proteins* **2004**, *54*, 247; b) G. R. Desiraju, *Acc. Chem. Res.* **1996**, *29*, 441; and references therein.
[26] See: a) S. Bahmanyar, K. N. Houk, *J. Am. Chem. Soc.* **2001**, *123*, 12911; b) C. E. Cannizzaro, K. N. Houk, *J. Am. Chem. Soc.* **2002**, *124*, 7163.
[27] However, we note that such anions may also act as X-type chiral ligands for enantioselective transition-metal catalysis, see ref. [3j].
[28] Asymmetric organocatalyzed reactions that involve hydrogen bonds can be carried out at elevated temperatures, see: M. Mečiarovà, Š. Toma, R. Šebesta, *Tetrahedron: Asymmetry* **2009**, *20*, 2403 and the references therein.
[29] Note added in proof: During the course of the reviewing process, the following articles, dealing with asymmetric, chiral-anion-directed, transition-metal catalysis, were published: a) G. Jiang, B. List, *Chem. Commun.* **2011**, *47*, 10022; b) G. Jiang, R. Halder, Y. Fang, B. List, *Angew. Chem.* **2011**, *123*, 9926; *Angew. Chem. Int. Ed.* **2011**, *50*, 9752; c) Y.-Y. Huang, A. Chakrabarti, N. Morita, U. Schneider, S. Kobayashi, *Angew. Chem.* **2011**, *123*, DOI:10.1002/ange.201105182; *Angew. Chem Int. Ed.* **2011**, *50*, DOI: 10.1002/anie.201105182.

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