Communication

# Highly Regio- and Enantioselective Alkoxycarbonylative Amination of Terminal Allenes Catalyzed by SKP/Pd(II) Complex

Jiawang Liu, Zhaobin Han, Xiaoming Wang, Zheng Wang, and Kuiling Ding

*J. Am. Chem. Soc.*, **Just Accepted Manuscript** • DOI: 10.1021/jacs.5b07764 • Publication Date (Web): 17 Sep 2015

# Highly Regio- and Enantioselective Alkoxycarbonylative Amination of Terminal Allenes Catalyzed by SKP/Pd(II) Complex

Jiawang Liu, Zhaobin Han, Xiaoming Wang, Zheng Wang* and Kuiling Ding*†

State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032; China

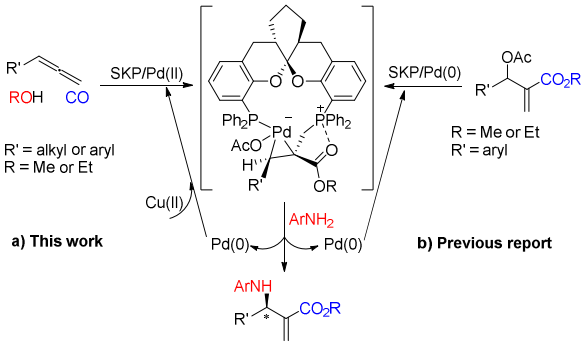
† and Collaborative Innovation Center of Chemical Science and Engineering (Tianjin), China

*Supporting Information Placeholder*

**ABSTRACT:** An enantioselective alkoxycarbonylation-amination cascade process of terminal allene with CO, methanol and arylamine has been developed under mild conditions (rt, ambient pressure CO) via oxidative Pd(II) catalysis using an aromatic spiroketal-based diphosphine (SKP) as chiral ligand and Cu(II) salt as oxidant, affording a wide range of α-methlene-β-arylamino acid esters (36 examples) in good yields with excellent enantioselectivity (up to 96% ee) and high regioselectivity (branched/linear > 92:8). Preliminary mechanistic studies suggested that the reaction is likely to proceed through alkoxylcarbonyl palladation of the allene followed by an amination process. The synthetic utility of the protocol is showcased in the asymmetric construction of a cycloheptene-fused chiral β-lactam.

Allenes have been recognized as versatile building blocks in organic synthesis,[1] enabling numerous efficient transformations for rapid generation of molecular complexity.[2] The unique reactivity of the 1,2-diene structure renders allenes excellent flexibility to perform multicomponent or tandem reactions, providing elegant access to multifunctional molecules from readily available chemicals.[3] In this context, a typical mode for transition metal catalyzed allene transformation involves insertion into R-M bond (hydrido-, carbo-, acyl-, or elemento-M in nature), to generate a transient π-allyl-M species that is trapped by an external or internal nucleophile, furnishing various functionalized olefins or cyclic compounds.[2,3] In the past two decades, this powerful strategy has been successfully extended to enantioselective functionalization of allenes[4] via asymmetric Pd,[5] Rh,[6] or Ni[7] catalysis. Despite the remarkable progresses, however, significant challenges still remain in the control of chemo-, regio-, and enantioselectivities, as multiple reactivities can be invoked on the two orthogonal cumulated C=C bonds in the catalysis.[2,3a,4,8] From synthetic perspective, development of new enantioselective tandem processes for allene functionalization, which can selectively combine several compounds in one-pot is a sought-after chemistry,[9] which holds the promise for rapid construction of chiral complex molecules without arduous and wasteful intermediate isolation in a multistep synthesis. Herein, we report the first regio- and enantioselective difunctionalization of simple terminal allenes with CO, methanol and arylamines, via a SKP/Pd(II)-catalyzed tandem alkoxycarbonylative amination process.

**Scheme 1. Reaction Design**

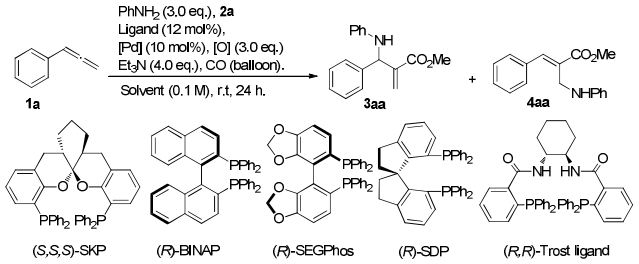



Recently we reported a Pd(0)-catalyzed asymmetric allylic amination of racemic Morita-Baylis–Hillman (MBH) adducts, wherein an aromatic spiroketal-based bisphosphine ligand (SKP)[10] demonstrated excellent control of regio- and enantioselectivity.[11] Mechanistic studies revealed that SKP ligand plays a bifunctional role in the catalysis, forming a C-P σ-bond with the terminal carbon of allyl moiety and concomitantly coordinating with Pd in the key catalytic species (Scheme 1b).[12] We envisaged such a phosphonium-Pd(II) species might be generated via an alternative route, i.e., by alkoxycarbonyl palladation of allenes with CO and alcohol as acylating agent via oxidative Pd(II) catalysis (Scheme 1a).[13] This would effectively steer the course of the catalysis through the same key Pd species, allowing for a more straightforward access to chiral α-methlene-β-arylamino acid esters[14] by obviating the tedious synthesis of MBH adducts. Though some studies have exploited Pd(II)-catalyzed oxidative carbonylation[15] of allenes to generate an 2-alkoxycarbonyl π-allylpalladium species in harness with attack by a nucleophile,[16] no asymmetric variant has been reported so far to our knowledge.

Initial studies were focused on examining the feasibility of the strategy and optimizing the reaction conditions, using 1-phenylallene **1a** and aniline **2a** as model substrates. The reactions were generally run at rt for 24 h under balloon pressure of CO in MeOH or MeOH-containing solvent, with a Pd(II) salt (10 mol%) and a chiral diphosphine (12 mol%) as the catalyst and $Et_3N$ (4.0 equiv) as the base. As shown in Table 1, the reaction catalyzed by $PdCl_2$/(*S,S,S*)-SKP in methanol gave the branched regioisomer **3aa** in only 7% yield in 24 h (entry 1), probably owing to the absence of a stoichiometric oxidant necessary for Pd(II) regeneration from Pd(0) species reduced in amination step. Introduction of 3.0 equiv of $CuCl_2$ as an oxidant led to an increased yield (19%) of **3aa**, albeit with poor branched/linear (**3aa**/**4aa**) ratio and ee

(entry 2). $Cu(OAc)_2$ proved to be superior to $CuCl_2$ in this reaction, affording preferentially branched product **3aa** in 52% yield with 74% ee (entry 3). Presumably, partial exchange of the acetate with the chloride in $PdCl_2$ gave coordinated acetate anions, which can serve as an internal base to facilitate the formation of a palladium alkoxide intermediate.[13a] Indeed, the beneficial effect of acetate was further corroborated with the use of $Pd(OAc)_2$ as Pd(II) source, whereby **3aa** was obtained in significantly enhanced yield (73%) with 89% ee and 95:5 branched selectivity (entry 4). After an extensive screening of reaction parameters (solvent, CO pressure, base, terminal oxidant, temperature, Pd precursor, etc) (for details, see Tables S1-S9 in SI), a solvent mixture of MeOH/PhF (9:1 v/v) was identified to be optimal, to give **3aa** in 89% yield with 92% ee and 96:4 B/L ratio (entry 5). This is in sharp contrast with the Pd(0)/SKP catalyzed asymmetric allylic amination of MBH acetates,[11] wherein $CH_2Cl_2$ was optimal but $CH_3OH$ was poor for catalysis. This distinction clearly indicated that different mechanistic details are present in the Pd(0)/SKP and Pd(II)/SKP routes to **3aa**/**4aa**, also reflected the need of high $CH_3OH$ concentration in the present catalysis (for catalyst activation). Further prolonging the reaction time from 24 to 40 h resulted in a slight improvement in yield of **3aa** (entry 6), and this set of conditions were identified as **condition A** in subsequent studies. Several other privileged chiral diphosphine ligands[17] were also evaluated in the catalysis, unfortunately all afforded less satisfactory results (entries 7–10). Some SKP ligands with different $PAr_2$ moieties were also found workable in the catalysis, but none showed significant improvement in activity or selectivities (Table S8 in SI). The use of 3.0 equiv of copper propionate [$Cu(OCOEt)_2$] as the oxidant at a reduced loading of SKP/$Pd(OAc)_2$ (5 mol %) afforded **3aa** in moderate 71% (entry 11), and extending the reaction time to 96 h afforded **3aa** in 87% yield with a 96:4 B/L ratio and 94% ee [entry 12, defined as **condition B**].

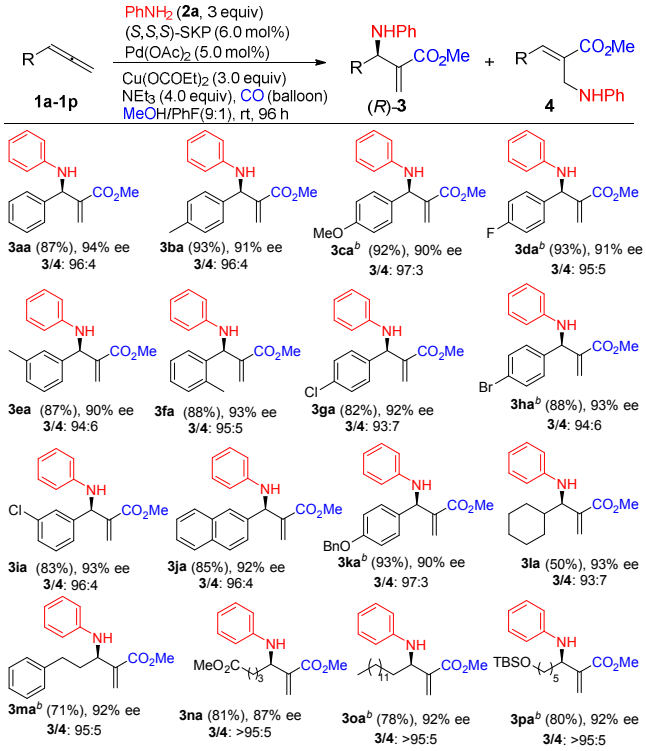
**Table 1. Methoxycarbonylative Amination of 1-Phenylallene (1a) with Aniline (2a), CO and MeOH** [a]




| Entry | [Pd]/ligand | [O] | **3aa**/**4aa**[b] | Yield(%)[c] | Ee(%)[d] |
|---|---|---|---|---|---|
| 1[e] | PdCl2/(*S,S,S*)-SKP | none | 36:64 | 7 | N.D. |
| 2[e] | PdCl2/(*S,S,S*)-SKP | CuCl2 | 50:50 | 19 | 40 |
| 3[e] | PdCl2/(*S,S,S*)-SKP | Cu(OAc)2 | 81:19 | 52 | 74 |
| 4[e] | Pd(OAc)2/(*S,S,S*)-SKP | Cu(OAc)2 | 95:5 | 73 | 89 |
| 5 | Pd(OAc)2/(*S,S,S*)-SKP | Cu(OAc)2 | 96:4 | 89 | 92 |
| 6[f] | Pd(OAc)2/(*S,S,S*)-SKP | Cu(OAc)2 | 96:4 | 93 | 93 |
| 7 | Pd(OAc)2/(*R*)-BINAP | Cu(OAc)2 | 64:36 | 54 | 3 |
| 8 | Pd(OAc)2/(*R*)-SEGPhos | Cu(OAc)2 | 79:21 | 68 | 49 |
| 9 | Pd(OAc)2/(*R*)-SDP | Cu(OAc)2 | 24:76 | 5 | 5 |
| 10 | Pd(OAc)2/Trost ligand | Cu(OAc)2 | 72:28 | <5 | 37 |
| 11[g] | Pd(OAc)2/(*S,S,S*)-SKP | Cu(OCOEt)2 | 95:5 | 71 | 92 |
| 12[g,h] | Pd(OAc)2/(*S,S,S*)-SKP | Cu(OCOEt)2 | 96:4 | 87 | 94 |

[a] Unless otherwise noted, all reactions were performed under 1 atm CO at rt for 24 h in the presence of **1a** (0.25 mmol), **2a** (0.75 mmol), [Pd] (10 mol%), ligand (12 mol%), Cu(II) salt (0.75 mmol), and $Et_3N$ (1.0 mmol), in a solvent mixture of methanol and fluorobenzene (2.5 mL, 9/1 v/v). [b] Determined by $^1H$ NMR analysis. [c] Yield of the isolated **3aa**. [d] Determined by chiral HPLC. [e] Methanol (2.5 mL) as solvent. [f] 40 h. [g] [Pd] (5 mol%), SKP (6 mol%). [h] 96 h.

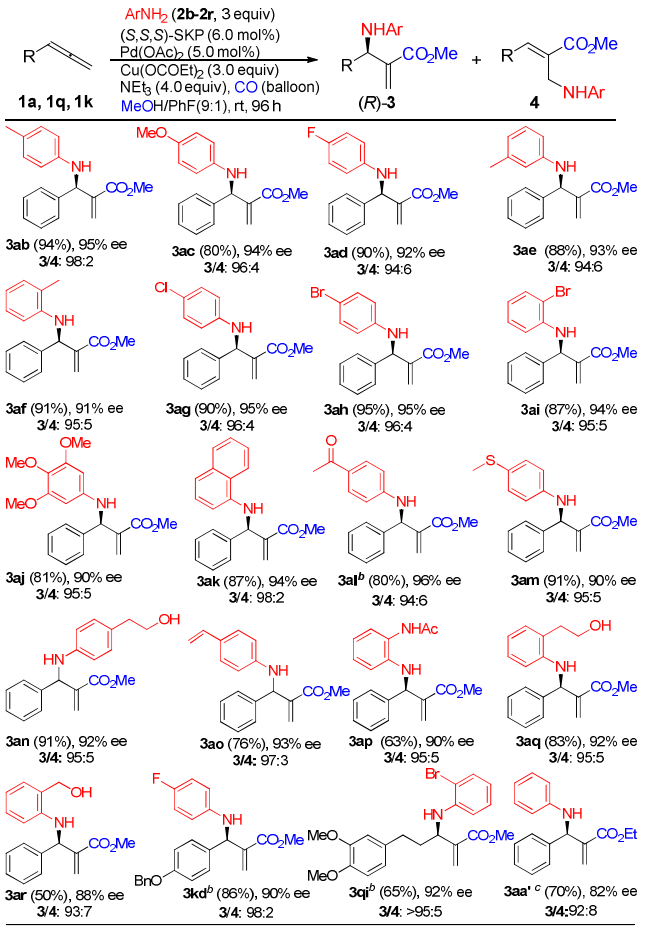
**Table 2. Substrate Scope Study for Allenes**




[a] Unless otherwise noted, the reactions were performed under **condition B**. The data in parentheses are the yields of isolated **3**. In each case, the branched/linear ratio of **3:4** was determined by $^1H$ NMR analysis of crude product, while the ee value of **3** was determined by chiral HPLC. [b] Reactions were conducted under **condition A**.

The substrate scope of allenes for the SKP/$Pd(OAc)_2$ catalyzed reaction was first examined using aniline (**2a**) as the nucleophile. In most cases, the reactions were conducted under **condition B**, and the results were summarized in Table 2. The reaction appears to be quite compatible with various types of terminal allenes (**1a-p**), consistently afforded the corresponding allylic amine products **3aa-3pa** in good to excellent yields (up to 93%), high branched regioselectivities (>93/7), and excellent enantioselectivities (87-94% ee), irrespective of whether aromatic (**1a-k**) or aliphatic (**1l-p**) substituents are tethered to the terminus of the allenes. The allenes bearing alkyl substituents on *o*-, *m*- or *p*-position of the phenyl terminus gave the corresponding products (**3ba**, **3ea**, **3fa**) in similar yields and selectivities, and functional groups such as TBSO (**3pa**) or halides (**3da**, **3ga**, **3ha**, **3ia**) were well tolerated in the catalysis. It is noteworthy that the present SKP/Pd(II) catalyzed process has effectively overcome some intrinsic limitations in aforementioned SKP/Pd(0) catalyzed allylic amination route to products **3**, whereby the presence of both 1-aryl and 2-$CO_2Et$ groups in the allylic acetate substrates have been found crucial for the reactivity, and hence the products were confined to **3** bearing a β-aryl group.[11,12] Finally, the absolute configuration of **3ha** was established to be *R* by X-ray crystal diffractional analysis.

**Table 3. Substrate Scope Study for Arylamines**

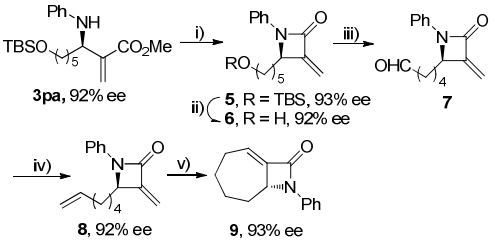



[a] Unless otherwise noted, the reactions were performed under **condition B**. The data in parentheses are the yields of isolated **3**. In each case, the branched/linear ratio of **3:4** was determined by $^1$H NMR analysis of crude product, while the ee value of **3** was determined by chiral HPLC. [b] Reactions were conducted under **condition A**. [c] The reaction was conducted under **condition B** using EtOH instead of MeOH.

A survey of various arylamines (**2a-r**) in the reactions with several terminal allenes (**1a**, **1k**, or **1q**), CO, and MeOH was also performed (Table 3). Substituents on the arylamines seemed to have no impact on the SKP/Pd(OAc)$_2$ catalysis, as both electron-rich and electron-poor arylamines were compatible with the procedure, and a broad functional group tolerance was observed in the reaction. The reactions of arylamines bearing F, Cl, Br, acyl, MeO, MeS, hydroxyalkyl, or vinyl substituent proceeded smoothly under **condition B** or **A**, to provide the corresponding products **3ab**-**3ar**, **3qi**, and **3aa'** in good yields (up to 95%), high B/L ratios (>94/6), and excellent ee values (up to 96%). Notably, product **3kd** as a synthetic intermediate for chiral drug Ezetimibe was obtained in good yield with high regioselectivity (98/2) and enantioselectivity (90% ee) using **condition A**. Preliminary studies on reactions involving other types of amines and allenes afforded less satisfactory results (SI), suggesting a large space for future development.

The synthetic utility of the methodology was exemplified in the asymmetric construction of **9**, a useful cycloheptene-fused chiral β-lactam.[18] As shown in Scheme 2, (*R*)-**3pa**, obtained in 80% yield and 92% ee from a gram-scale synthesis (SI) using the present protocol, was treated with Sn[N(TMS)$_2$]$_2$ to give the silyl-protected β-lactam **5**. Deprotection of **5** using TBAF afforded alcohol **6**, which on Swern oxidation furnished aldehyde **7**. Wittig methylenation afforded β-lactam **8** with two terminal alkene groups, which underwent RCM with 2$^{nd}$ generation Grubbs catalyst[19] to give β-lactam **9** in overall yield of 50% over five steps with 93% ee.

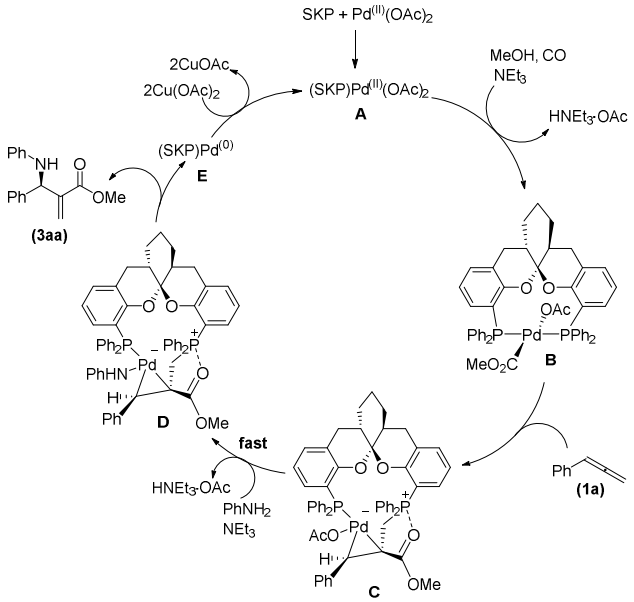
**Scheme 2. Synthetic Transformation of (*R*)-3pa into β-Lactam 9**




Reagents and conditions: i) Sn[N(TMS)$_2$]$_2$, toluene, reflux, 12h, 93%; ii) *n*-Bu$_4$NF, 0°C-rt, 6 h, 95%; iii) SO$_3$.Pyr, DMSO, NEt$_3$, CH$_2$Cl$_2$, 0°C-rt, 8 h, 88%; iv) Ph$_3$PMeBr, *n*-BuLi, THF, 0°C-rt, 10 h, 80%; v) Grubbs catalyst 2$^{nd}$ generation, *n*-hexane, 55°C, 6 h, 79%.

While the exact mechanism of the titled catalysis is not clear at this stage, the results from a series of comparative studies (for details, see SI) seem to be consistent with the proposed catalytic cycle in Scheme 3. Herein the catalysis is likely to be initiated by a *trans*-[(SKP)(AcO)Pd-COOMe] species **B**, generated via exchange of OAc in the [(SKP)Pd(OAc)$_2$] (**A**) with methoxy group followed by carbonyl insertion. Methoxycarbonylpalladation of allene **1a** by intermediate **B**, followed by intramolecular rearrangement would give the phosphonium-Pd(II) species **C**, which is the same key intermediate in the mechanism for SKP/Pd(0) catalyzed allylic amination of MBH acetates reported previously by our group.[12] The following ligand exchange of intermediate **C** with the amido from aniline is expected to be fast under basic conditions, affording the amido-Pd(II) species **D**. Reductive elimination of **D** followed by an intramolecular Pd-assisted phosphonium dissociation furnishes the product **3aa**, with concomitant release of (SKP)Pd(0) species **E**. Oxidation of **E** by a Cu(II) salt regenerates the active Pd(II) species **A**, thus accomplishing the catalytic cycle. It is noteworthy that clear distinctions exist in the courses to the intermediate **C** for SKP/Pd(II)-catalyzed methoxycarbonylative amination of allenes and SKP/Pd(0) catalyzed allylic amination of MBH acetates. Control experiments using Hg(0) test suggested Pd(0) reoxidation tends to be sluggish in the catalytic cycle, and a significant fraction of Pd species lay dormant as Pd(0) in the system, which may account for relatively high catalyst loading needed in the Pd(II) catalysis.

**Scheme 3. A Plausible Mechanism**




In conclusion, we have developed the first highly chemo-, regio- and enantioselective alkoxycarbonylation-amination cascade process of terminal allenes with arylamines, carbon monoxide and methanol, via oxidative SKP/Pd(II) catalysis with a Cu(II) salt as oxidant, affording a range of β-aryl-β-arylamine-α-methylene-carboxylic acid derivatives in good yields with excellent regio- and enantioselectivities (B/L > 92:8, up to 96% ee) with a broad substrate scope. Preliminary mechanistic studies suggested that the reaction is likely to proceed through alkoxylcarbonyl palladation of the allene followed by an amination process. The synthetic utility of the protocol is exemplified in the asymmetric construction of a cycloheptene-fused chiral β-lactam. We anticipate that the strategy of present Pd-catalyzed cascade process may find wider applications in the efficient synthesis of multifunctional compounds starting from simple olefinic molecules.

## ASSOCIATED CONTENT

### Supporting Information

Synthetic procedures, characterization and additional data. This material is available free of charge via the Internet at http://pubs.acs.org.

## AUTHOR INFORMATION

### Corresponding Author

kding@mail.sioc.ac.cn

## ACKNOWLEDGMENT

We are grateful for financial support from National Natural Science Foundation of China (21232009, 20421091, 21172237), the Chinese Academy of Sciences, and the Science and Technology Commission of Shanghai Municipality.

## REFERENCES

[1] Modern Allene Chemistry, ed. Krause, N and Hashmi, A. S. K.; Wiley-VCH, Weinheim, **2004**.

[2](a) Zimmer, R.; Dinesh, C. U.; Nandanan, E.; Khan, F. A. *Chem. Rev.***2000**,*100*, 3067; (b) Lechel, T.; Pfrengle, F.; Reissig, H. U.; Zimmer, R. *ChemCatChem,* **2013**, *5*, 2100.

[3] (a) Jeganmohan, M.; Cheng, C.-H. *Chem. Commun*. **2008**, 3101. (b)Jonasson, C.; Horvath, A.; Backvall, J. E. *J. Am. Chem. Soc*. **2000**, *122*, 9600; (c) Tonogaki, K.; Itami, K.; Yoshida, J. *J. Am. Chem. Soc*. **2006**, *128*, 1464.

[4] Yu, S.; Ma, S. *Angew. Chem. Int. Ed*. **2012**, *51*, 3074.

[5] (a) Larock, R. C.; Zenner, J. M. *J. Org. Chem*. **1995**, *60*, 482; (b) Trost, B. M.; Jakel, C.; Plietker, B. *J. Am. Chem. Soc*. **2003**, *125*, 4438; (c) Pelz, N. F.; Woodward, A. R.; Burks, H. E.; Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc*. **2004**, *126*, 16328; (d) Ohmura, T.; Taniguchi, H.; Suginome, M. *J. Am. Chem. Soc.* **2006**, *128*, 13682; (e) Shu, W.; Ma, S. *Chem. Commun*. **2009**, 6198.

[6] (a) Koschker, P.; Lumbroso, A.; Breit, B. *J. Am. Chem. Soc*. **2011**, *133*, 20746; (b) Cooke, M. L.; Xu, K.; Breit, B. *Angew. Chem. Int. Ed*. **2012**, *51*, 10876; (c) Li, C.; Kahny, M.; Breit, B. *Angew. Chem. Int. Ed.* **2014**, *53*, 13780; (d) Xu, K.; Thieme, N.; Breit, B. *Angew. Chem. Int. Ed*. **2014**, *53*, 2162; (e) Pritzius, A. B.; Breit, B. *Angew. Chem. Int. Ed*. **2015**, *54*, 3121.

[7] (a) Miura, T.; Morimoto, M.; Murakami, M. *J. Am. Chem. Soc.* **2010**, *132*, 15836; (b) Yamauchi, M.; Morimoto, M.; Miura, T.; Murakami, M. *J. Am. Chem. Soc*. **2010**, *132*, 54.

[8] Hashmi, A. S. K. *Angew. Chem. Int. Ed*. **2000**, *39*, 3590.

[9] (a) Ramon, D. J.; Yus, M. *Angew. Chem. Int. Ed*. **2005**, *44*, 1602; (b) Burks, H. E.; Morken, J. P. *Chem. Commun*. **2007**, 4717.

[10] (a) Wang, X.; Han, Z.; Wang, Z.; Ding, K. *Angew. Chem. Int. Ed.* **2012**, *51*, 936; (b) Wang, X.; Guo, P.; Wang, X.; Wang, Z.; Ding, K. *Adv. Synth. Catal*. **2013**, *355*, 2900; (c) Cao, Z.-Y.; Wang, X.; Tan C.; Zhao, X.-L.; Zhou, J.; Ding, K. *J. Am. Chem. Soc.* **2013**, *135*, 8197; (d) Miyazaki, Y.; Ohta, N.; Semba, K.; Nakao, Y. *J. Am. Chem. Soc*. **2014**, *136*, 3732. For selected reviews on the uses of chiral spiro ligands in asymmetric catalysis, see: (e) Xie, J.-H.; Zhou, Q.-L. *Acc. Chem. Res.* **2008**, *41*, 581; (f) Ding, K.; Han, Z.; Wang, Z. *Chem. Asian J.* **2009**, *4*, 32.

[11] Wang, X.; Meng, F.; Wang, Y.; Han, Z.; Chen, Y.; Liu, L.; Wang, Z.; Ding, K. *Angew. Chem. Int. Ed*. **2012**, *51*, 9276.

[12] Wang, X.; Guo, P.; Han, Z.; Wang, X.; Wang, Z.; Ding, K. *J. Am. Chem. Soc*. **2014**, *136*, 405.

[13] For reviews, see: (a) Stahl, S. S. *Angew. Chem. Int. Ed*. **2004**, *43*, 3400; (b) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Sottocornola, S. *Chem. Rev*. **2007**, *107*, 5318; (c) McDonald, R. I.; Liu, G. S.; Stahl, S. S. *Chem. Rev*. **2011**, *111*, 2981.

[14] For an elegant example, see: Yukawa, T.; Seelig, B.; Xu, Y.-J.; Morimoto, H.; Matsunaga, S.; Berkessel, A.; Shibasaki, M. *J. Am. Chem. Soc*. **2010**, *132*, 11988.

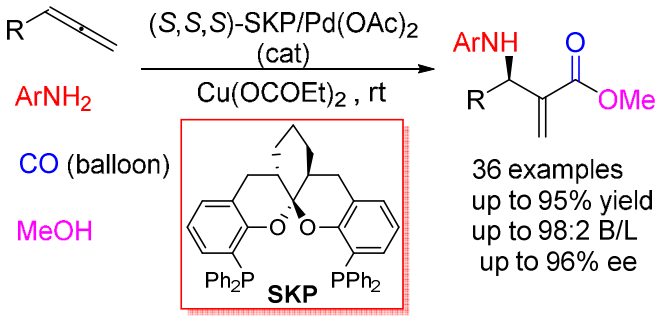
[15] For reviews, see: (a) Gabriele, B.; Salerno, G.; Costa, M. *Top. Organomet. Chem*. **2006**, *18*, 239; (b) Wu, X. F.; Neumann, H.; Beller, M. *ChemSusChem*, **2013**, *6*, 229.

[16] (a) Alper, H.; Hartstock, F. W.; Despeyroux, B. *J. Chem. Soc., Chem. Commun.* **1984**, 905; (b) Shaw, R.; Lathbury, D.; Anderson, M.; Gallagher, T. *J. Chem. Soc., Perkin Trans. 1*, **1991**, 659; (c) Grigg, R.; Pratt, R. *Tetrahedron Lett*. **1997**, *38*, 4489; (d) Okuro, K.; Alper, H. *J. Org. Chem.* **1997**, *62*, 1566; (e) Grigg, R.; Monteith, M.; Sridharan, V.; Terrier, C. *Tetrahedron*, **1998**, *54*, 3885; (f) Xiao, W. J.; Vasapollo, G.; Alper, H. *J. Org. Chem*. **1998**, *63*, 2609; (g) Grigg, R.; MacLachlan, W.; Rasparini, M. *Chem. Commun*. **2000**, 2241; (h) Wang, L.; Wang, Y. X.; Liu, C.; Lei, A. W. *Angew. Chem. Int. Ed*. **2014**, *53*, 5657; (i) Liu, J.; Liu, Q.; Franke, R.; Jackstell, R.; Beller, M. *J. Am. Chem. Soc*. **2015**, *137*, 8556.

[17] (a) *Privileged Chiral Ligandsand Catalysts,* Ed. Zhou, Q.-L.; Wiley-VCH, Weinheim, **2011**; (b) Xie, J.-H.; Zhou, Q.-L. *Acta Chim. Sinica* **2014**, *72*, 778.

[18] Grainger, R. S.; Betou, M.; Male, L.; Pitak, M. B.; Coles, S. J. *Org. Lett*. **2012**, *14*, 2234.

[19] Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett*. **1999**, *1* 953.


R
ArNH2
CO (balloon)
MeOH
(S,S,S)-SKP/Pd(OAc)2
(cat)
Cu(OCOEt)2 , rt
Ph2P
PPh2
SKP
ArNH
O
R
OMe
36 examples
up to 95% yield
up to 98:2 B/L
up to 96% ee