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Communication

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# Nickel-Catalyzed Enantioselective Hydroarylation and Hydroalkenylation of Styrenes

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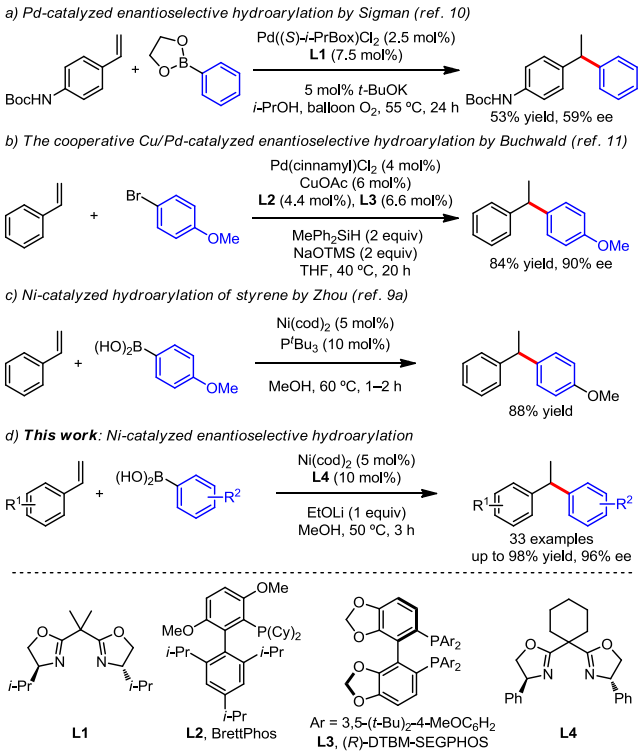
*Supporting Information Placeholder*

**ABSTRACT:** We have developed a Ni-catalyzed enantioselective hydroarylations of styrenes with arylboronic acids using MeOH as the hydrogen source, providing an efficient method to access 1,1-diarylalkanes, which are essential structural units in many biologically active compounds. In addition, Ni-catalyzed enantioselective hydrovinylation of styrenes with vinylboronic acids is also realized with good yields and enantioselectivities. The synthetic utility was demonstrated by the efficient synthesis of (*R*)-(-)-Ibuprofen.

Construction of a tertiary stereogenic center bearing two different aryl groups, an essential structure units found in both natural products and pharmaceuticals, is of great importance in organic synthesis.[1] In this context, various methods employing asymmetric catalysis have been developed for the synthesis of enantioenriched 1,1-diarylalkanes,[2] including the hydrogenation of 1,1-diarylalkenes,[3] the conjugate addition of aryl nucleophiles to 1-arylalkenes,[4] the cross-coupling benzylic reagents with nucleophiles or electrophiles,[5,6] and arylation via C–H functionalization.[7] Alternatively, transition-metal-catalyzed enantioselective hydroarylation of styrenes offers a straightforward method to the synthesis of 1,1-diaryl alkanes, in which active catalyst species metal–hydride (M–H) is involved.[8,9] Due to the requirement for ligand to obtain high branch selectivity, the development of an enantioselctive hydroarylation of styrenes was still challenging. To date, only two examples have been developed for the enantioselective hydroarylation of styrenes. In 2011, Sigman and co-workers elegantly developed palladium-catalyzed enantioselective hydroarylation of styrenes with aryl boron esters using *i*-PrOH as the hydride source with moderate yields and enantioselectivities (Scheme 1a).[10] This work was a milestone in the field of enantioselective hydroarylation, as it inspired further studies to address the issues. In 2016, Buchwald and co-workers reported the cooperative Cu/Pd-catalyzed hydroarylation of styrenes with arylbromides using $MePh_2SiH$ as the hydride source, affording 1,1-diarylethanes in good yields with good to excellent enantioselectivities (Scheme 1b).[11] Recently, Zhou and co-workers elegantly developed a Ni-catalyzed hydroarylation of styrenes and 1,3-dienes with organoboron compounds (Scheme 1c).[9a] Nevertheless, nickel-catalyzed enantioselective hydroarylation of styrenes remains undeveloped. Herein, we report a Ni-catalyzed enantioselective hydroarylation of styrenes with arylboronic acids using MeOH as the hydride source and chiral bis(oxazoline) ligand **L4** (Scheme 1d). In addition, we have successfully developed a catalytic hydrovinylation of styrenes with vinylboronic acids with good to excellent enantioselectivities.

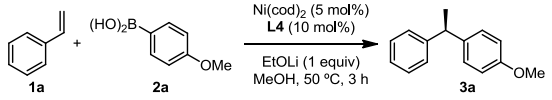
**Scheme 1. Catalytic Enantioselective Hydroarylation**



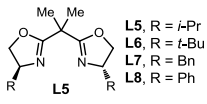

Initially, we chose styrene (**1a**) and 4-methoxyphenylboronic acids (**2a**) as model substrates and MeOH as a hydride source, and probed various reaction conditions for the envisioned hydroarylation. After extensive optimization, we found that 92% isolated yield of 1,1,-diarylethane (**3a**) could be obtained with 92% ee value in the presence of 5 mol% of $Ni(cod)_2$, 10 mol% of bis(oxazoline) ligand **L4**, and one equivalent of

EtOLi in MeOH at 50 °C after 3 h (Table 1, entry 1). $NiCl_2$ is not effective for this reaction (entry 2). The reactivity diminished significantly if $Ni(PPh_3)_4$ was used (entry 3). The addition of base is helpful for the achievement of high enantioselectivity and LiOEt is optimal among the bases we tried (entry 4–7). Evaluating different substituents on the Box ligands bearing a gem-dimethyl linkage revealed that phenyl substituent is optimal and 49% $^1$H NMR yield with 85% ee value was achieved using chiral bis(oxazoline) ligand **L8** (entries 8–11). Subsequent investigations focused on ligands **L9–L12** since the bite-angle (θ) of Box ligands could affect the enantioselectivity. Generally, when ring size of Box ligands become larger (from n = 3 to 6), the bite angle (θ) decreased.[12] Evaluating different ring size of Box ligands (from n = 3 to 7) revealed that **L4** is optimal and 92% isolated yield with 92% ee value was achieved (entries 12–15).

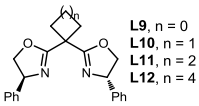
**Table 1. Reaction Optimization with Substrate 1a**




| entry | variation from standard conditions[a] | yield (%)[b] | ee (%)[c] |
|---|---|---|---|
| 1 | none | 96 (92)[d] | 92 |
| 2 | $NiCl_2$ in lieu of $Ni(cod)_2$ | <5 | – |
| 3 | $Ni(PPh_3)_4$ in lieu of $Ni(cod)_2$ | <5 | – |
| 4 | no EtOLi | 64 | 63 |
| 5 | MeOLi in lieu of EtOLi | 82 | 90 |
| 6 | *i*-PrOLi in lieu of EtOLi | 90 | 89 |
| 7 | *t*-BuOLi in lieu of EtOLi | 95 | 89 |
| 8 | **L5** in lieu of **L4** | <5 | – |
| 9 | **L6** in lieu of **L4** | <5 | – |
| 10 | **L7** in lieu of **L4** | 76 | 40 |
| 11 | **L8** in lieu of **L4** | 49 | 85 |
| 12 | **L9** in lieu of **L4** | 11 | 17 |
| 13 | **L10** in lieu of **L4** | 88 | 84 |
| 14 | **L11** in lieu of **L4** | 96 | 76 |
| 15 | **L12** in lieu of **L4** | 62 | 90 |




**L5**, R = *i*-Pr
**L6**, R = *t*-Bu
**L7**, R = Bn
**L8**, R = Ph

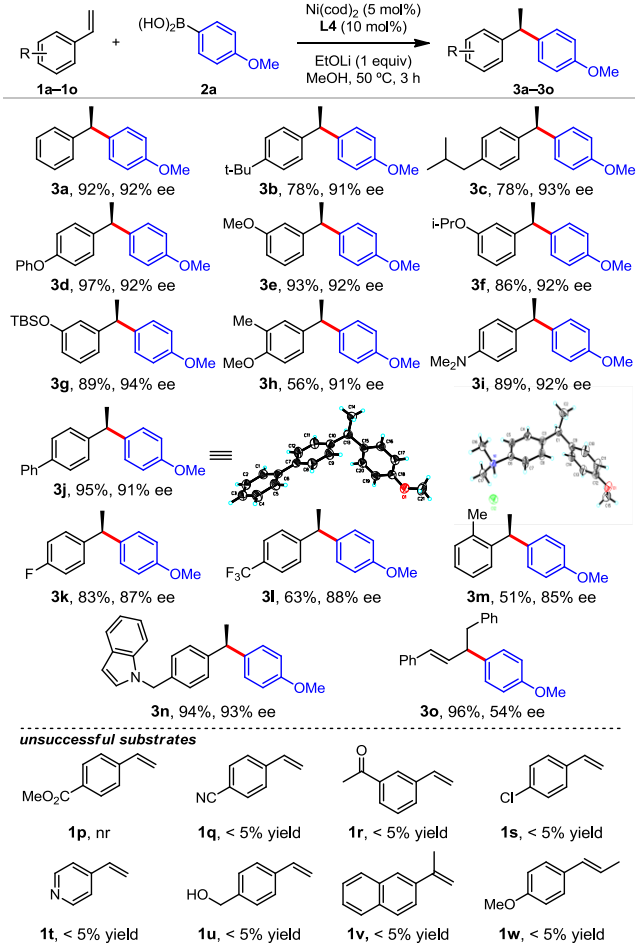



**L9**, n = 0
**L10**, n = 1
**L11**, n = 2
**L12**, n = 4

[a]Reaction conditions: **1a** (0.25 mmol), **2a** (0.5 mmol), $Ni(cod)_2$ (5 mol%), ligand (10 mol%), additives (0.25 mmol), in MeOH (1 mL) at 50 °C for 3 h. EtOLi is 1.0 M solution in ethanol. [b]Yields were determined by $^1$H NMR using $CH_2Br_2$ internal. [c]Enantioselectivities were determined by chiral HPLC analysis. [d]Yield of isolated product **3a**.

With the optimized reaction conditions in hand, the substrate scope was evaluated to test the generality and limitation of this Ni-catalyzed hydroarylation. As shown in Scheme 2, styrene derivatives substituted with a variety of functional groups such as alkyl, ether, OTBS, phenyl, fluoro, and trifluoromethyl groups were well tolerated under standard conditions (**3a–3m**). In general, hydroarylation of styrenes with electron-rich or electron-neutral substituents resulted in 91–94% ee values with good to excellent yields (**3a–3j**). A strongly electron withdrawing group, such as $CF_3$, afforded a 87% ee value with slightly lower yield (**3l**). An *ortho*-substituted styrene is also tolerated, affording slightly lower yield and enantioselectivity (**3m**). To our satisfaction, indole substituted styrene also gave an excellent yield and enantioselectivity (**3n**). It is worth noting that 1,3-diene substrate reacted particularly well (96% yield), although low enantioselectivity was obtained (**3o**). In addition, the structures of **3i** and **3j** were unambiguously confirmed by X-ray analysis. Although this reaction is useful for the enantioselective hydroarylation of numerous styrenes, it is not without its limitations. For examples, although fluoro and trifluoromethyl substituted styrenes are reactive (**3k** and **3l**), styrenes bearing ester, nitrile, ketone, and chloro group, are not reactive at current reaction conditions (**1p–1s**). 4-Vinylpyridine and styrene containing a free alcohol, are not tolerated (**1t** and **1u**). In addition, α- and β-substituted styrenes are not reactive at current reaction conditions (**1v** and **1w**).

**Scheme 2. Evaluation of Styrene Scope**[a,b]

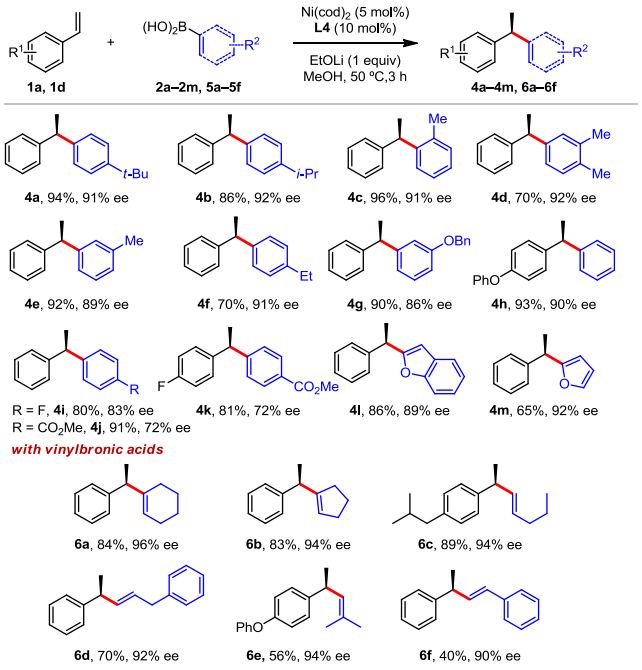



[a]Isolated yields are reported unless otherwise noted.Yields of isolated products on 0.25 mmol scale. [b]Enantioselectivities were determined by chiral HPLC analysis.

Encouraged by the feasibility of Ni-catalyzed hydroarylation using substituted styrenes, we moved on to examine the reactivity of a series of arylboronic acids, which are readily available. As shown in Scheme 3, substrates containing various functional groups, including alkyl, ether, and ester group were tolerated, affording good to excellent yields (**4a–4m**). In general, arylboronic acids with electron-rich or electron-neutral substituents resulted in 86–91% ee values with excellent yields (**4a–4h**). A strongly electron withdrawing group, such as ester, afforded excellent yields with moderate enan-

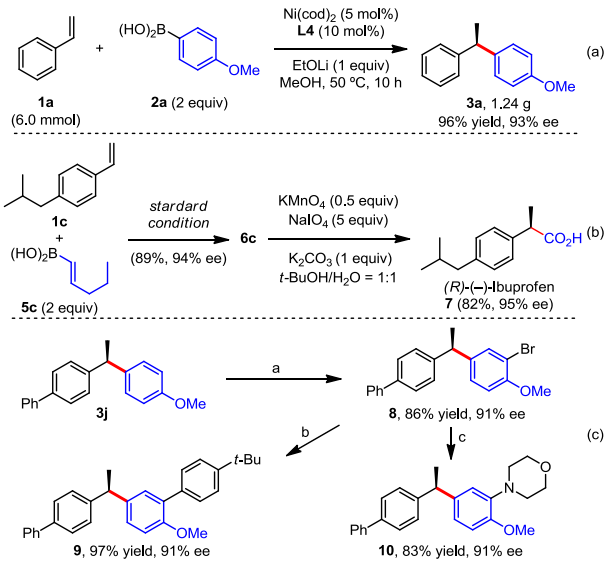
tioselectivity (**4j** and **4k**). To our delight, heteroaromatic rings such as benzofuran and furan are tolerated under standard conditions, which results in good enantioselectivities and yields (**4l** and **4m**). Furthermore, this protocol could also be applied to enantioselective hydrovinylation of styrenes with various vinylboronic acids. To the best our knowledge, enantioselective Ni-catalyzed enantioselective hydroalkenylation of styrene with vinylboronic acids is unknown.[13] As shown in Scheme 3, cyclic and acyclic vinylboronic acids were well tolerated under the standard conditions, affording good yields with 89–96% ee values (**6a–6f**).

**Scheme 3. Evaluation of Arylboronic Acid Scope**[a,b]




[a]Isolated yields are reported unless otherwise noted. Yields of isolated products on 0.25 mmol scale. [b]Enantioselectivities were determined by chiral HPLC analysis.

**Scheme 4. Gram-Scale Experiment and Synthetic Applications**

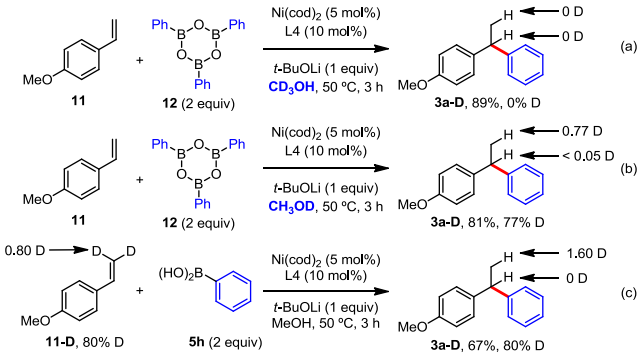



Reaction conditions for Scheme 5c: a) *N*-bromosuccinimide (1 equiv), $CH_3CN$, rt, 3 h; b) $Pd(PPh_3)_4$ (5 mol%), $K_2CO_3$ (3 equiv), 4-*t*-Bu-ArB$(OH)_2$ (3 equiv), PhMe/EtOH/$H_2O$ = 1:1:1, 100 °C, 3 h; c) $Pd(OAc)_2$ (5 mol%), rac-BINAP (7.5 mol%), morpholine (2 equiv), $Cs_2CO_3$ (1.3 equiv), PhMe, 100 °C, 5 h.

The scalability of this hydroarylation was evaluated using a reaction containing 6.0 mmol of substrate **1a,** giving 1.24 gram of desired product **3a** in 96% yield with 93% ee value which showcases the preparative utility of this hydroarylation (Scheme 4a). The synthetic utility of this catalytic hydrovinylation was demonstrated by efficient synthesis of the drug molecular, (*R*)-ibuprofen with good yield and excellent enantioselectivity (Scheme 4b). In addition, bromination of the hydroarylation product **3j** results in **8**, which could be converted into **9** and **10** with coupling reactions (Scheme 4c).

To gain insight into the reaction mechanism, deuterium-labelling experiments were carried out. As shown in Scheme 5, subjection of **11** and **12** to the reaction conditions using $CD_3OH$ as solvent in lieu of $CH_3OH$ resulted in **3a-D** with no deuterium incorporation (Scheme 5a). However, 77% deuterium incorporation was observed using $CH_3OD$ as solvent in lieu of $CH_3OH$, which indicates that the hydride is deriving from methanol O–H group instead of the C–H bond of the alcohol (Scheme 5b). To gain further insight into this hydroarylation system, deuterium-labelled **11-D** was prepared and subjected to the reaction and the H/D scrambling between methyl and benzyl groups was not observed, which is distinct from previous report.[9a]

**Scheme 5. Deuterium-Labeling Experiment**




In conclusion, we have demonstrated the first example of Ni-catalyzed enantioselective hydroarylation of styrenes with aryboronic acids using methanol as the hydride source. In addition, catalytic enantioselective hydroalkenylation was demonstrated, which could be applied to efficient synthesis of drug molecular (*R*)-ibuprofen. More work to better understand the mechanistic intricacies of this process are currently underway in our laboratory.

## ASSOCIATED CONTENT

### Supporting Information

Text, Figures, Tables, and CIF files giving experimental procedure, compound characterization data, and crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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**Notes**

The authors declare no competing financial interests.

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## REFERENCES

1. For biological activity of 1,1-diarylalkanes, see: (a) Soussi, M. A.; Provot, O.; Bernadat, G.; Bignon, J.; Desravines, D.; Dubois, J.; Brion, J.-D.; Messaoudi, S.; Alami, M. *Iso*CombretaQuinazolines: Potent Cytotoxic Agents with Antitubulin Activity. *ChemMedChem* **2015**, *10*, 1392–1402. (b) Messaoudi, S.; Hamze, A.; Provot, O.; Tréguier, B.; De Losada, J. R.; Bignon, J.; Liu, J.-M.; Wdzieczak-Bakala, J.; Thoret, S.; Dubois, J.; Brion, J.-D.; Alami, M. Discovery of Isoerianin Analogues as Promising Anticancer Agents. *ChemMedChem* **2011**, *6*, 488–497. (c) Cheltsov, A. V. Aoyagi, M. Aleshin, A.; Yu, E. C.-W.; Gilliland, T.; Zhai, D.; Bobkov, A. A.; Reed, J. C.; Liddington, R. C.; Abagyan, R. Vaccinia Virus Virulence Factor NIL is a Novel Promising Target for Antiviral Therapeutic Intervention. *J. Med. Chem.* **2010**, *53*, 3899–3906.

2. For selected reviews, see: (a) Jia, T.; Cao, P.; Liao, J. Enantioselective synthesis of *gem*-diarylalkanes by transition metal-catalyzed asymmetric arylations (TMCAAr). *Chem. Sci.* **2018**, *9*, 546–559. (b) Cherney, A. H.; Kadunce, N. T.; Reisman, S. E. Enantioselective and Enantiospecific Transition-Metal-Catalyzed Cross-Coupling Reactions of Organometallic Reagents To Construct C–C Bonds. *Chem. Rev.* **2015**, *115*, 9587–9652. (c) Tollefson, E. J.; Hanna, L. E.; Jarvo, E. R. *Acc. Chem. Res.* **2015**, *48*, 2344–2353. (d) Swift, E. C.; Jarvo, E. R. Asymmetric transition metal-catalyzed cross-coupling reactions for the construction of teriary stereocenters. *Tetrahedron* **2013**, *69*, 5799–5817.

3. For selected examples, see: (a) Bess, E. N.; Sigman, M. S. Distinctive *Meta*-Directing Group Effect for Iridium-Catalyzed 1,1-Diarylalkene Enantioselective Hydrogenation. *Org. Lett.* **2013**, *15*, 646–649. (b) Woodmansee, D. H.; Pfaltz, A. Asymmetric hydrogenation of alkenes lacking coordinating groups. *Chem. Commun.* **2011**, *47*, 7912–7916. (c) Tolstoy, P.; Engman, M.; Paptchikhine, A.; Bergquist, J.; Church, T. L.; Leung, A. W.-M.; Andersson, P. G. Iridium-Catalyzed Asymmetric Hydrogenation Yielding Chiral Diarylmethines with Weakly Coordinating or Noncoordinating Substituents. *J. Am. Chem. Soc.* **2009**, *131*, 8855–8860.

4. For selected examples, see: (a) Wu, C.; Yue, G.; Nielsen, C. D.-T.; Xu, K.; Hirao, H.; Zhou, J. Asymmetric Conjugate Addition of Organoboron Reagents to Common Enones Using Copper Catalysts. *J. Am. Chem. Soc.* **2016**, *138*, 742–745. (b) Takatsu, K. Shintani, R. Hayashi, T. Copper-Catalyzed 1,4-Addition of Orgaoboronates to Alkylidene Cyanoacetates: Mechanistic Insight and Application to Asymmetric Catalysis. *Angew. Chem. Int. Ed.* **2011**, *50*, 5548–5552. (c) Wang, Z. Q.; Feng, C. G.; Zhang, S. S.; Xu, M. H.; Lin, G.-Q. Rhodium-Catalyzed Asymmetric Conjugate Addition of Organoboronic Acids to Nitroalkenes Using Chiral Bicyclo[3.3.0] Diene Ligands. *Angew. Chem. Int. Ed.* **2010**, *49*, 5780–5783. (d) Paquin, J.-F.; Defieber, C.; Stephenson, C. R. J.; Carreira, E. M. Asymmetric Synthesis of 3,3-Diarylpropanals with Chiral Diene-Rhodium Catalysts *J. Am. Chem. Soc.* **2005**, *127*, 10850–10851.

5. For the enantioselective cross-coupling, see: (a) Woods, B. P.; Orlandi, M.; Huang, C.-Y.; Sigman, M.-S. Doyle, A. G. Nickel-Catalyzed Enantioselective Reductive Cross-Coupling of Styrenyl Aziridines. *J. Am. Chem. Soc.* **2017**, *139*, 5688–5691. (b) Poremba, K. E.; Kadunce, N. T.; Suzuki, N.; Cherney, A. H.; Reisman, S. E. Nickel-Catalyzed Asymmetric Reductive Cross-Coupling To Access 1,1-Diarylalkanes. *J. Am. Chem. Soc.* **2017**, *139*, 5684–5687. (c) Ackerman, L. K. G.; Anka-Lufford, L. L.; Naodovic, M.; Weix, D. J. Cobalt co-catalysis for cross-electrophile coupling: diarylmethanes from benzyl mesylates and aryl halides. *Chem. Sci.* **2015**, *6*, 1115. (d) Gutierrez, O.; Tellis, J. C.; Primer, D. N.; Molander, G. A.; Kozlowski, M. C. Nickel-Catalyzed Cross-Coupling of Photoredox-Generated Radicals: Uncovering a General Manifold for Stereoconvergence in Nickel-Catalyzed Cross-Couplings. *J. Am. Chem. Soc.* **2015**, *137*, 4896–4899. (e) Tellis, J. C.; Primer, D. N.; Molander, G. A. Single-electron transmetalation in organoboron cross-coupling by photoredox/nickel dual catalysis. *Science* **2014**, *345*, 433–436. (f) Do, H.-Q.; Chandrashekar, E. R. R.; Fu, G. C. Nickel/Bis(Oxazoline)-Catalyzed Asymmetric Negishi Arylations of Racemic Secondary Benzylic Electrophiles to Genrate Enantioenriched 1,1-Diarylalkanes. *J. Am. Chem. Soc.* **2013**, *135*, 16288–16291.

6. For selected examples on the stereospecific cross-couplings, see: (a) Rygus, J. P. G.; Crudden, C. M. Enantiospecific and Iterative Suzuki-Miyaora Cross-Couplings. *J. Am. Chem. Soc.* **2017**, *139*, 18124–18137. (b) Zhou, Q.; Srinivas, H. D.; Dasgupta, S.; Watson, M. P. Nickel-Catalyzed Cross-Couplings of Benzylic Pivalates with Arylboroxines: Stereospecific Formation of Diarylalkanes and Triarylmethanes. *J. Am. Chem. Soc.* **2013**, *135*, 3307–3310. (c) Taylor, B. L. H.; Swift, E. C.; Waetzig, J. D.; Jarvo, E. R. Stereospecific Nickel-Catalyzed Cross-Coupling Reactions of Alkyl Ethers: Enantioselective Synthesis of Diarylethanes. *J. Am. Chem. Soc.* **2011**, *133*, 389–391. (d) He, A.; Falck, J. R. Stereospecific Suzuki Cross-Coupling of Alkyl α-Cyanohydrin Triflates. *J. Am. Chem. Soc.* **2010**, *132*, 2524–2525. (f) López-Pérez, A.; Adrio, J.; Carretero, J. C. Palladium-Catalyzed Cross-Coupling Reaction of Secondary Benzylic Bromides with Grignard Reagents. *Org. Lett.* **2009**, *11*, 5514–5517. (g) Imao, D.; Glasspoole, B. W.; Laberge, V. S.; Crudden, C. M. Cross Coupling Reactions of Chiral Secondary Organoboronic Esters With Retention of Configuration. *J. Am. Chem. Soc.* **2009**, *131*, 5024–5025.

7. For selected examples, see: (a) Grélaud, S.; Cooper P.; Feron, L. J.; Bower, J. F. Branch-Selective and Enantioselective Iridium-Catalyzed Alkene Hydroarylation via Anilide-Directed C–H Oxidative Addition. *J. Am. Chem. Soc.* **2018**, *140*, 9351–9356. (b) Loup, J.; Zell, D.; Oliveira, J. C. A.; Keil, H.; Stalke, D.; Ackermann, L. *Angew. Chem. Int. Ed.* **2017**, *56*, 14197–14201. (c) Ebe, Y.; Onoda, M.; Nishimura, T.; Yorimitsu, H. Iridium-Catalyzed Regio- and Enantioselective Hydroarylation of Alkenyl Ethers by Olefin Isomerization. *Angew. Chem. Int. Ed.* **2017**, *56*, 5607–5611. (d) Crisenza, G. E. M.; Bower, J. F. Branch Selective Murai-Type Alkene Hydroarylation Reactions. *Chem. Lett.* **2016**, *45*, 2–9; this reference includes a discussion of other approaches to the synthesis of 1,1-diarylalkanes. (e) Lee, P.-S.; Yoshikai, N. Cobalt-Catalyzed Enantioselective Directed C–H Alkylation of Indole with Styrenes. *Org. Lett.* **2015**, *17*, 22-25.

8. For selected examples on Pd-catalyzed hydroarylation with olefins, see: (a) Wang, H.; Bai, Z.; Jiao, T.; Deng, Z.; Tong, H.; He, G.; Peng, Q.; Chen, G. Palladium-Catalyzed Amide-Directed Enantioselective Hydrocarbofunctionalization of Unactivated Alkenes Using a Chiral Monodentate Oxazoline Ligand. *J. Am. Chem. Soc.* **2018**, *140*, 3542–3546. (b) Matsuura, R.; Jankins, T. C.; Hill, D. E.; Yang, K. S.; Gallego, G. M.; Yang, S.; He, M.; Wang, F.; Marsters, R. P.; McAlpine,

I.; Engle, K. M. Palladium(II)-catalyzed γ-selective hydroarylation of alkenyl carbonyl compounds with arylboronic acids. *Chem. Sci.* **2018**, *9*, 8363–8368. (c) Friis, S. D.; Pirnot, M. T.; Dupuis, L. N.; Buchwald, S. L. A Dual Palladium and Copper Hydride Catalyzed Approach for Alkyl-Aryl Cross-Coupling of Aryl Halides and Olefins. *Angew. Chem. Int. Ed.* **2017**, *56*, 7242–7246. (d) Semba, K.; Ariyama, K.; Zheng, H.; Kameyama, R.; Sakaki, S.; Nakao, Y. Reductive Cross-Coupling of Conjugated Arylalkenes and Aryl Bromides with Hydrosilanes by Cooperative Palladium/Copper Catalysis. *Angew. Chem. Int. Ed.* **2016**, 55, 6275–6279. (e) Liao, L.; Sigman, M. S. Palladium-Catalyzed Hydroarylation of 1,3-Dienes with Boronic Esters via Reductive Formation of π-allyl Palladium Intermediates under Oxidative Conditions. *J. Am. Chem. Soc.* **2010**, *132*, 10209–10211. (f) Iwai, Y.; Gligorich, K. M.; Sigman, M. S. Aerobic Alcohol Oxidation Coupled to Palladium-Catalyzed Alkene Hydroarylation with Boronic Esters. *Angew. Chem. Int. Ed.* **2008**, *47*, 3219–3222. (g) Gligorich, K. M.; Cummings, S. A.; Sigman, M. S. Palladium-Catalyzed Reductive Coupling of Styrenes and Organostannanes under Aerobic Conditions. *J. Am. Chem. Soc.* **2007**, *129*, 14193–14195.

9. For Ni-catalyzed hydroarylation with olefins, see: (a) Xiao, L.-J.; Chen, L.; Feng, W.-M. Li, M.-L.; Xie, J.-H.; Zhou, Q.-L. Nickel(0)-catalyzed hydroarylation of Styrenes and 1,3-Dienes with Organoboron Compounds. *Angew. Chem. Int. Ed.* **2018**, *57*, 461–464. (b) Lv, H.; Xiao, L.-J.; Zhao, D.; Zhou, Q.-L. Nickel(0)-catalyzed linear-selective hydroarylation of unactivated alkenes and styrenes with aryl boronic acids. *Chem. Sci.* **2018**, *9*, 6839–6843. (c) Lu, K.; Han, X.-W.; Yao, W.-W.; Luan, Y.-X.; Wang, Y.-X.; Chen, H.; Xu, X.-T.; Zhang, K.; Ye, M. DMF-Promoted Redox-Neutral Ni-catalyzed Intramolecular Hydroarylation of Alkene with Simple Arene. *ACS Catal.* **2018**, *8*, 3913–3917. (d) Chen, F.; Chen, K.; Zhang, Y.; He, Y.; Wang, Y.-M.; Zhu, S. Remote Migratory Cross-Electrophile Coupling and Olefin Hydroarylation Reactions Enabled by in Situ Generation of NiH. *J. Am. Chem. Soc.* **2017**, *139*, 13929–13935. (e) He, Y.; Vai, Y.; Zhu, S. Mild and Regioselective Benzylic C–H Functionalization: Ni-Catalyzed Reductive Arylation of Remote and Proximal Olefins. *J. Am. Chem. Soc.* **2017**, *139*, 1061-1064. (f) Green, S. A.; Matos, J. L. M.; Yagi, A.; Shenvi, R. A. Branch-Selective Hydroarylation: Iodoarene-Olefin Cross-Coupling. *J. Am. Chem. Soc.* **2016**, *138*, 12779–12782. For the review on Ni-hydride Complex, see: (g) Eberhardt, N. A.; Guan, H. Nickel Hydride Complexes. *Chem. Rev.* **2016**, *116*, 8373–8426.

10. Podhajsky, S. M.; Iwai, Y.; Cook-Sneathen, A.; Sigman, M. S. Asymmetric palladium-catalyzed hydroaryltion of styrens and dienes. *Tetrahedron* **2011**, *67*, 4435–4441.

11. Friis, S. D.; Pirnot, M. T.; Buchwald, S. L. Asymmetric Hydroarylation of Vinylarenes Using a Synergistic Combination of CuH and Pd Catalysis. *J. Am. Chem. Soc.* **2016**, *138*, 8372–8375.

12. (a) Wu, L.; Wang, F.; Wan, X.; Wang, D.; Chen, P.; Liu, G. Asymmetric Cu-Catalyzed Intermolecular Trifluoromethylarylation of Styrenes: Enantioselective Arylation of Benzylic Radicals. *J. Am. Chem. Soc.* **2017**, *139*, 2904–2907. (b) Davis, I. W.; Gerena, L.; Castonguay, L.; Senanayake, C. H.; Larsen, R. D.; Verhoeven, T. R.; Reider, P. J. The influence of ligand bite angle on the enantioselectivity of copper(II)-catalyzsed Diels-Alder reactions. *Chem. Commun.* **1996**, 1753–1754.

13. For selected examples on enantioselective hydroalkenylation, see: (a) Li, K.; Li, M.-L.; Zhang, Q.; Zhu, S.-F.; Zhou, Q.-L. Highly Enantioselective Nickel-Catalyzed Intramolecular Hydroalkenylation of N- and O-Tethered 1,6-Dienes To Form Six-Membered Heterocycles. *J. Am. Chem. Soc.* **2018**, *140*, 7458–7461. (b) Ho, C.-Y.; Chan, C.-W.; He, L. Catalytic Asymmetric Hydroakenylation of Vinylarenes: Electronic Effects of Substrates and Chiral N-Heterocyclic Carbene Ligands. *Angew. Chem. Int. Ed.* **2015**, *54*, 4512–4516. (c) Shi, W.-J.; Zhang, Q.; Xie, J.-H.; Zhu, S.-F.; Hou, G.-H.; Zhou, Q.-L. Highly Enantioselective Hydrovinylation of α-Alkyl Vinylarenes. An Approach to the Construction of All-Carbon Quaternary Stereocenters. (d) RajanBabu, T. V. Asymmetric Hydrovinylation Reaction. *Chem. Rev.* **2003**, *103*, 2845–2860.

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