JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Communication
pubs.acs.org/JACS

Synthesis and Application of Chiral Spiro Cp Ligands in Rhodium-Catalyzed Asymmetric Oxidative Coupling of Biaryl Compounds with Alkenes

Jun Zheng,[†] Wen-Jun Cui,[†] Chao Zheng,[†] and Shu-Li You*[,†,‡]

[†]State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Lu, Shanghai 200032, China

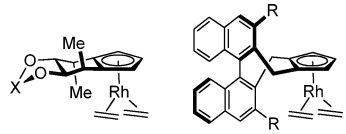
[‡]Collaborative Innovation Center of Chemical Science and Engineering, Tianjin 300072, China

Supporting Information

ABSTRACT: The vastly increasing application of chiral Cp ligands in asymmetric catalysis results in growing demand for novel chiral Cp ligands. Herein, we report a new class of chiral Cp ligands based on 1,1′-spirobiindane, a privileged scaffold for chiral ligands and catalysts. The corresponding Rh complexes are shown to be excellent catalysts in asymmetric oxidative coupling reactions, providing axially chiral biaryls in 19−97% yields with up to 98:2 er.

Cyclopentadienyl (Cp) has been recognized as a powerful, easy-to-access, and versatile ligand for the construction of robust and catalytically competent transition-metal complexes.[1] However, compared with the exponentially increased reports on the syntheses and applications of diverse chiral ligands in asymmetric catalysis, the research that aims to devise synthetically useful chiral Cp ligands by imparting chiral element into the Cp moiety remains rather underdeveloped. As a pioneering work in this area, Vollhardt and Halterman reported in 1986 the first C_2-symmetric annulated Cp ligand from tartrate derivatives, which avoids the detrimental formation of diastereomers upon metal coordination.[2] Although in the following years, sporadic examples of C_2-symmetric Cp ligands were published,[3,4] there was a continuous lack of broad interest in this area, probably due to the absence of efficient benchmark transformations. Recently, the rapid development of CpRh-catalyzed C−H activation proposed great demand of novel derivation of Cp ligands.[5] In this respect, Ward, Rovis et al. successfully synthesized a biotinylated [Cp*Rh(III)] complex which found utility in catalytic asymmetric C−H bond functionalization reactions.[6] On the other hand, the Cramer group disclosed two generations of C_2-symmetric Cp ligands whose Rh-complexes (**K1** and **K2**) exhibit great potentials in asymmetric C−H activation processes (Figure 1).[7] Notably, the complexes of other transition metals (Ru,[8] Ir,[9] and Sc[10]) with these Cp ligands also found successful applications in asymmetric catalysis.

Despite these remarkable contributions, developing Cp ligands bearing other chiral backbones is still an urgent but very challenging task. On the other hand, 1,1′-spirobiindane, as a privileged chiral scaffold, provides an excellent platform for chiral ligand and catalyst diversification.[11] Pioneered by the Zhou group, an array of 1,1′-spirobiindane-derived phosphine,[12] phosphoramidite,[13] oxazoline ligands[14] has emerged and shown impressive activity in versatile catalytic asymmetric transformations. Inspired by these elegant pioneering studies, we recently designed and synthesized a series of 1,1′-spirobiindane-derived Cp ligands (SCps) and successfully applied their Rh-complexes [(*S*)-**K3a-d**] in asymmetric oxidative coupling of biaryls with alkenes. Herein, we report the preliminary results of this study.



K1 **K2a** (R = OMe) **K2b** (R = O^{i}Pr) **K2c** (R = OTIPS) **K2d** (R = H)

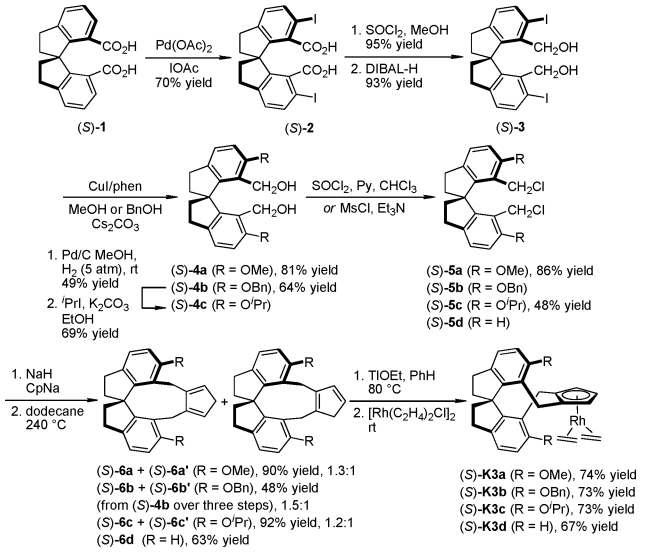
Figure 1. Rh(I) complexes of two generations of Cramer's chiral Cp^x ligands.

The syntheses of SCps started from known dicarboxylic acid (*S*)-**1**[15] (Scheme 1). The Pd-catalyzed directed *ortho*-C−H iodination, a procedure introduced by Yu et al.,[16] afforded diiodide (*S*)-**2**. The subsequent esterification and reduction provided diol (*S*)-**3** which was ready for the critical steric manipulation at the 6,6′-positions of the spirobiindane skeleton. The Cu-catalyzed methoxylation and benzyloxylation, introduced by the Buchwald group,[17] at the 6,6′-positions furnished modified diols (*S*)-**4a** and (*S*)-**4b**, respectively. Isopropoxy-substituted diol (*S*)-**4c** was obtained by debenzylation of (*S*)-**4b** and etherification. Then, the chlorination of (*S*)-**4a−c** with $SOCl_2$ or MsCl led to dichlorides (*S*)-**5a−c**. Double alkylation of cyclopentadiene followed by thermal rearrangement[7c,d,h] yielded a mixture of the precursors of cyclopentadienyl ligands (*S*)-**6a−c** and (*S*)-**6a′−c′**. The final metalation with $[Rh(C_2H_4)_2Cl]_2$ completed the syntheses of chiral SCpRh(I) complexes (*S*)-**K3a−c**. Analogue complex (*S*)-**K3d** with 6,6′-unsubstituted SCp was obtained via a similar procedure from known dichloride (*S*)-**5d**.[15] The structures of (*S*)-**K3a** and (*S*)-**K3d** were confirmed unambiguously by X-ray crystallographic analyses (Figure 2).[18]

Received: March 2, 2016
Published: April 12, 2016

DOI: 10.1021/jacs.6b02302
J. Am. Chem. Soc. 2016, 138, 5242−5245

Scheme 1. Synthesis of SCp Ligands and Their Rh(I) Complexes



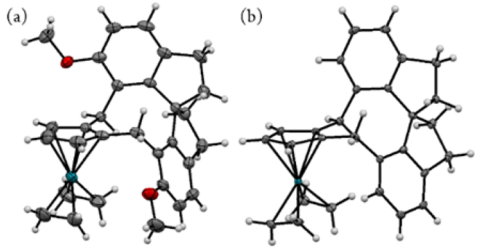


Figure 2. X-ray crystal structures of Rh(I) complexes (*S*)-**K3a** (a) and (*S*)-**K3d** (b).

A comparison between the structures of (*S*)-**K3a** and the BINOL-derived Cp^{x}Rh(I) complex (*R*)-**K2a** (R = OMe, Figure 1)[7d] revealed some interesting aspects (Figure 3). Compared

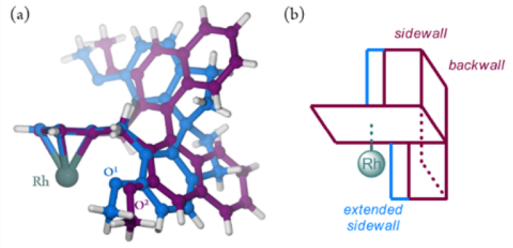
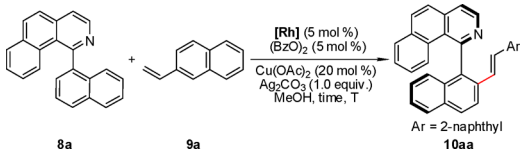


Figure 3. (a) The overlay of the X-ray crystal structures of (*R*)-**K2a** and (*S*)-**K3a**. Ethylene moieties are omitted for clarity. The BINOL backbone of (*R*)-**K2a** is in purple, and the 1,1′-spirobiindane backbone is in blue. (b) The schematic depiction of the asymmetric environment of C_2-symmetric Cp ligands.

with the BINOL skeleton, 1,1′-spirobiindane pushes the methoxy groups at the 6,6′-positions toward the Rh center more effectively, which is exemplified by a closer Rh···O distance in (*S*)-**K3a** (B(Rh···O^1) = 3.762 Å in (*S*)-**K3a** vs B(Rh···O^2) = 3.897 Å in (*R*)-**K2a**). According to the steric model suggested by Cramer et al.,[7d] relatively extended sidewalls are incorporated in SCp. Therefore, a better chiral environment around the Rh center in (*S*)-**K3a** might be expected.

Encouraged by the above structural information, we next tested the catalytic activity of Rh-complexes (*S*)-**K3**. Since axially chiral biaryls are of high importance in natural products as well as asymmetric synthesis, we have previously demonstrated that the axially chiral biaryls could be obtained through an oxidative coupling from 1-(naphthalen-1-yl)benzo-[*h*]isoquinoline with olefins by Cramer Cp^{x}Rh catalyst (*R*)-**K2a**. However, the average enantioselectivity could only reach around 90:10 er (entry 1, Table 1).[7g] To our delight, with the

Table 1. Optimization of the Enantioselective Oxidative Coupling Reaction[a]



entry	[Rh]	*T* (°C)	time (h)	yield (%)[b]	er[c]
1	(*R*)-**K2a**	80	24	94	90:10[d]
2	(*S*)-**K3a**	80	19	97	93:7
3	(*S*)-**K3b**	80	19	97	87:13
4	(*S*)-**K3c**	80	24	83	91:9
5	(*S*)-**K3d**	80	24	92	79:21
6	(*S*)-**K3a**	60	36	93	94:6
7	(*S*)-**K3a**	45	48	90	95:5
8[e]	(*S*)-**K3a**	**25**	**63**	**92**	**95:5**

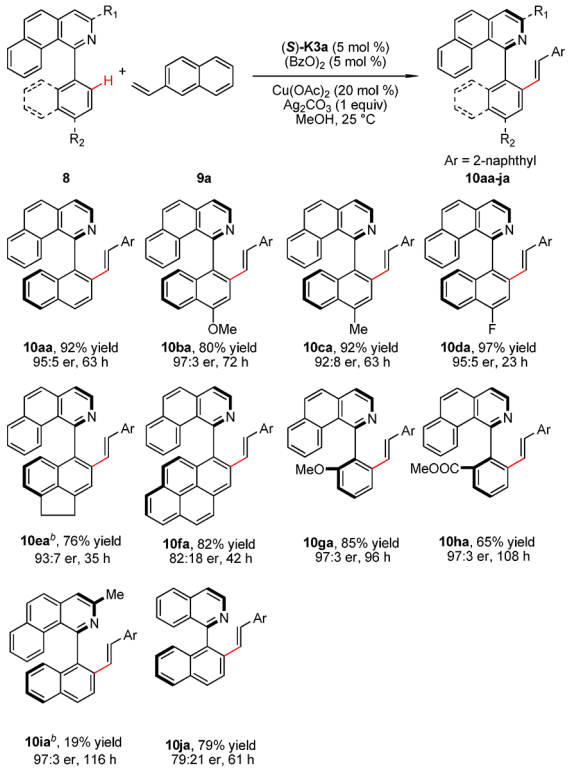
[a]Unless otherwise noted, all reactions were carried out under the following conditions: **8a** (0.1 mmol), **9a** (1.2 equiv), $Cu(OAc)_2$ (20 mol %), Ag_2CO_3 (1 equiv) in MeOH (0.2 M). [b]Isolated yields. [c]Determined by HPLC analysis on a chiral stationary phase. [d]The results are taken from ref 7g. [e]Reaction was performed on 0.2 mmol scale.

newly synthesized (*S*)-**K3a** (5 mol %) as the catalyst, the model reaction between **8a** and **9a** proceeded smoothly under the previously optimized conditions, giving the desired chiral biaryl **10aa** in 93:7 er (entry 2). It was found that the steric bulkiness of the substituents at the 6,6′-positions of 1,1′-spirobiindane scaffold exerts great influence on the reaction outcomes. The catalysts either with larger substituents such as (*S*)-**K3b** (R = OBn) and (*S*)-**K3c** (R = O^{i}Pr) or bearing no substituent on these positions [(*S*)-**K3d**, R = H] all resulted in diminished enantioselectivity (entries 3−5). Interestingly, the enantioselectivity could be increased slightly by reducing the temperature (entries 6 and 7), and the optimal results (**10aa** in 92% yield and 95:5 er) could be delivered at 25 °C (entry 8).

With the optimized conditions in hand, we next evaluated the generality of (*S*)-**K3a** as the catalyst in this transformation. As shown in Scheme 2, with **9a** as the coupling partner, an array of biaryls was well tolerated, and the corresponding alkenylated products **10aa−fa** could be afforded in satisfying yields (up to 97%) with excellent enantioselective control (up to 97:3 er). To our delight, phenyl ring bearing either an electron-donating (OMe) or electron-withdrawing group (CO_2Me) was well tolerated, and the desired products (**10ga−ha**) were obtained in good yields (65−85%) and excellent enantioselectivity (97:3 er). Notably, the reaction proceeded well with the challenging isoquinoline-derived substrate providing **10ja** with good yield, albeit in moderate enantioselectivity. Moreover, the reaction of sterically demanding substrate became retarded and delivered **10ia** in 19% yield with 97:3 er, probably due to the more congested chiral pocket of (*S*)-**K3a**.

DOI: 10.1021/jacs.6b02302
J. Am. Chem. Soc. 2016, 138, 5242−5245

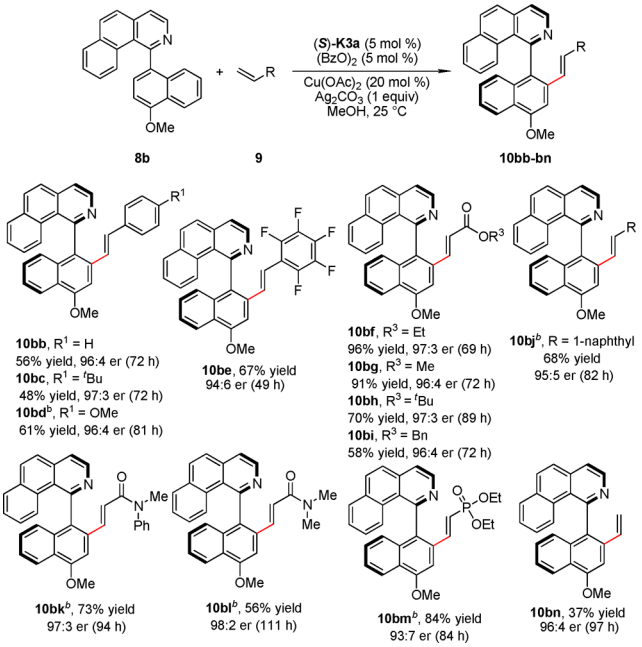
Scheme 2. Substrate Scope: Biaryls[a]



[a]Reaction conditions: **8** (0.2 mmol), **9a** (1.2 equiv), (*S*)-**K3a** (5 mol %), $(BzO)_2$ (5 mol %), $Cu(OAc)_2$ (20 mol %), and Ag_2CO_3 (1 equiv) in MeOH (0.2 M) at 25 °C. [b]At 60 °C.

The scope of olefins was also examined (Scheme 3). Almost for all the olefins tested, the oxidative coupling reaction worked with uniformly better enantioselectivity than that obtained using (*R*)-**K2a** as the catalyst.[7g] No matter with electronically and sterically varied styrenes, polarized olefins like α,β-unsaturated esters, amides, phosphonate ester, or even simple ethylene, the reactions led to the corresponding chiral biaryls (**10bb**–**bn**) in reasonable yields (37–91%) with excellent er values (93:7 to 98:2).

Scheme 3. Substrate Scope: Olefins[a]



[a]Reaction conditions: **8** (0.2 mmol), **9a** (1.2 equiv), (*S*)-**K3a** (5 mol %), $(BzO)_2$ (5 mol %), $Cu(OAc)_2$ (20 mol %), and Ag_2CO_3 (1 equiv) in MeOH (0.2 M) at 25 °C. [b]At 60 °C.

In summary, we have developed a series of novel cyclopentadienyl ligands (SCps) based on 1,1′-spirobiindane scaffold, and one of their corresponding Rh(I) complexes behaved as a superior catalyst in asymmetric oxidative coupling of biaryl derivatives with olefins. Notably, excellent enantioselectivity could be achieved in most cases, and the reaction could be run even at room temperature. Expanding the applications of SCp ligands to other synthetically useful enantioselective transformations is currently under investigation in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b02302.

Experimental details and data (PDF)
Crystallographic data (CIF)
Crystallographic data (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*slyou@sioc.ac.cn

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the National Basic Research Program of China (973 Program 2015CB856600) and National Natural Science Foundation of China (21332009, 21421091) for generous financial support.

■ REFERENCES

(1) For a review, see: Halterman, R. L. *Chem. Rev.* **1992**, *92*, 965.
(2) Halterman, R. L.; Vollhardt, K. P. C. *Tetrahedron Lett.* **1986**, *27*, 1461.
(3) For examples of C_2-symmetric Cp ligands, see: (a) Colletti, S. L.; Halterman, R. L. *Tetrahedron Lett.* **1989**, *30*, 3513. (b) Erker, G.; Schamberger, J.; van der Zeijden, A. A. H.; Dehnicke, S.; Krüger, C.; Goddard, R.; Nolte, M. *J. Organomet. Chem.* **1993**, *459*, 107. (c) Li, Z.; Vasella, A. *Helv. Chim. Acta* **1996**, *79*, 2201. (d) Paquette, L. A.; Bzowej, E. I.; Kreuzholz, R. *Organometallics* **1996**, *15*, 4857. (e) Gutnov, A.; Heller, B.; Drexler, H.-J.; Spannenberg, A.; Oehme, G. *Organometallics* **2003**, *22*, 1550. (f) McGlacken, G. P.; O'Brien, C. T.; Whitwood, A. C.; Fairlamb, I. J. S. *Organometallics* **2007**, *26*, 3722.
(4) For other examples of chiral Cp ligands, see: (a) Halterman, R. L.; Vollhardt, K. P. C. *Organometallics* **1988**, *7*, 883. (b) Schumann, H.; Stenzel, O.; Dechert, S.; Girgsdies, F.; Blum, J.; Gelman, D.; Halterman, R. L. *Eur. J. Inorg. Chem.* **2002**, *2002*, 211. (c) Halterman, R. L.; Crow, L. D. *Tetrahedron Lett.* **2003**, *44*, 2907. (d) Zhang, X.; Prosenc, M. H.; Meyer-Friedrichsen, T.; Heck, J. *Eur. J. Inorg. Chem.* **2003**, *2003*, 313. (e) Gutnov, A.; Drexler, H.-J.; Spannenberg, A.; Oehme, G.; Heller, B. *Organometallics* **2004**, *23*, 1002. (f) Gutnov, A.; Heller, B.; Fischer, C.; Drexler, H.-J.; Spannenberg, A.; Sundermann, B.; Sundermann, C. *Angew. Chem., Int. Ed.* **2004**, *43*, 3795. (g) Heller, B.; Gutnov, A.; Fischer, C.; Drexler, H.-J.; Spannenberg, A.; Redkin, D.; Sundermann, C.; Sundermann, B. *Chem. - Eur. J.* **2007**, *13*, 1117. (h) Laï, R.; Daran, J.-C.; Nuel, D.; Sanz, M.; Summerton, N.;

DOI: 10.1021/jacs.6b02302
J. Am. Chem. Soc. 2016, 138, 5242–5245

Vanthuyne, N.; Zaragori-Benedetti, A. *Dalton Trans.* **2013**, *42*, 7980. (i) Turner, Z. R.; Buffet, J.-C.; O'Hare, D. *Organometallics* **2014**, *33*, 3891. (j) Gajewski, P.; Renom-Carrasco, M.; Facchini, S. V.; Pignataro, L.; Lefort, L.; de Vries, J. G.; Ferraccioli, R.; Forni, A.; Piarulli, U.; Gennari, C. *Eur. J. Org. Chem.* **2015**, *2015*, 1887. (k) Gajewski, P.; Renom-Carrasco, M.; Facchini, S. V.; Pignataro, L.; Lefort, L.; de Vries, J. G.; Ferraccioli, R.; Piarulli, U.; Gennari, C. *Eur. J. Org. Chem.* **2015**, *2015*, 5526.

(5) For selected reviews on Rh(III)-catalyzed C−H functionalization reaction, see: (a) Satoh, T.; Miura, M. *Chem. - Eur. J.* **2010**, *16*, 11212. (b) Wencel-Delord, J.; Dröge, T.; Liu, F.; Glorius, F. *Chem. Soc. Rev.* **2011**, *40*, 4740. (c) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215. (d) Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2012**, *45*, 814. (e) Song, G.; Wang, F.; Li, X. *Chem. Soc. Rev.* **2012**, *41*, 3651. (f) Kuhl, N.; Schröder, N.; Glorius, F. *Adv. Synth. Catal.* **2014**, *356*, 1443. (g) Zhang, X.-S.; Chen, K.; Shi, Z.-J. *Chem. Sci.* **2014**, *5*, 2146. (h) Song, G.; Li, X. *Acc. Chem. Res.* **2015**, *48*, 1007. (i) Shin, K.; Kim, H.; Chang, S. *Acc. Chem. Res.* **2015**, *48*, 1040.

(6) Hyster, T. K.; Knörr, L.; Ward, T. R.; Rovis, T. *Science* **2012**, *338*, 500.

(7) For reviews, see: (a) Ye, B.; Cramer, N. *Acc. Chem. Res.* **2015**, *48*, 1308. (b) Newton, C. G.; Kossler, D.; Cramer, N. *J. Am. Chem. Soc.* **2016**, *138*, 3935. For selected examples, see: (c) Ye, B.; Cramer, N. *Science* **2012**, *338*, 504. (d) Ye, B.; Cramer, N. *J. Am. Chem. Soc.* **2013**, *135*, 636. (e) Ye, B.; Donets, P. A.; Cramer, N. *Angew. Chem., Int. Ed.* **2014**, *53*, 507. (f) Ye, B.; Cramer, N. *Angew. Chem., Int. Ed.* **2014**, *53*, 7896. (g) Zheng, J.; You, S.-L. *Angew. Chem., Int. Ed.* **2014**, *53*, 13244. (h) Ye, B.; Cramer, N. *Synlett* **2015**, *26*, 1490. (i) Zheng, J.; Wang, S.-B.; Zheng, C.; You, S.-L. *J. Am. Chem. Soc.* **2015**, *137*, 4880. (j) Chidipudi, S. R.; Burns, D. J.; Khan, I.; Lam, H. W. *Angew. Chem., Int. Ed.* **2015**, *54*, 13975. (k) Pham, M. V.; Cramer, N. *Chem. - Eur. J.* **2016**, *22*, 2270.

(8) Kossler, D.; Cramer, N. *J. Am. Chem. Soc.* **2015**, *137*, 12478.

(9) Dieckmann, M.; Jang, Y.-S.; Cramer, N. *Angew. Chem., Int. Ed.* **2015**, *54*, 12149.

(10) Song, G.; O, W. W. N.; Hou, Z. *J. Am. Chem. Soc.* **2014**, *136*, 12209.

(11) For selected reviews, see: (a) Xie, J.-H.; Zhou, Q.-L. *Acc. Chem. Res.* **2008**, *41*, 581. (b) Ding, K.; Han, Z.; Wang, Z. *Chem. - Asian J.* **2009**, *4*, 32. (c) Bajracharya, G. B.; Arai, M. A.; Koranne, P. S.; Suzuki, T.; Takizawa, S.; Sasai, H. *Bull. Chem. Soc. Jpn.* **2009**, *82*, 285. (d) Xie, J.-H.; Zhou, Q.-L. *Huaxue Xuebao* **2014**, *72*, 778. (e) Xie, J.-H.; Bao, D.-H.; Zhou, Q.-L. *Synthesis* **2015**, *47*, 460. (f) Zhu, S.-F.; Zhou, Q.-L. *Acc. Chem. Res.* **2012**, *45*, 1365. For a book, see: (g) *Privileged Chiral Ligands and Catalysts*; Zhou, Q.-L., Ed.; Wiley-VCH: Weinheim, Germany, 2011.

(12) Xie, J.-H.; Wang, L.-X.; Fu, Y.; Zhu, S.-F.; Fan, B.-M.; Duan, H.-F.; Zhou, Q.-L. *J. Am. Chem. Soc.* **2003**, *125*, 4404.

(13) (a) Fu, Y.; Xie, J.-H.; Hu, A.-G.; Zhou, H.; Wang, L.-X.; Zhou, Q.-L. *Chem. Commun.* **2002**, 480. (b) Hu, A.-G.; Fu, Y.; Xie, J.-H.; Zhou, H.; Wang, L.-X.; Zhou, Q.-L. *Angew. Chem., Int. Ed.* **2002**, *41*, 2348.

(14) Liu, B.; Zhu, S.-F.; Wang, L.-X.; Zhou, Q.-L. *Tetrahedron: Asymmetry* **2006**, *17*, 634.

(15) Zhu, S.-F.; Yang, Y.; Wang, L.-X.; Liu, B.; Zhou, Q.-L. *Org. Lett.* **2005**, *7*, 2333.

(16) For palladium-catalyzed *ortho* iodination of simple arene carboxylic acids, see: Mei, T.-S.; Giri, R.; Maugel, N.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2008**, *47*, 5215.

(17) For copper-catalyzed coupling of aryl iodides with aliphatic alcohols, see: Wolter, M.; Nordmann, G.; Job, G. E.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 973.

(18) For details, see the Supporting Information. CCDC 1455371−1455372 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

DOI: 10.1021/jacs.6b02302
J. Am. Chem. Soc. 2016, 138, 5242−5245