

Copper-Catalyzed Asymmetric Umpolung Hydroamination: an Unified Strategy for the Synthesis of Chiral β -Amino Acid and Its Derivatives

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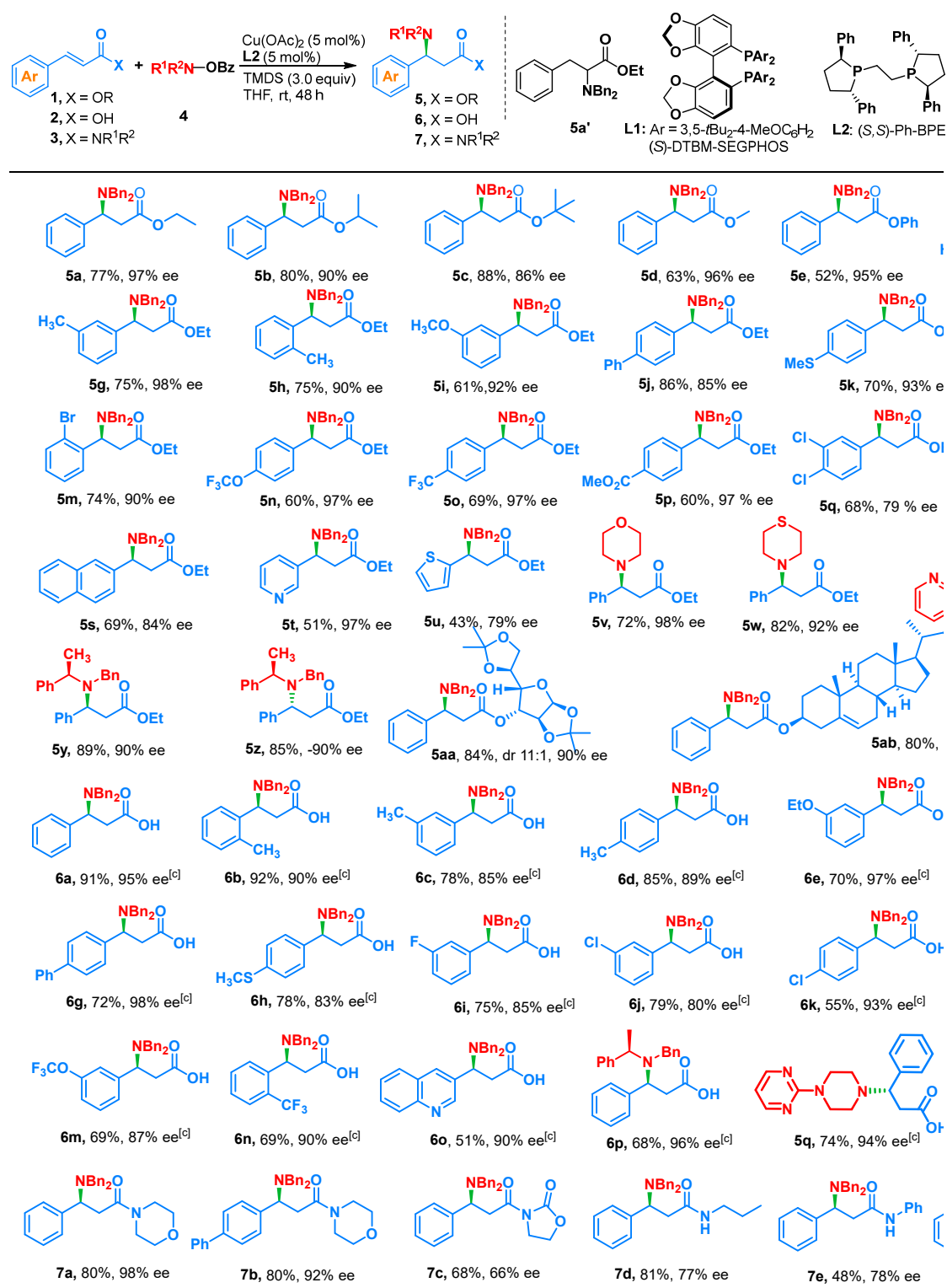
Abstract: Catalytic asymmetric aza-Michael represents one of the most convenient and atom-economical approach for the rapid construction of biologically active chiral β -amino acid frameworks. However, the direct enantioselective addition of nitrogen-based nucleophiles to intrinsically low reactivity of α , β -unsaturated carboxylic acid, ester, and amide, as well as simple α , β -unsaturated nitrile, remains a long-standing challenge. Herein, we reported an unified Cu-catalyzed asymmetric umpolung hydroamination, which is capable of direct preparation of a series of β -amino acid, ester, amide, and nitrile in a highly regio- and enantioselective manner, without the requirement of traditional pre-installation of stoichiometric quantities of auxiliaries.

Catalytic asymmetric 1,4-addition of nitrogen-based nucleophiles to the Michael acceptors, namely aza-Michael addition reaction, has attracted continuous attention in recent decades,¹ owing to furnishing one of the most convenient and atom-economical approach for the rapid construction of biologically and synthetically extremely important chiral β -amino acid frameworks from readily accessible feedstocks.² In this regard, impressive advances have been made for the chemo- and enantioselective addition of nitrogen-based nucleophiles to highly reactive Michael acceptors,¹ such as α , β -unsaturated aldehydes, ketones, nitroolefins and vinyl sulfones. However, the corresponding addition to intrinsically less reactive α , β -unsaturated acid, ester, and amide has far less been well established.^{1,3} Inspired by enzymatic systems activated unreactive carboxylic acids, the preponderant strategy up to now typically relies on the pre-installation of an activating functional group on the carbonyl to enhance the reactivity and increase enantioselectivity (Scheme 1 A, top).⁴ Nevertheless, the requirement of pre-installation and subsequent deprotection of stoichiometric quantities of activating auxiliaries are time-consuming multistep sequences, and sometimes might lead to chiral products racemization and/or incompatible with delicate molecular architectures when removal of these auxiliaries. To our knowledge, only some sporadic examples described the direct addition to α , β -unsaturated acid⁵ and α , β -unsaturated ester⁶ as well as enzyme-catalyzed transformations so far.⁷ Furthermore, the simple α , β -unsaturated nitriles (β -substituted acrylonitrile), another typical kind of Michael acceptor and versatile building blocks in synthetic chemistry,⁸ the enantioselective addition with nitrogen-based nucleophiles to form a chiral center at the β -position of the nitrile group is only up to 22% enantiomeric excess (ee) value (Scheme 1 A,

At the outset of our studies, we selected ethyl cinnamate **1a** and *O*-benzoylhydroxylamine **4a** as the model substrates in the presence of 5 mol% of Cu(OAc)₂ and (*S*)-DTBM-SEGPHOS **L1**, the extremely powerful catalytic system of CuH-catalyzed asymmetric hydroamination pioneered by the group of Buchwald, with an excess of TMDS (1,1,3,3-tetramethyldisiloxane) at room temperature under N₂ atmosphere in THF for 48 h (Table. 1). In line with the regioselectivity of previous CuH-catalyzed transformations of α , β -unsaturated ester,^[11b,14] the α -alkylaminyl substituted product **5a'** was obtained in 39% yield but without enantioinduction. During a thorough evaluation of various chiral ligands, we were surprised to discover that the regioreversed β -alkylaminyl substituted ester **5a**, namely formal aza-Michael addition product, could be obtained and (*S,S*)-Ph-BPE **L2** showed most efficiency in terms of reactivity, regio- and stereocontrol (77% yield and 97% ee).¹⁷ Moreover, we did not observe the regioisomer **5a'** with **L2** as the ligand. Examining other commercially available hydrosilanes and solvents were also performed and slightly inferior either the yield or enantiocontrol under the otherwise optimal reaction conditions were observed.¹⁷

In assessing the scope of the catalytic reaction (Table 1), we found that an array of α , β -unsaturated esters **1** bearing different steric hindrance functional groups could be efficiently transformed to the corresponding chiral β -aminyl esters **5a-5e** in generally high yields with excellent enantioselectivities. Various substituents including alkyl, methoxyl, phenyl and methylthiyl at either *ortho*-, *meta*- or *para*-position on the aromatic rings of the unsaturated esters **1** were also efficiently converted into chiral products **5f-5k** with high level of enantiocontrol. An array of electronic-withdrawing groups, including -F, -Cl, -Br, -OCF₃, -CF₃, -C(O)OMe, and some privileged heteroaromatic ring motifs widespread in bioactive molecules and pharmaceuticals, such as pyridine and thiophene, were also readily accommodated and provided expected hydroamination products **5l-5u** in good yields with excellent enantioselectivities. In addition to examining the scope of α , β -unsaturated esters, we also surveyed the substrate scope with respect to the hydroxylamine ester component. We found that electron-rich or electron-deficient hydroxylamine esters, nitrogen-containing heterocyclic hydroxylamine esters, as well as the enantiomeric hydroxylamine esters were all applicable to this hydroamination and provided β -aminyl esters **5v-5z** with high efficiency and good to excellent enantiocontrol. Structurally more complicated diacetone-D-glucose and cholesterol-derived α , β -unsaturated esters could also be transferred smoothly into corresponding β -amino ester **5aa** and **5ab** in good yield with excellent diastereo- and enantiocontrol. The success of this asymmetric hydroamination strategy for α , β -unsaturated ester encouraged us to continue examining whether this approach could also be applied to synthesize chiral β -aminyl acids and amides. To our delight, without the requirement of further optimizing reaction conditions, a diverse range of α , β -unsaturated acids with various electronic-withdrawing or donating functional groups on the aromatic rings (**2a-2n**), including methyl, ethoxyl, ester, phenyl, methylthiyl, halogens, trifluoromethoxyl and trifluoromethyl, and (*E*)-3-(quinolin-3-yl)acrylic acid (**2o**) were suitable coupling partners for this amination, providing corresponding β -alkylaminyl substituted acid **6a-6o** with high efficiency and generally excellent level of enantiocontrol. In addition, some representative hydroxylamine esters were also examined and could be readily converted into chiral β -aminyl acids **6p-6r** with over 90% ee. α , β -Unsaturated amides **3a-3f** could also be converted into corresponding β -aminyl amides **7a-7f** under this catalytic system with high efficiency, despite showing relatively low enantiocontrol compared with that of α , β -Unsaturated ester and acid.

Table 1: Scope of hydroamination of α , β -unsaturated ester, acid and amide.^{a,b}

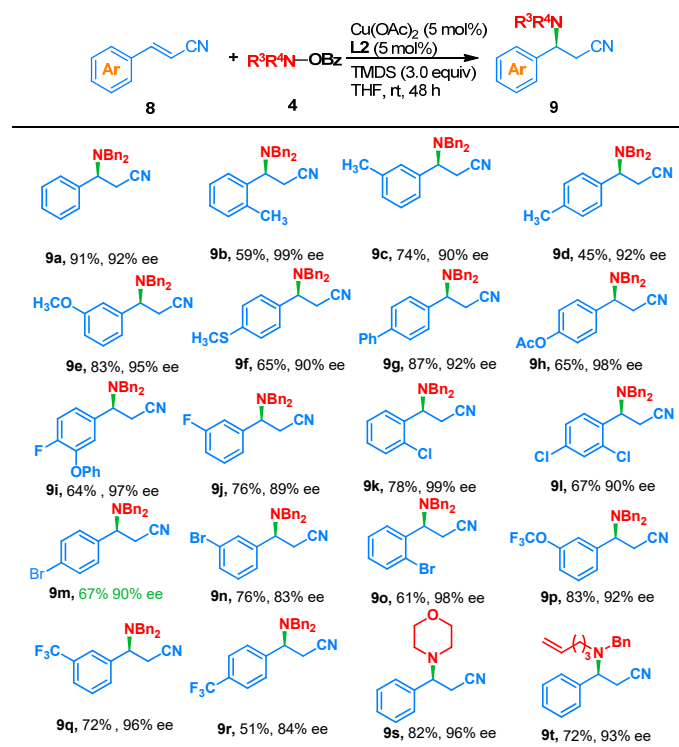


a Reaction conditions: α , β -unsaturated carbonyl compounds (0.2 mmol), **4** (0.3 mmol, 1.5 equiv), TMDS (3.0 equiv), Cu(OAc)₂ (5 mol%) and chiral ligand **L2** (5 mol%) in 2.0 mL dry THF at room temperature for 48 h. b Yield determined by ¹H NMR spectroscopy using CH₂Br₂ as an internal standard and ee value determined by HPLC. c 6.0 equiv TMDS was used and the reactions were performed at 50 °C.

Inspired by the above encouraging results, we next particularly interested that whether this umpolung hydroamination strategy could be applicable to α , β -unsaturated nitriles to form synthetically formidable challenging chiral β -amino nitriles. We then began our investigation using

(*E*)-cinnamonitrile **8** as the Michael acceptor. To our delight, the expected β -amino substituted nitrile **9a** was indeed generated in 91% yield and 92% ee without any further optimization reaction conditions. Encouraged by this result, we then commenced assessment of substrate scope and the functional group compatibility (Table 2). In general, this reaction also showed good functional group tolerance and had nearly negligible electronic effect. For example, either electron-donating functional groups (-CH₃, -OCH₃, -SCH₃, -C₆H₅, -OAc, and -OC₆H₅) or electron-withdrawing functional groups (-F, -Cl, -Br, -OCF₃, and -CF₃) on the aromatic rings of the α , β -unsaturated nitriles, all of which tolerated well and corresponding substrates converted smoothly into desired chiral β -amino nitriles **9b-9r** in good to excellent yields with more than 90% ee values in most cases. Two representative aminating reagents were also examined and could enable the nitrogen-containing substructures to integrate into the expected chiral products **9s** and **9t** with high efficiency and good enantiocontrol. In addition, the absolute configuration of the product **9o** was unequivocally determined by single-crystal X-ray diffraction.

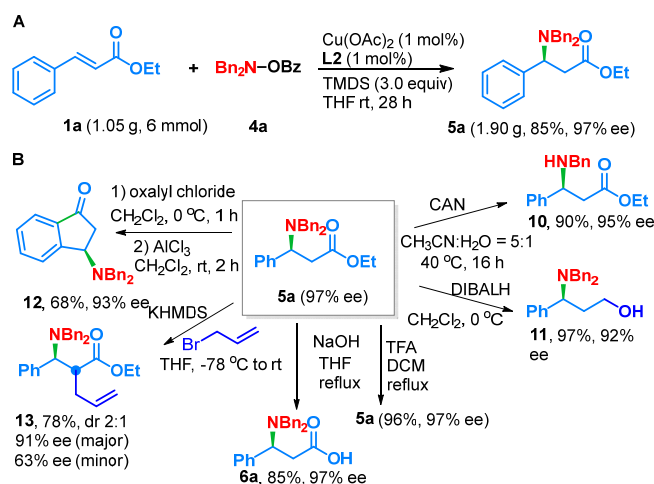
Table 2: Scope of hydroamination of α , β -unsaturated nitrile.^{a,b}



^a Reaction conditions: α , β -unsaturated nitrile **8** (0.2 mmol), **4** (0.3 mmol, 1.5 equiv), TMDS (3.0 equiv), Cu(OAc)₂ (5 mol%) and chiral ligand **L2** (5 mol%) in 2.0 mL dry THF at room temperature for 48 h. ^b Yield determined by ¹H NMR spectroscopy using CH₂Br₂ as an internal standard and ee value determined by HPLC.

A gram-scale synthesis was conducted to demonstrate the practicability of this method, the target chiral β -amino ester **5a** was obtained in good yield without any erosion in enantioselectivity with 1 mol% CuCl and 1 mol % chiral ligand **L2** (Scheme 2A). We also examined further applications of this chiral compound (Scheme 2B). For instance, chiral β -amino ester **5a** would undergo a selective mono-debenzylation or reduction process, offering chiral β -amino ester **10** and important chiral γ -amino alcohol **11** in excellent yield with 95% and 92% ee, respectively. In addition, ester **5a** can also convert into the chiral cyclic β -amino ketone **12** smoothly in 68% yield with slightly erosion of enantioselectivity. The chiral β -amino ester **5a** could be further functionalized at the α -

position of the ester group and deliver more complex molecules. For example, **5a** could be efficiently allylated with allyl bromide in the presence of KHMDS, providing synthetically versatile compound **13** with 2:1 diastereoselectivity. Moreover, without any racemization at the chiral center in **5a** was observed under harsh conditions (e.g. in the presence of NaOH or TFA), that indicate these types of chiral compounds might have the capacity to transfer into more complicated chiral compounds, meanwhile maintaining the enantioselectivity.



Scheme 2. Gram-scale synthesis and applications of chiral β -amino ester

In summary, we have developed an efficient umpolung hydroamination strategy of α , β -unsaturated carboxylic acid, ester, amide, and nitrile through precious choice of chiral ligand, providing an unified approach for the convenient and rapid synthesis of an array of important chiral β -amino acids and their derivatives with high level of regio- and enantiocontrol. Although further studies need to carry out to illuminate the origin of this unusual regio- and enantioselectivity, this approach not only provides an alternative route to traditional aza-Michael addition, but also opens a new door for the challenging asymmetric addition of other nucleophiles to low reactivity of Michael acceptors. Mechanism studies are currently under way in our lab.

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Keywords: asymmetric catalysis • umpolung hydroamination • chiral β -amino acid and its derivatives • copper catalysis

- 1 a) L.-W. Xu, C.-G. Xia, *Eur. J. Org. Chem.* **2005**, 633–639; b) D. Enders, C. Wang, J. X. Liebich, *Chem. Eur. J.* **2009**, *15*, 11058–11076; c) M. Sánchez-Roselló, J. L. Aceña, A. Simón-Fuentes, C. del Pozo, *Chem. Soc. Rev.* **2014**, *43*, 7430–7453; d) G. Desimoni, G. Faita, P. Quadrelli, *Chem. Rev.* **2015**, *115*, 9922–9980; e) J. Wang, P. Li, P. Y. Choy, A. S. C. Chan, F. Y. Kwong, *ChemCatChem* **2012**, *4*, 917–925; f) K. Zheng, X. Liu, X. Feng, *Chem. Rev.* **2018**, *118*, 7586–7656.
- 2 a) *Enantioselective Synthesis of β -Amino Acids*. (Ed. Juaristi, E), Wiley-VCH: New York, **1997**; b) Z. Amara, J. Caron, D. Joseph, *Nat. Prod. Rep.* **2013**, *30*, 1211–1225; c) *Highlights in Bioorganic Chemistry*; (Eds.: C. Schmuck, H. Wennemers), Wiley-VCH: Weinheim, **2004**. d) G. Cardillo, C. Tomasini, *Chem. Soc. Rev.* **1996**, *25*, 117–128; e) *Cephalosporins and Penicillins Chemistry and Biology*; (Ed.: Flynn, E. H), Academic Press: New York and London, **1972**.
- 3 a) *Comprehensive Asymmetric Catalysis I-III*, (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **1999**. b) *Catalytic Asymmetric Conjugate Reactions*, (Ed.: A. Córdova), Wiley-VCH, **2010**.

- 4 For reviews, see: a) B. Weiner, W. Szymański, D. B. Janssen, A. J. Minnaard, B. L. Feringa, *Chem. Soc. Rev.* **2010**, *39*, 1656–1691; b) D. Monge, H. Jiang, Y. Alvarez-Casao, *Chem. Eur. J.* **2015**, *21*, 4494–4504; c) K. M. Byrd, *Beilstein J. Org. Chem.* **2015**, *11*, 530–562. For leading examples: see: c) L. Falborg, K. A. Jørgensen, *J. Chem. Soc., Perkin Trans. 1* **1996**, 2823–2826; d) H. Jiang, M. W. Paixão, D. Monge, K. A. Jørgensen, *J. Am. Chem. Soc.* **2010**, *132*, 2775–2783; e) M. P. Sibi, J. J. Shay, M. Liu, C. P. Jasperse, *J. Am. Chem. Soc.* **1998**, *120*, 6615–6616; f) M. P. Sibi, M. Liu, *Org. Lett.* **2001**, *3*, 4181–4184; g) M. P. Sibi, N. Prabakaran, S. G. Ghorpade, C. P. Jasperse, *J. Am. Chem. Soc.* **2003**, *125*, 11796–11797; h) J. K. Myers, E. N. Jacobsen, *J. Am. Chem. Soc.* **1999**, *121*, 8959–8960; i) M. Gandelman, E. N. Jacobsen, *Angew. Chem. Int. Ed.* **2005**, *44*, 2393–2397; *Angew. Chem.* **2005**, *117*, 2445–2449; j) N. Yamagiwa, H. Qin, S. Matsunage, M. Shibasaki, *J. Am. Chem. Soc.* **2005**, *127*, 13419–13427; k) S. Matsunage, T. Kinoshita, S. Okada, S. Harada, M. Shibasaki, *J. Am. Chem. Soc.* **2004**, *126*, 7559–7570; l) T. E. Horstmann, D. J. Guerin, S. J. Miller, *Angew. Chem. Int. Ed.* **2000**, *39*, 3635–3638; *Angew. Chem.* **2000**, *112*, 3781–3784 m) D. J. Guerin, S. J. Miller, *J. Am. Chem. Soc.* **2002**, *124*, 2134–2136; n) S. Kikuchi, H. Sato, S. Fukuzawa, *Synlett* **2006**, *7*, 1023–1026; o) B. E. Uno, R. D. Dicken, L. R. Redfern, C. M. Stern, G. G. Krzywicki, K. A. Scheidt, *Chem. Sci.* **2018**, *9*, 1634–1639
- 5 N. Hayama, R. Kuramoto, T. Földes, K. Nishibayashi, Y. Kobayashi, I. Pápai, Y. Takemoto, *J. Am. Chem. Soc.* **2018**, *140*, 12216–12225;
- 6 a) M. Bandini, A. Eichholzer, M. Tragni, A. Umami-Ronchi, *Angew. Chem. Int. Ed.* **2008**, *47*, 3238–3241; *Angew. Chem.* **2008**, *120*, 3282–3285; b) Y. Lin, W. J. Hirschi, A. Kunadia, A. Paul, I. Ghiviriga, K. A. Abboud, R. W. Karugu, M. J. Vetticatt, J. S. Hirschi, D. Seidel, *J. Am. Chem. Soc.* **2020**, *142*, 5627–5635.
- 7 a) N. J. Weise, F. Parmeggiani, S. T. Ahmed, N. J. Turner, *J. Am. Chem. Soc.* **2015**, *137*, 12977–12983; b) R. Li, H. J. Wijma, L. Song, Y. Cui, M. Otzen, Y. Tian, J. Du, T. Li, D. Niu, Y. Chen, J. Feng, J. Han, H. Chen, Y. Tao, D. B. Janssen, B. Wu, *Nature Chemical Biology* **2018**, *14*, 664–670.....
- 8 A. J. Fatiadi, In *Preparation and Synthetic Applications of Cyano Compounds*, (Eds.: S. Patai and Z. Rappaport), Wiley, New York, **1983**.
- 9 a) L. Fadini, A. Togni, *Chem. Commun.* **2003**, 30–31; b) L. Fadini, A. Togni, *Helvetica Chimica Acta* **2007**, *90*, 411–424; c) Z. Yang, D. Liu, Y. Liu, M. Sugiya, T. Imamoto, W. Zhang, *Organometallics* **2015**, *34*, 1228–1237.
- 10 For selected recent reviews, see: a) T. E. Müller, M. Beller, *Chem. Rev.* **1998**, *98*, 675–704; b) F. Alonso, I. P. Beletskaya, M. Yus, *Chem. Rev.* **2004**, *104*, 3079–3159; c) T. E. Müller, K. C. Hultsch, M. Yus, F. Foubelo, M. Tada, *Chem. Rev.* **2008**, *108*, 3795–3892; d) L. Huang, M. Arndt, K. Gooßen, H. Heydt, L. Gooßen, *Chem. Rev.* **2015**, *115*, 2596–2697; For asymmetric hydroamination of alkenes, see: e) A. L. Reznichenko, A. J. Nawara-Hultsch, K. C. Hultsch, *Top. Curr. Chem.* **2013**, *343*, 191–260; f) J. Hannedouche, E. Schulz, *Chem. Eur. J.* **2013**, *19*, 4972–4985; g) G. Zi, *J. Organomet. Chem.* **2011**, *696*, 68–75; h) G. Zi, *Dalton Trans.* **2009**, 9101–9109; i) S. R. Chmaler, *Org. Biomol. Chem.* **2009**, *7*, 3009–3019; j) I. Aillaud, J. Collin, J. Hannedouche, E. Schulz, *Dalton Trans.* **2007**, 5105–5118; k) K. K. Hii, *Pure Appl. Chem.* **2006**, *78*, 341–349.
- 11 For reviews, see: a) S. Rendler, M. Oestreich, *Angew. Chem. Int. Ed.* **2007**, *46*, 498–504; *Angew. Chem.* **2007**, *119*, 504–510; b) C. Deutsch, N. Krause, B. H. Lipshutz, *Chem. Rev.* **2008**, *108*, 2916–2927; c) T. Fujihara, K. Semba, J. Terao, Y. Tsuji, *Catal. Sci. Technol.* **2014**, *4*, 1699–1709; d) M. T. Pirnot, Y.-M. Wang, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2016**, *55*, 48–57; *Angew. Chem.* **2016**, *128*, 48–57; e) A. J. Jordan, G. Lalic, J. P. Sadighi, *Chem. Rev.* **2016**, *116*, 8318–8372; f) Chen, J., Guo, J., Lu, Z. *Chin. J. Chem.* **2018**, *36*, 1075–1109.
- 12 a) S. Zhu, S. L. Buchwald, *J. Am. Chem. Soc.* **2014**, *136*, 15913–15916; b) N. Niljianskul, S. Zhu, S. L. Buchwald, *Angew. Chem., Int. Ed.* **2015**, *54*, 1638–1641; *Angew. Chem.* **2015**, *127*, 1658–1661; c) S.-L. Shi, S. L. Buchwald, *Nat. Chem.* **2015**, *7*, 38–44; d) Y. Miki, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2014**, *16*, 1498–1501; e) Y. Xi, T. W. Butcher, J. Zhang, J. F. Hartwig, *Angew. Chem., Int. Ed.* **2016**, *55*, 776–780; f) D. Nishikawa, K. Hirano, M. Miura, *J. Am. Chem. Soc.* **2015**, *137*, 15620–15623; g) Y. Yang, S.-L. Shi, D. Niu, P. Liu, S. L. Buchwald, *Science* **2015**, *349*, 62–66; h) J. S. Bandar, M. T. Pirnot, S. L. Buchwald, *J. Am. Chem. Soc.* **2015**, *137*, 14812–14818; i) S.-L. Shi, Z. L. Wong, S. L. Buchwald, *Nature* **2016**, *532*, 353–356; j) S. Tobisch, *Chem. Eur. J.* **2016**, *22*, 8290–8300; k) S. Zhu, N. Niljianskul, S. L. Buchwald, *Nat. Chem.* **2016**, *8*, 144–150; l) H. Wang, J. C. Yang, S. L. Buchwald, *J. Am. Chem. Soc.* **2017**, *139*, 258428–8431; m) G. Lu, R. Y. Liu, Y. Yang, C. Fang, D. S. Lambrecht, S. L. Buchwald, P. Liu, *J. Am. Chem. Soc.* **2017**, *139*, 16548–16555; n) Y. Zhou, O. Engl, J. S. Bandar, E. D. Chant, S. L. Buchwald, *Angew. Chem., Int. Ed.* **2018**, *57*, 6672–6675; *Angew. Chem.* **2018**, *130*, 6782–6785; o) Q.-F. Xu-Xu, Q.-Q. Liu, X. Zhang, S.-L. You, *Angew. Chem. Int. Ed.* **2018**, *57*, 15204–15208; *Angew. Chem.* **2018**, *130*, 15424–15428; p) S. Ichikawa, S. Zhu, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2018**, *57*, 8714–8718; *Angew. Chem.* **2018**, *130*, 8850–8854; q) S. Guo, J. C. Yang, S. L. Buchwald, *J. Am. Chem. Soc.* **2018**, *140*, 15976–15984; r) F. Xie, B. Shen, X. Li, *Org. Lett.* **2018**, *20*, 7154–7157; s) A. A. Thomas, K. Speck, I. Kevlishvili, Z. Lu, P. Liu, S. L. Buchwald, *J. Am. Chem. Soc.* **2018**, *140*, 13976–13984; t) L. Yu, P. Somfai, *Angew. Chem. Int. Ed.* **2019**, *58*, 8551–8555; *Angew. Chem.* **2019**, *131*, 8639–8643; u) T. Takata, K. Hirano, M. Miura, *Org. Lett.* **2019**, *21*, 4284–4288; v) S. Ichikawa, X.-J. Dai, S. L. Buchwald, *Org. Lett.* **2019**, *21*, 4370–4373.
- 13 a) a) Y. Miki, K. Hirano, T. Satoh, M. Miura, *Angew. Chem. Int. Ed.* **2013**, *52*, 10830–10834; *Angew. Chem.* **2013**, *125*, 11030–11034; b) S. Zhu, N. Niljianskul, S. L. Buchwald, *J. Am. Chem. Soc.* **2013**, *135*, 15746–15749.
- 14 a) B. H. Lipshutz, W. Chrisman, K. Noson, P. Papa, J. A. Scalfani, R. W. Vivian, J. M. Keith, *Tetrahedron* **2000**, *56*, 2779–2788; b) D. H. Apella, Y. Moritani, R. Shintani, E. M. Ferreira, S. L. Buchwald, *J. Am. Chem. Soc.* **1999**, *121*, 9473–9474; c) Y. Moritani, D. H. Apella, V. Jurkauskas, S. L. Buchwald, *J. Am. Chem. Soc.* **2000**, *122*, 6797–6798; d) G. Hughes, M. Kimura, S. L. Buchwald, *J. Am. Chem. Soc.* **2003**, *125*, 11253–11258;

- e) M. P. Rainka, Y. Aye, S. L. Buchwald, *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5821–5823; f) B. H. Lipshutz, J. M. Servesko, B. R. Taft, *J. Am. Chem. Soc.* **2004**, *126*, 8352–8353.
- 15 a) G. Xu, H. Zhao, B. Fu, A. Cang, G. Zhang, Q. Zhang, T. Xiong, Q. Zhang, *Angew. Chem. Int. Ed.* **2017**, *56*, 13130–13134; *Angew. Chemie.* **2017**, *129*, 13310–13314; b) G. Xu, B. Fu, H. Zhao, Y. Li, G. Zhang, Y. Wang, T. Xiong, Q. Zhang, *Chem. Sci.*, **2019**, *10*, 1802–1806; c) B. Fu, X. Yuan, Y. Li, Y. Wang, Q. Zhang, T. Xiong, Q. Zhang, *Org. Lett.* **2019**, *21*, 3576–3580.
- 16 S. Guo, J. Zhu, S. L. Buchwald, *Angew. Chem. Int. Ed.* Doi: 10.1002/anie.202007005.
- 17 See Supplementary Information for details.

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