OL | Organic Letters

pubs.acs.org/OrgLett Letter

Synthesis of Axially Chiral Olefin−Oxazoline Ligands via Pd-Catalyzed Multiple C−H Functionalization

Ling-Jun Li, Jun-Jie Chen, Chen-Fei Feng, Han-Yuan Li, Xing Wang, Hui Xu, and Hui-Xiong Dai*

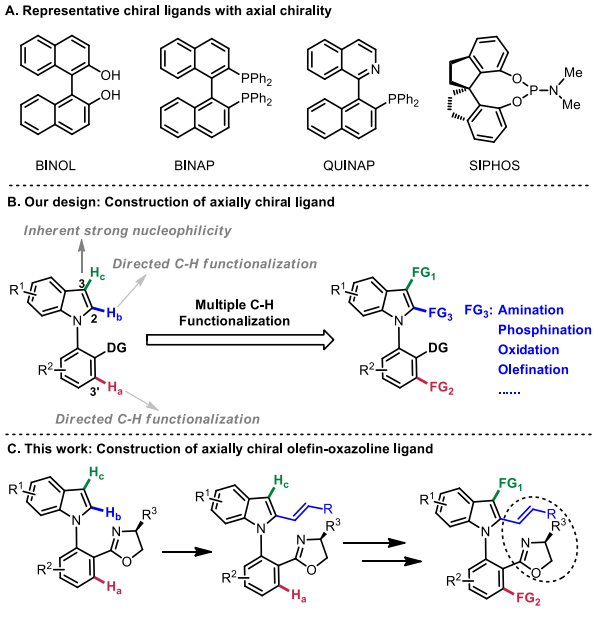
Cite This: https://dx.doi.org/10.1021/acs.orglett.0c03093 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: We report herein the Pd-catalyzed oxazoline-directed C−H olefination of the *N*-arylindole skeleton, affording two diastereomers of axially chiral olefin−oxazoline ligands in a one-step procedure. Modifications at the 3- and 3′-positions were facilely achieved via electrophilic substitution of the indole fragment and subsequent oxazoline-directed C−H amidation or olefination of the arene fragment.

Chiral ligands possessing axial chirality have been widely employed in transition-metal-catalyzed enantioselective synthesis (Scheme 1A).[1] Many types of axially chiral ligands have been developed in the past decades. For example, the P,P-ligand BINAP, discovered by Noyori, is a powerful ligand in Ru-catalyzed asymmetric hydrogenation.[2] The P,N-ligand QUINAP shows broad catalytic utility in Rh-catalyzed asymmetric hydroboration of alkenes and asymmetric cycloaddition.[3] The monodentate spiro phosphorus ligand SIPHOS, developed by Zhou, has proved to be highly efficient in asymmetric hydrogenation and C−C bond formation.[4] Despite the significant achievements, there has been ongoing interest in ligand modification to improve the catalytic efficiency and enantioselectivity in some asymmetric syntheses. Modifications at the *ortho* positions of the coordinating group are highly appealing because of the significant influence of the electron density and steric hindrance. Zhou demonstrated that 6,6′-diaryl substitution of SIPHOS resulted in remarkable improvement in the Ni-catalyzed asymmetric reductive coupling of 1,3-dienes with benzaldehyde.[5] Very recently, Shi investigated a series of BINOLs and found that 3,3′-disubstituted BINOLs can significantly enhance the reactivity and enantioselectivity in Pd(II)-catalyzed methylene C−H alkynylation.[6] However, ligand modifications often require excess organolithium reagents, prefunctionalization of the ligand, and multistep synthesis.[1] Direct C−H functionalization at the 3- and 3′-positions to diversify the axially chiral ligands is the most efficient and straightforward way. However, only a few examples have been reported in the literature.[7] To develop a practical methodology for ligand modifications, we turned our attention to *N*-arylindole, which is an important structure motif in organic chemistry.[8] We envisioned that direct C2−H amination, phosphination, oxidation, or olefination assisted by a coordination group could be used to construct axially chiral bidentate ligands. The 3- and 3′-positions of the ligand could be facilely modified via electrophilic substitution at the 3-position of the indole fragment and directed C−H

Scheme 1. 3,3′-Modification of the Axially Chiral Ligand



Received: September 15, 2020

https://dx.doi.org/10.1021/acs.orglett.0c03093
Org. Lett. XXXX, XXX, XXX−XXX

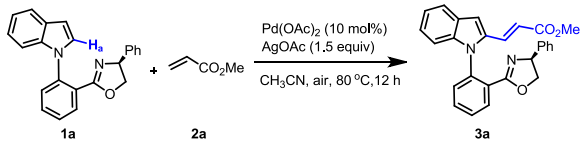
functionalization at the 3′-position of the arene fragment (Scheme 1B).

In recent years, chiral olefin ligands have emerged as powerful ligands in asymmetric catalysis.[9] In 2003, Hayashi and co-workers reported Rh-catalyzed asymmetric conjugate additions employing bicyclo[2.2.1]heptadiene as the ligand.[10] Since then, chiral diene ligands,[11] chiral phosphine−olefin ligands,[12] and chiral sulfur−olefin ligands have been developed.[13] By combining olefins with oxazolines, in 2010 Glorius and co-workers reported the bidentate olefin−oxazoline (OlefOx) ligands, which were successfully applied in asymmetric 1,4-conjugate addition.[14] Inspired by the successful applications of axially chiral ligands and the bidentate olefin−oxazoline skeleton in asymmetric catalysis, we report herein the synthesis of axially chiral olefin−oxazoline ligands via Pd-catalyzed oxazoline-directed C−H olefination (Scheme 1C). The 3- and 3′-positions of the ligands were conveniently modified by electrophilic C−H bromination and oxazoline-directed C−H amidation and olefination.

Over the past decades, several practical strategies have been developed for the synthesis of axially chiral biaryls via transition-metal-catalyzed asymmetric C−H bond functionalization.[15] Considering the wide application of the oxazoline moiety in asymmetric synthesis,[16] we commenced our studies by choosing indole−phenyloxazoline skeleton **1a** as the model substrate for the synthesis of axially chiral olefin−oxazoline ligand **3a**. The optimization of the reaction conditions is shown in Table 1. To our delight, in the presence of 10 mol % $Pd(OAc)_2$ and 1.5 equiv of AgOAc in CH_3CN, C−H bond olefination occurred smoothly, affording two diastereomeric ligands **3a** with (*S*,*R*) and (*S*,*S*) configurations in 82% yield with 1.2:1 *d.r.* (entry 1). As expected, no desired product was obtained in the absence of $Pd(OAc)_2$ (entry 2), indicating that the palladium catalyst was essential in the reaction. Other palladium salts were also effective, including $PdCl_2$, $Pd(acac)_2$, $Pd(dppf)Cl_2$, and $Pd_2(dba)_3$, albeit in lower yields (entries 3−6). When AgTFA, Ag_2SO_4, Ag_2CO_3, and $AgBF_4$ were employed as the oxidants, 27−53% yields of olefin−oxazoline ligand **3a** were obtained (entries 7−10). Further investigation of solvents, including DCE, DMF, and THF, showed that CH_3CN was the optimal solvent (entries 11−13). Although the *d.r.* value was improved to 4.2:1, the total yield significantly decreased to 54% when we lowered the reaction temperature to 60 °C (entry 14). Furthermore, when the reaction was carried out under a N_2 atmosphere, the desired product was formed in only 34% yield (entry 15). The reason for the low diastereoselectivity may be that the stereogenic center is too far away or the lower rotational barriers of axially chiral scaffolds containing five-membered rings cause racemization of products (see the Supporting information).

With the optimal reaction conditions in hand, we turned our attention to examine the substrate scope of indole−phenyloxazoline derivatives **1** and various acrylates **2** (Scheme 2). To our delight, regardless of their electronic properties, methyl-, methoxy-, fluoro-, chloro-, bromo-, and trifluoromethyl-substituted indole−phenyloxazoline derivatives **1** were well-tolerated in the reaction (Scheme 2A). The corresponding olefin−oxazoline ligands were obtained in moderate to good

Table 1. Optimization of the Reaction Conditions[a]

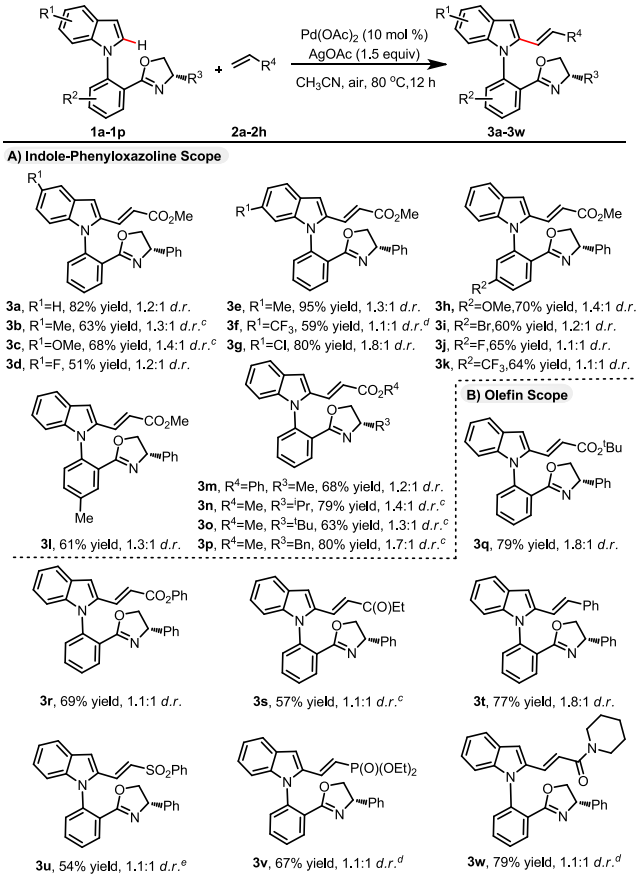


1a 2a 3a

entry	variation from the standard conditions	yield (%)[b]	*d.r.*[c]
1	none	82	1.2:1
2	no Pd	–	–
3	$PdCl_2$	52	1.3:1
4	$Pd(acac)_2$	30	1.6:1
5	$Pd(dppf)Cl_2$	46	1.2:1
6	$Pd_2(dba)_3$	16	1.3:1
7	AgTFA	46	1.3:1
8	Ag_2SO_4	27	1.2:1
9	Ag_2CO_3	53	1.2:1
10	$AgBF_4$	34	1.1:1
11	DCE instead of CH_3CN	40	1.1:1
12	DMF instead of CH_3CN	43	1.4:1
13	THF instead of CH_3CN	68	1.5:1
14	at 60 °C	54	4.2:1
15	N_2 atmosphere	34	1.2:1

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), $Pd(OAc)_2$ (10 mol %), AgOAc (0.15 mmol), CH_3CN (1.0 mL), air, 80 °C, 12 h. [b]Determined by ^1H NMR analysis of the crude products using CH_2Br_2 as an internal standard. [c]Determined by ^1H NMR analysis.

Scheme 2. Substrate Scope of Indole−Phenyloxazoline Derivatives[a,b]



[a]Reaction conditions: **1** (0.1 mmol), **2** (0.15 mmol), $Pd(OAc)_2$ (10 mol %), AgOAc (0.15 mmol), CH_3CN (1.0 mL), air, 80 °C, 12 h. [b]Total yields of two diastereomers are shown. [c]9 h. [d]24 h. [e]100 °C, 36 h.

https://dx.doi.org/10.1021/acs.orglett.0c03093
Org. Lett. XXXX, XXX, XXX−XXX

yields (**3a–l**). The *d.r.* values of diastereomeric ligands ranged from 1.1:1 to 1.8:1. Different chiral oxazoline moieties were compatible with the standard conditions, affording the diastereomeric ligands **3m–p** in 63–80% yield. Next, the scope of olefins was briefly surveyed (Scheme 2B). Olefin coupling partners, including α,β-unsaturated esters, amide, ketone, sulfone, phosphonate, and styrene, afforded olefin–oxazoline ligands **3q–w** in 54–79% yield with *d.r.* values ranging from 1.1:1 to 1.8:1.

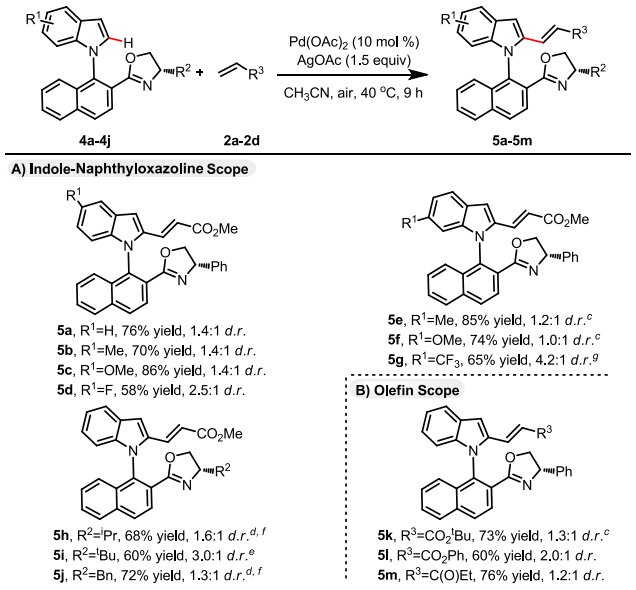
Next, we began to examine the scope of indole–naphthyloxazoline derivatives (Scheme 3). As shown in Scheme 3A, indole–naphthyloxazolines **4** bearing methyl, methoxy, fluoro, and trifluoromethyl substituents were compatible with the standard conditions, giving the corresponding products **5a–g** in moderate to good yields. Substrates **4h–j** with chiral oxazolines bearing *i*-Pr, *t*-Bu, and Bn groups, respectively, were also investigated and substrate **4i** with a *t*-Bu group on the oxazoline gave the highest *d.r.* in the coupling reaction with methyl acrylate. When *tert*-butyl acrylate, phenyl acrylate, and ethyl vinyl ketone were employed as coupling reagents, the desired products **5k–m** were obtained in 60–76% yield (Scheme 3B).

To demonstrate the utility of this protocol, a gram-scale synthesis using substrate **1a** and methyl acrylate **2a** was carried out under the standard conditions, affording the corresponding product **3a** in 78% yield (Scheme 4).

The 3- and 3′-positions of axially chiral olefin–oxazoline ligand **3a** could be conveniently modified via electrophilic bromination at the 3-position and subsequent Rh-catalyzed olefination or amidation at the 3′-position to give compounds **6** and **7** in 60% and 78% yield, respectively (Scheme 5A,B). The brominated products are versatile stepping stones for further structure elaboration at the 3-position. For example, compound **7** could be further transformed to **8** via Pd-catalyzed Suzuki coupling (Scheme 5C).

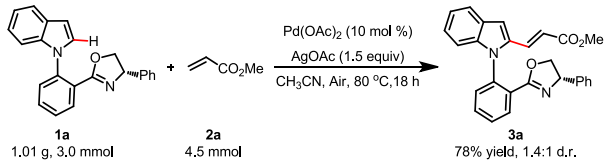
In summary, we have reported herein the synthesis of axially chiral olefin–oxazoline ligands via palladium-catalyzed C–H olefination. Two diastereomeric ligands were obtained in a one-step procedure. Our protocol showed broad substrate scope and good functional group tolerance. The 3- and 3′-positions of the axially chiral olefin–oxazoline ligands could be facilely modified via electrophilic bromination at the 3-position of the indole fragment and Rh-catalyzed amidation or olefination at the 3′-position of the arene fragment. Further applications of these ligands in asymmetric synthesis are currently ongoing in our laboratory.

Scheme 3. Substrate Scope of Indole–Naphthyloxazoline Derivatives[a,b]

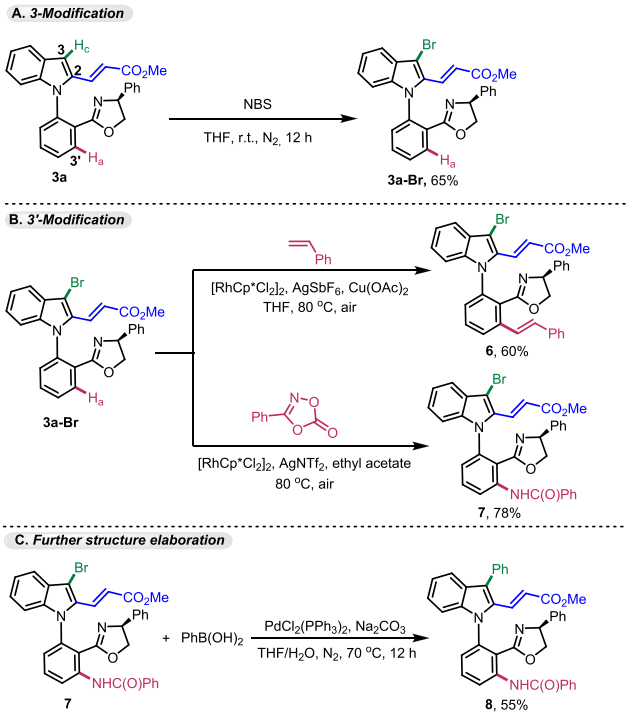


[a]Reaction conditions: **4** (0.1 mmol), **2** (0.15 mmol), $Pd(OAc)_2$ (10 mol %), AgOAc (0.15 mmol), CH_3CN (2.0 mL), air, 40 °C, 9 h. [b]Total yields of two diastereomers are shown. [c]12 h. [d]60 °C. [e]5 h. [f]7 h. [g]130 °C, 24 h.

Scheme 4. Gram-Scale Synthesis



Scheme 5. 3,3′-Modification of Olefin–Oxazoline Ligand 3a



■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c03093.

Experimental procedures, characterizations of new compounds, and NMR spectra (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Hui-Xiong Dai – *Chinese Academy of Sciences Key Laboratory of Receptor Research, Shanghai Institute of Materia Medica, University of Chinese Academy of Sciences, Shanghai 201203, China; University of Chinese Academy of Sciences, Beijing*

https://dx.doi.org/10.1021/acs.orglett.0c03093
Org. Lett. XXXX, XXX, XXX–XXX

100049, China; orcid.org/0000-0002-2937-6146; Email: hxdai@simm.ac.cn

Authors

Ling-Jun Li − *Chinese Academy of Sciences Key Laboratory of Receptor Research, Shanghai Institute of Materia Medica, University of Chinese Academy of Sciences, Shanghai 201203, China; University of Chinese Academy of Sciences, Beijing 100049, China*

Jun-Jie Chen − *Chinese Academy of Sciences Key Laboratory of Receptor Research, Shanghai Institute of Materia Medica, University of Chinese Academy of Sciences, Shanghai 201203, China*

Chen-Fei Feng − *Chinese Academy of Sciences Key Laboratory of Receptor Research, Shanghai Institute of Materia Medica, University of Chinese Academy of Sciences, Shanghai 201203, China*

Han-Yuan Li − *Chinese Academy of Sciences Key Laboratory of Receptor Research, Shanghai Institute of Materia Medica, University of Chinese Academy of Sciences, Shanghai 201203, China*

Xing Wang − *Chinese Academy of Sciences Key Laboratory of Receptor Research, Shanghai Institute of Materia Medica, University of Chinese Academy of Sciences, Shanghai 201203, China; University of Chinese Academy of Sciences, Beijing 100049, China*

Hui Xu − *Chinese Academy of Sciences Key Laboratory of Receptor Research, Shanghai Institute of Materia Medica, University of Chinese Academy of Sciences, Shanghai 201203, China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.0c03093

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We gratefully acknowledge Shanghai Institute of Materia Medica, Chinese Academy of Sciences, the National Natural Science Foundation of China (21772211), the Youth Innovation Promotion Association of CAS (2014229 and 2018293), Institutes for Drug Discovery and Development, Chinese Academy of Sciences (CASIMM0120163006), the Science and Technology Commission of Shanghai Municipality (17JC1405000 and 18431907100), the Program of Shanghai Academic Research Leader (19XD1424600), the National Science & Technology Major Project "Key New Drug Creation and Manufacturing Program", China (2018ZX09711002-006), and the State Key Laboratory of Natural and Biomimetic Drugs for financial support.

■ REFERENCES

(1) For selected reviews, see: (a) Berthod, M.; Mignani, G.; Woodward, G.; Lemaire, M. Modified BINAP: The How and the Why. *Chem. Rev.* **2005**, *105*, 1801−1836. (b) Noyori, R.; Takaya, H. BINAP: An Efficient Chiral Element for Asymmetric Catalysis. *Acc. Chem. Res.* **1990**, *23*, 345−350. (c) Brunel, J. M. BINOL: A Versatile Chiral Reagent. *Chem. Rev.* **2005**, *105*, 857−898. (d) Rokade, B. V.; Guiry, P. J. Axially Chiral P,N-Ligands: Some Recent Twists and Turns. *ACS Catal.* **2018**, *8*, 624−643. (e) Xie, J. H.; Zhou, Q. L. Chiral Diphosphine and Monodentate Phosphorus Ligands on a Spiro Scaffold for Transition-Metal-Catalyzed Asymmetric Reactions. *Acc. Chem. Res.* **2008**, *41*, 581−593.

(2) Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. Synthesis of 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP), an atropisomeric chiral bis(triaryl)phosphine, and its use in the rhodium(I)-catalyzed asymmetric hydrogenation of α-(acylamino)acrylic acids. *J. Am. Chem. Soc.* **1980**, *102*, 7932−7934.

(3) (a) Alcock, N. W.; Brown, J. M.; Hulmes, D. I. Synthesis and resolution of 1-(2-diphenylphosphino-1-naphthyl)isoquinoline; a P-N chelating ligand for asymmetric catalysis. *Tetrahedron: Asymmetry* **1993**, *4*, 743−756. (b) Brown, J. M.; Hulmes, D. I.; Layzell, T. P. Effective asymmetric hydroboration catalysed by a rhodium complex of 1-(2-diphenylphosphino-1-naphthyl)isoquinoline. *J. Chem. Soc., Chem. Commun.* **1993**, 1673−1674. (c) Valk, J. M.; Whitlock, G. A.; Layzell, T. P.; Brown, J. M. Catalytic asymmetric hydroboration with heterotopic P-N ligands: Trends in enantioselectivity with increased steric demand. *Tetrahedron: Asymmetry* **1995**, *6*, 2593−2596. (d) Doucet, H.; Fernandez, E.; Layzell, T. P.; Brown, J. M. The Scope of Catalytic Asymmetric Hydroboration/Oxidation with Rhodium Complexes of 1,1′-(2-Diarylphosphino-1-naphthyl)-isoquinolines. *Chem. - Eur. J.* **1999**, *5*, 1320−1330. (e) Chen, C.; Li, X.; Schreiber, S. L. Catalytic Asymmetric [3+2] Cycloaddition of Azomethine Ylides. Development of a Versatile Stepwise, Three-Component Reaction for Diversity-Oriented Synthesis. *J. Am. Chem. Soc.* **2003**, *125*, 10174−10175. (f) Lim, A. D.; Codelli, J. A.; Reisman, S. E. Catalytic asymmetric synthesis of highly substituted pyrrolizidines. *Chem. Sci.* **2013**, *4*, 650−654. (g) Miura, T.; Yamauchi, M.; Kosaka, A.; Murakami, M. Nickel-Catalyzed Regio- and Enantioselective Annulation Reactions of 1,2,3,4-Benzothiatriazine-1,1(2*H*)-dioxides with Allenes. *Angew. Chem., Int. Ed.* **2010**, *49*, 4955−4957.

(4) (a) Fu, Y.; Xie, J.; Hu, A.; Zhou, H.; Wang, L.; Zhou, Q. Novel monodentate spiro phosphorus ligands for rhodium-catalyzed hydrogenation reactions. *Chem. Commun.* **2002**, 480−481. (b) Hu, A.; Fu, Y.; Xie, J.; Zhou, H.; Wang, L.; Zhou, Q.-L. Monodentate Chiral Spiro Phosphoramidites: Efficient Ligands for Rhodium-Catalyzed Enantioselective Hydrogenation of Enamides. *Angew. Chem., Int. Ed.* **2002**, *41*, 2348−2350.

(5) Yang, Y.; Zhu, S.-F.; Zhou, C.-Y.; Zhou, Q.-L. Nickel-Catalyzed Enantioselective Alkylative Coupling of Alkynes and Aldehydes: Synthesis of Chiral Allylic Alcohols with Tetrasubstituted Olefins. *J. Am. Chem. Soc.* **2008**, *130*, 14052−14053.

(6) Han, Y.-Q.; Ding, Y.; Zhou, T.; Yan, S.-Y.; Song, H.; Shi, B.-F. Pd(II)-Catalyzed Enantioselective Alkynylation of Unbiased Methylene C(sp^3)−H Bonds Using 3,3′-Fluorinated-BINOL as a Chiral Ligand. *J. Am. Chem. Soc.* **2019**, *141*, 4558−4563.

(7) (a) Xiao, B.; Fu, Y.; Xu, J.; Gong, T.-J.; Dai, J.-J.; Yi, J.; Liu, L. Pd(II)-Catalyzed C−H Activation/Aryl-Aryl Coupling of Phenol Esters. *J. Am. Chem. Soc.* **2010**, *132*, 468−469. (b) Yang, J.; Wang, R.; Wang, Y.; Yao, W.; Liu, Q.; Ye, M. Ligand-Accelerated Direct C−H Arylation of BINOL: A Rapid One-Step Synthesis of Racemic 3,3′-Diaryl BINOLs. *Angew. Chem., Int. Ed.* **2016**, *55*, 14116−14120.

(8) (a) Hulcoop, D. G.; Lautens, M. Palladium-Catalyzed Annulation of Aryl Heterocycles with Strained Alkenes. *Org. Lett.* **2007**, *9*, 1761−1764. (b) Yang, Z.; Möller, M.; Koenigs, R. M. Synthesis of gem-Difluoro Olefins through C−H Functionalization and β-fluoride Elimination Reactions. *Angew. Chem., Int. Ed.* **2020**, *59*, 5572−5576.

(9) (a) Feng, X.; Du, H. Synthesis of Chiral Olefin Ligands and their Application in Asymmetric Catalysis. *Asian J. Org. Chem.* **2012**, *1*, 204−213. (b) Dong, H.-Q.; Xu, M.-H.; Feng, C.-G.; Sun, X.-W.; Lin, G.-Q. Recent applications of chiral N-tert-butanesulfinyl imines, chiral diene ligands and chiral sulfur−olefin ligands in asymmetric synthesis. *Org. Chem. Front.* **2015**, *2*, 73−89. (c) Defieber, C.; Grützmacher, H.; Carreira, E. M. Chiral Olefins as Steering Ligands in Asymmetric Catalysis. *Angew. Chem., Int. Ed.* **2008**, *47*, 4482−4502. (d) Johnson, J. B.; Rovis, T. More than Bystanders: The Effect of Olefins on Transition-Metal-Catalyzed Cross-Coupling Reactions. *Angew. Chem., Int. Ed.* **2008**, *47*, 840−871.

(10) Hayashi, T.; Ueyama, K.; Tokunaga, N.; Yoshida, K. A Chiral Chelating Diene as a New Type of Chiral Ligand for Transition Metal

Catalysts: Its Preparation and Use for the Rhodium-Catalyzed Asymmetric 1,4-Addition. *J. Am. Chem. Soc.* **2003**, *125*, 11508−11509.
(11) (a) Glorius, F. Chiral Olefin Ligands—New "Spectators" in Asymmetric Catalysis. *Angew. Chem., Int. Ed.* **2004**, *43*, 3364−3366. (b) Shintani, R.; Hayashi, T. Chiral Diene Ligands for Asymmetric Catalysis. *Aldrichimica Acta* **2009**, *42*, 31−38. (c) Tian, P.; Dong, H.-Q.; Lin, G.-Q. Rhodium-Catalyzed Asymmetric Arylation. *ACS Catal.* **2012**, *2*, 95−119.
(12) (a) Maire, P.; Deblon, S.; Breher, F.; Geier, J.; Böhler, C.; Rüegger, H.; Schönberg, H.; Grützmacher, H. Olefins as Steering Ligands for Homogeneously Catalyzed Hydrogenations. *Chem. - Eur. J.* **2004**, *10*, 4198−4205. (b) Shintani, R.; Duan, W.-L.; Nagano, T.; Okada, A.; Hayashi, T. Chiral Phosphine−Olefin Bidentate Ligands in Asymmetric Catalysis: Rhodium-Catalyzed Asymmetric 1,4-Addition of Aryl Boronic Acids to Maleimides. *Angew. Chem., Int. Ed.* **2005**, *44*, 4611−4614. (c) Kasák, P.; Arion, V. B.; Widhalm, M. A chiral phosphepine−olefin rhodium complex as an efficient catalyst for the asymmetric conjugate addition. *Tetrahedron: Asymmetry* **2006**, *17*, 3084−3090. (d) Defieber, C.; Ariger, M. A.; Moriel, P.; Carreira, E. M. Iridium-Catalyzed Synthesis of Primary Allylic Amines from Allylic Alcohols: Sulfamic Acid as Ammonia Equivalent. *Angew. Chem., Int. Ed.* **2007**, *46*, 3139−3143. (e) Hoffman, T. J.; Carreira, E. M. Catalytic Asymmetric Intramolecular Hydroacylation with Rhodium/Phosphoramidite−Alkene Ligand Complexes. *Angew. Chem., Int. Ed.* **2011**, *50*, 10670−10674.
(13) Li, Y.; Xu, M.-H. Simple sulfur−olefins as new promising chiral ligands for asymmetric catalysis. *Chem. Commun.* **2014**, *50*, 3771−3782.
(14) Hahn, B. T.; Tewes, F.; Fröhlich, R.; Glorius, F. Olefin-Oxazolines (OlefOx): Highly Modular, Easily Tunable Ligands for Asymmetric Catalysis. *Angew. Chem., Int. Ed.* **2010**, *49*, 1143−1146.
(15) (a) Giri, R.; Chen, X.; Yu, J.-Q. Palladium-Catalyzed Asymmetric Iodination of Unactivated C−H Bonds under Mild Conditions. *Angew. Chem., Int. Ed.* **2005**, *44*, 2112−2115. (b) Liao, G.; Zhou, T.; Yao, Q.-J.; Shi, B.-F. Recent advances in the synthesis of axially chiral biaryls via transition metal-catalysed asymmetric C−H functionalization. *Chem. Commun.* **2019**, *55*, 8514−8523. (c) He, C.; Hou, M.; Zhu, Z.; Gu, Z. Enantioselective Synthesis of Indole-Based Biaryl Atropisomers via Palladium-Catalyzed Dynamic Kinetic Intramolecular C−H Cyclization. *ACS Catal.* **2017**, *7*, 5316−5320. (d) Liu, Z.-S.; Hua, Y.; Gao, Q.; Ma, Y.; Tang, H.; Shang, Y.; Cheng, H.; Zhou, Q. Construction of axial chirality via palladium/chiral norbornene cooperative catalysis. *Nature Catalysis* **2020**, *3*, 727−733. (e) Wang, Y.-B.; Tan, B. Construction of Axially Chiral Compounds via Asymmetric Organocatalysis. *Acc. Chem. Res.* **2018**, *51*, 534−547. (f) Zheng, J.; You, S.-L. Construction of Axial Chirality by Rhodium-Catalyzed Asymmetric Dehydrogenative Heck Coupling of Biaryl Compounds with Alkenes. *Angew. Chem., Int. Ed.* **2014**, *53*, 13244−13247. (g) Zheng, J.; Cui, W.-J.; Zheng, C.; You, S.-L. Synthesis and Application of Chiral Spiro Cp Ligands in Rhodium-Catalyzed Asymmetric Oxidative Coupling of Biaryl Compounds with Alkenes. *J. Am. Chem. Soc.* **2016**, *138*, 5242−5245. (h) Luo, J.; Zhang, T.; Wang, L.; Liao, G.; Yao, Q.-J.; Wu, Y.-J.; Zhan, B.-B.; Lan, Y.; Lin, X.-F.; Shi, B.-F. Enantioselective Synthesis of Biaryl Atropisomers by Pd-Catalyzed C−H Olefination using Chiral Spiro Phosphoric Acid Ligands. *Angew. Chem., Int. Ed.* **2019**, *58*, 6708−6712. (i) Yao, Q.-J.; Zhang, S.; Zhan, B.-B.; Shi, B.-F. Atroposelective Synthesis of Axially Chiral Biaryls by Palladium-Catalyzed Asymmetric C−H Olefination Enabled by a Transient Chiral Auxiliary. *Angew. Chem., Int. Ed.* **2017**, *56*, 6617−6621. (j) Zhang, J.; Xu, Q.; Wu, J.; Fan, J.; Xie, M. Construction of N−C Axial Chirality through Atroposelective C−H Olefination of N-Arylindoles by Palladium/Amino Acid Cooperative Catalysis. *Org. Lett.* **2019**, *21*, 6361−6365. (k) Ma, Y.-N.; Zhang, H.-Y.; Yang, S.-D. Pd(II)-Catalyzed P(O)R^1R^2-Directed Asymmetric C−H Activation and Dynamic Kinetic Resolution for the Synthesis of Chiral Biaryl Phosphates. *Org. Lett.* **2015**, *17*, 2034−2037.
(16) (a) Desimoni, G.; Faita, G.; Jørgensen, K. A. C2-Symmetric Chiral Bis(Oxazoline) Ligands in Asymmetric Catalysis. *Chem. Rev.* **2006**, *106*, 3561−3651. (b) Yang, G.; Zhang, W. Renaissance of pyridine-oxazolines as chiral ligands for asymmetric catalysis. *Chem. Soc. Rev.* **2018**, *47*, 1783−1810. (c) Hargaden, G. C.; Guiry, P. J. Recent Applications of Oxazoline-Containing Ligands in Asymmetric Catalysis. *Chem. Rev.* **2009**, *109*, 2505−2550. (d) Rechavi, D.; Lemaire, M. Enantioselective Catalysis Using Heterogeneous Bis-(oxazoline) Ligands: Which Factors Influence the Enantioselectivity? *Chem. Rev.* **2002**, *102*, 3467−3494. (e) McManus, H. A.; Guiry, P. J. Recent Developments in the Application of Oxazoline-Containing Ligands in Asymmetric Catalysis. *Chem. Rev.* **2004**, *104*, 4151−4202.

https://dx.doi.org/10.1021/acs.orglett.0c03093
Org. Lett. XXXX, XXX, XXX−XXX