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Copper(I)-Catalyzed Intramolecular Asymmetric Double C-Arylation for the Formation of Chiral Spirocyclic Bis-oxindoles

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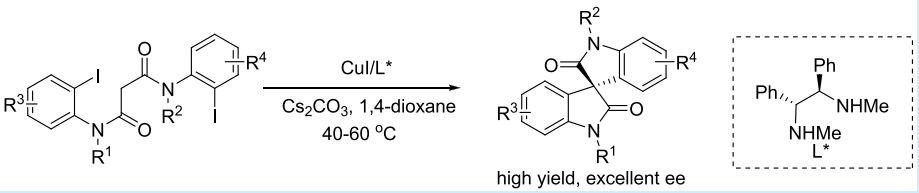
Supporting Information



ABSTRACT: A copper-catalyzed intramolecular asymmetric double C-arylation reaction was developed. The method provides a facile approach to chiral spiro bis-oxindoles in high yields and with good to excellent enantioselectivities. It also shows a broad substrate scope and good functional group tolerance. Density functional theory (DFT) calculations were conducted and revealed that the enantioselectivity is determined at the oxidative addition of Cu(I) into the second C−I bond.

Copper-catalyzed coupling reaction of aryl halides with nucleophiles has become one of the most important methods for the construction of aryl C−C and C−heteroatom bonds.[1] However, the research on copper-catalyzed asymmetric aryl C−C coupling reaction is rare. That was until 2006, when the pioneering study for copper-catalyzed asymmetric C-arylation was reported by Ma and co-workers.[2] In this work, the enantioselective coupling of 2-methylacetoacetates with 2-halotrifluoroacetanilides afforded the C-arylation product with a quaternary chiral carbon center under the catalysis of CuI and trans-4-hydroxyl-L-proline. Moderate to high yields and enantioselectivities were obtained. No further research on copper-catalyzed asymmetric coupling of aryl halides with C-nucleophiles was reported since then,[3−7] and it has remained a great challenge in coupling chemistry.

The spirooxindole moiety has been found as a core structure in many bioactive natural products and synthetic pharmaceutical compounds.[8,9] The unique structures and broad biological activities of such compounds have attracted great attention in the synthetic community and many elegant methods have been developed for their syntheses.[10,11] Among various spirooxindoles, spirocyclic bis-oxindoles, in which two oxindoles are connected through a single carbon at the 3-position, have a very rigid and crowded spirocarbon stereogenic center. The presence of two bulky aryl rings in such compounds makes their synthesis challenging, but also provides a good opportunity for intramolecular double C-arylation of N^1,N^3-diarylmalonamides to access the spirocyclic structures. In 2012, Du and Zhao reported a synthesis of racemic spirocyclic bis-oxindoles from N^1,N^3-diarylmalonamides through a PIFA[PhI-(TFA)$_2$]-promoted intramolecular oxidative coupling (Scheme 1a).[12,13] In 2014, Gong and co-workers developed such reactions further, achieving an elegant catalytic asymmetric version with chiral iodoarenes and oxidants (Scheme 1b).[14]

Scheme 1. Copper-Catalyzed Intramolecular Asymmetric Double C-Arylation for the Formation of Spiro Bis-oxindoles

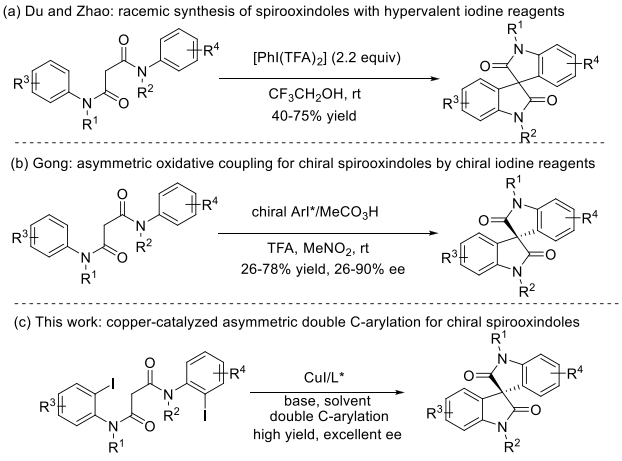


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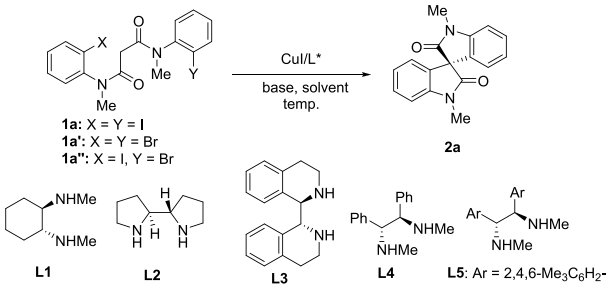
Table 1. Reaction Condition Screening[a]



entry	L*	base	solvent	temperature (°C)	yield[b] (%)	enantiomeric excess, ee[c] (%)
1	**L1**	Cs_2CO_3	toluene	80	82	33
2	**L1**	Cs_2CO_3	DMF	80	80	20
3	**L1**	Cs_2CO_3	THF	80	95	20
4	**L1**	Cs_2CO_3	MeCN	80	98	23
5	**L1**	Cs_2CO_3	dioxane	80	34	53
6	**L1**	Cs_2CO_3	dioxane	60	76	62
7	**L1**	K_3PO_4	dioxane	60	91	56
8	**L1**	K_2CO_3	dioxane	60	72	52
9	**L2**	Cs_2CO_3	dioxane	60	60	41
10	**L3**	Cs_2CO_3	dioxane	60	80	<10
11	***L4***	***Cs_2CO_3***	***dioxane***	***60***	***86***	***91***
12	**L5**	Cs_2CO_3	dioxane	60	72	55
13[d]	**L4**	Cs_2CO_3	dioxane	60	91	90
14[e]	**L4**	Cs_2CO_3	dioxane	60	88	88
15[f]	**L4**	Cs_2CO_3	dioxane	60	–	–
16[g]	**L4**	Cs_2CO_3	dioxane	60	67	85

[a]Reagents and conditions: entries 1−14, **1a** (0.2 mmol), CuI (0.04 mmol, 20 mol %), **L*** (0.08, 40 mol %), base (0.75 mmol, 3 equiv), solvent 2 mL, 24 h. [b]Isolated yield. [c]Determined by chiral HPLC. [d]CuI (10 mol %), **L*** (20 mol %), 48 h. [e]CuI (5 mol %), **L*** (10 mol %), 48 h. [f]**1a′** was used. [g]**1a′′** was used.

However, because of the incompatibility of some functional groups with oxidative conditions and the complexity of reactions mediated by iodine reagents, serious limitations and challenges to these synthetic efforts still persisted, including limited substrate scope, moderate reaction efficiency, and poor regioselectivity.[15] Further efforts may also be needed for further improvement of the enantioselectivity of such reactions. Consequently, a highly efficient and enantioselective method for the asymmetric synthesis of spiro bis-oxindoles will be very useful.

To overcome the regioselective and enantioselective problems, as well as substrate limitations in the asymmetric synthesis of spiro bis-oxindoles, we envisioned that copper-catalyzed double C-arylation may be a possible solution. During our research on asymmetric coupling reactions, we have developed several CuI/chiral ligand catalytic systems for asymmetric aryl C−N/O bond coupling.[16,17] The high efficiency of these catalytic systems encouraged us for further exploration in asymmetric C-arylation. In this work, an enantioselective double aryl C−C coupling was developed for the formation of chiral spirocyclic bis-oxindoles (Scheme 1c). The details of this research are reported in this paper.

The reaction of N^1,N^3-dimethyl-N^1,N^3-bis(2-iodophenyl)-malonamide (**1a**) was taken as a model case. As shown in Table 1, the CuI-catalyzed double C-arylation of **1a** was performed in toluene at 80 °C, with (1*R*,2*R*)-N^1,N^2-dimethylcyclohexane-1,2-diamine (**L1**) as a chiral ligand and Cs_2CO_3 as the base. The reaction proceeded smoothly, furnishing the spirocyclic product (**2a**) in 82% yield and 33% enantiomeric excess (ee) (see Table 1, entry 1). Further screening of solvents revealed that better enantioselectivity (53% ee) but a reduced yield (34% yield) was obtained in 1,4-dioxane (Table 1, entries 2−5). The poor yield in 1,4-dioxane is mainly due to the competitive hydrolysis of amide bonds at 80 °C. Thus, we reduced the reaction temperature to 60 °C and a better yield (76%) and enantioselectivity (62% ee) were obtained (Table 1, entry 6). Other bases were explored, and better reaction efficiency, but slightly reduced enantioselectivity, was achieved by changing the base to K_3PO_4 (see Table 1, entry 7). Further screening of different chiral diamine ligands (**L2**−**L5**) revealed that good yields and excellent enantioselectivity were obtained with ligand **L4** at 60 °C (Table 1, entry 11, 86% yield, 91% ee). Reducing the catalyst loading to 10 mol % or 5 mol % of CuI (20 mol % or 10 mol % of L4), the reaction still worked well and the spiro bis-oxindole product **2a** was obtained in 91% yield and 90% ee or 88% yield and 88% ee, respectively, albeit a prolonged reaction time of 48 h was needed for complete conversion (see Table 1, entries 13 and 14). Although the formation of spiro bis-oxindole **2a** was supposed to proceed through a double C-arylation process, it is noteworthy that no monocyclized byproduct was observed during the reaction. This means that the monocyclized intermediates are very reactive and can easily undergo a second C-arylation step. To compare with the reaction of diiodo substrate **1a**, the reactions of dibromo substrate **1a′** and N^1-(2-bromophenyl)-N^3-(2-iodophenyl)-N^1,N^3-dimethylmalonamide **1a′′** were explored under the same reaction conditions. Spirocyclic product **2a** was not detected when the less-reactive dibromo substrate **1a′** was used (Table 1, entry 15). Meanwhile, the reaction of **1a′′** proceeded smoothly to deliver

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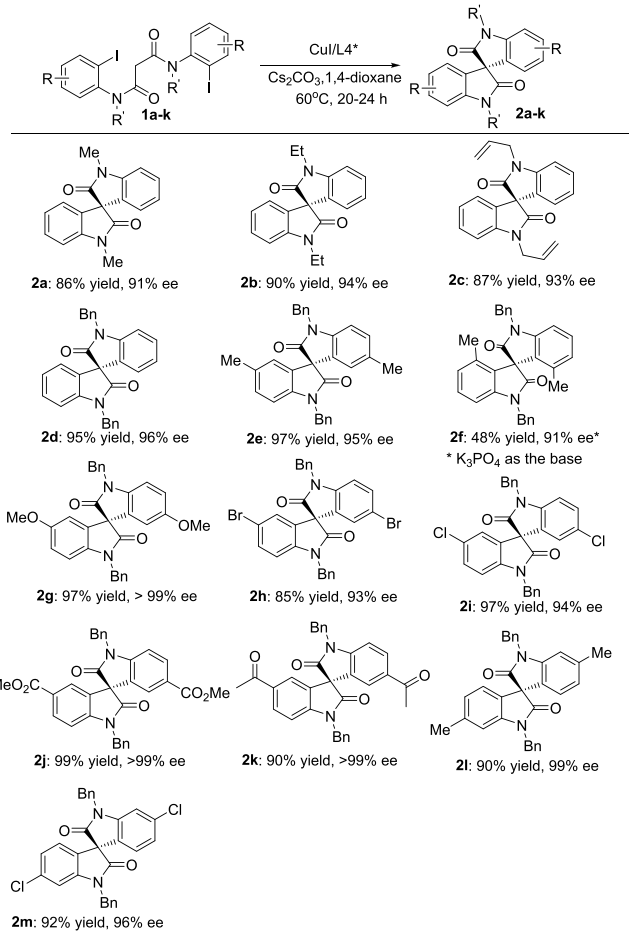
the desired spirocyclic product **2a** in moderate yield and good enantioselectivity (Table 1, entry 16, 67% yield, 85% ee).

With these optimized conditions (Table 1, entry 11), we explored the reaction scope with a variety of symmetric diamide substrates, obtaining the results shown in Scheme 2.

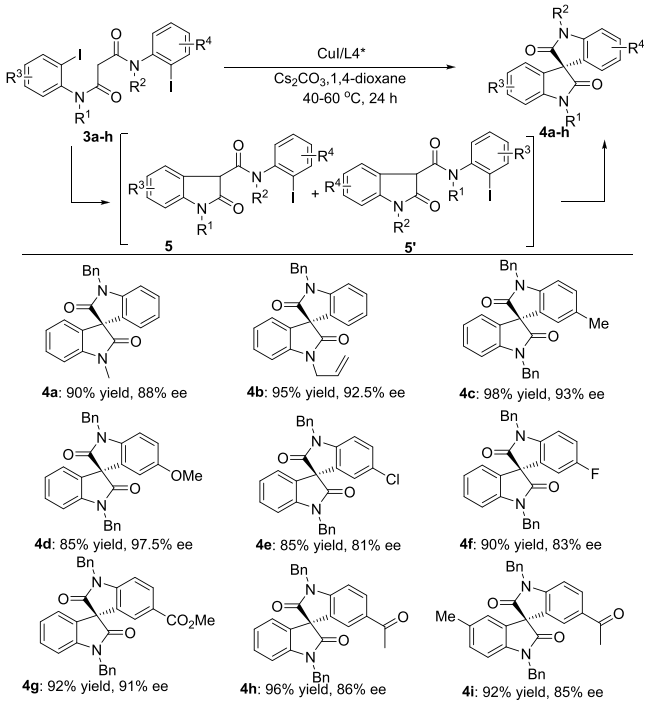
Scheme 2. Substrate Scope of Symmetric Diamides



First, different substituents such as methyl, ethyl, allyl, and benzyl group on the N atom of amides were explored, and all delivered the corresponding spiro *bis*-oxindoles in high yields and with excellent enantioselectivity. A variety of diamide substrates with symmetric substituents on both aryl rings were explored. Both electron-donating and electron-withdrawing groups, including alkyl, methoxy, halide, ester, and carbonyl groups, were well-tolerated in the reactions and all afforded the desired double C-arylation products in high yields and with excellent enantioselectivity. In some cases, such as products **2g**, **2j**, **2k**, and **2l**, the enantioselectivities even reached >99% ee. An exception was compound **1f**, with two methyl groups ortho to the two coupling iodo sites. The coupling reaction of **1f** at 60 °C with Cs_2CO_3 as the base was slow, presumably because of steric hindrance. However, such a problem could be solved by switching the base to K_3PO_4, with which the spirocyclic product **2f** was produced in moderate yield and with excellent enantioselectivity (48% yield, 91% ee). The absolute configuration of product **2a** was assigned as *S* by comparison with reported data.[14] The absolute configurations of other products were assigned by analogy.

A variety of unsymmetric diamide substrates were then explored, and the results are shown in Scheme 3. The reactions

Scheme 3. Substrate Scope of Symmetric Diamides



of unsymmetric diamides were expected to afford a mixture of two monocyclic intermediates at the first C-arylation step, but lead to the same chiral spirocyclic products through the second C-arylation. Several examples of unsymmetrical diamides with different substituents on the N atom or aryl rings were explored. All these reactions were observed to proceed smoothly under our optimized conditions, delivering the corresponding spiro bis-oxindoles in high yields and with good to excellent enantioselectivities. It is noteworthy that the substrates bearing electron-withdrawing groups such as F, ester, or carbonyl groups were found to deliver high enantioselectivities at 40 °C. The absolute configuration of product **4b** was confirmed as *S* by X-ray crystallography.[18] The absolute configurations of other products were assigned by analogy.

The formation of spirocyclic bis-oxindoles was supposed to proceed through two C-arylation steps (see Scheme 4). The nucleophilic carbon in monocyclic intermediate **INT1**, activated by two amide bonds and a phenyl group, can be easily deprotonated and undergo racemization under basic conditions.[2,6] Thus, the enantioselectivity is mainly determined in the second C-arylation step. To understand the origin of the high enantioselectivity, density functional theory (DFT) calculations were conducted.[18] The potential energy surface of the second Cu^{I}/Cu^{III} catalytic cycle is shown in Figure S1 in the Supporting Information (SI).[19] A systematic conformational search was conducted to obtain the lowest pathway leading to the products (see Figures S1 and S2 in the SI). The transition state for the oxidative addition (**TS4**) is generally comparable or higher in free energy than the transition state associated with reductive elimination (**TS5**), suggesting that oxidative addition (**TS4**) is the enantioselectivity-determining step.[20] The most stable transition states for oxidative addition

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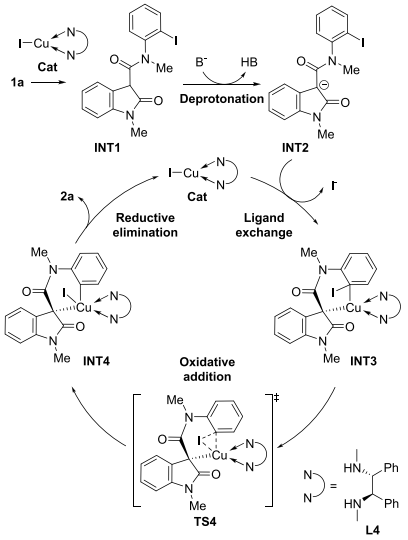
Scheme 4. Proposed Reaction Mechanism



(**TS4-R** and **TS4-S**) leading to two enantiomers are depicted in Figure 1. The relative free energy of **TS4-R** is higher than

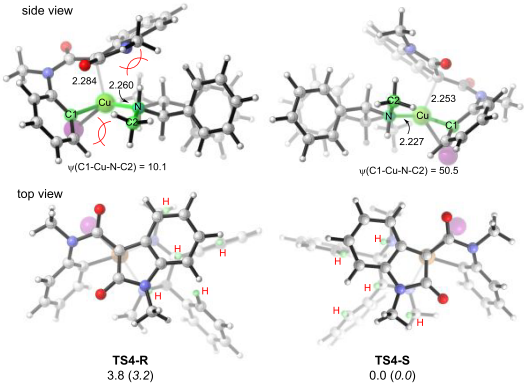


Figure 1. Structures of **TS4-R** and **TS4-S**. Relative free energies and enthalpies (shown in parentheses) are given in units of kcal/mol, and dihedral angles and distances are presented in units of degrees and Å, respectively.

that of **TS4-S**, which is in good agreement with the experimental observed reference on the *S*-product. In **TS4**, CuI adopts a tetrahedral geometry. The substrate **INT2** complex with CuI has two orientations and the main difference between them is the orientation of the methyl group (C2) of the amine. The dihedral angle ψ(C1−Cu−N−C2) in **TS4-R** is 10.1°, indicating that the methyl group and the incoming aryl group are eclipsed, and repulsion between the methyl group and the aryl group destabilizes **TS4-R**. On the other hand, in **TS4-S**, the corresponding methyl group and aryl group adopt a comfortable staggered conformation, with a dihedral angle of ψ(C1−Cu−N−C2) = 50.5°. The repulsion in **TS4-R** can also be seen in the fact that the Cu−N bond in **TS4-R** is longer that in **TS4-S**. Another effect of discrimination is the repulsion between the indole with the 1,2-diamine ligand. As shown from the top view of the transition states, the indole ring of **TS4-R** occupies a more crowded position which suffers from the repulsion of those H atoms of 1,2-diamine ligand. By switching the face, the indole in **TS4-S** can be accommodated at a sterically relaxed position.

In summary, we have developed a copper-catalyzed double C-arylation process for the enantioselective formation of spiro bis-oxindoles. This method provides a highly efficient and enantioselective approach to the asymmetric synthesis of spiro bis-oxindoles. Further explorations and applications of this method are in progress in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.9b01373.

Full experimental and characterization data, including ^{1}H and ^{13}C NMR for all the new compounds, chiral HPLC spectra for the products (PDF)

Accession Codes

CCDC 1912332 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For selected reviews, see: (a) Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400. (b) Beletskaya, I. P.; Cheprakov, A. V. *Coord. Chem. Rev.* **2004**, *248*, 2337. (c) Evano, G.; Blanchard, N.; Toumi, M. *Chem. Rev.* **2008**, *108*, 3054. (d) Monnier, F.; Taillefer, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 6954−6971. (e) Ma, D.; Cai, Q. *Acc. Chem. Res.* **2008**, *41*, 1450. (f) Surry, D. S.; Buchwald, S. L. *Chem. Sci.* **2010**, *1*, 13. (g) Sambiagio, C.; Marsden, S. P.; Blacker, A. J.; McGowan, P. C. *Chem. Soc. Rev.* **2014**, *43*, 3525.

(2) Xie, X.; Chen, Y.; Ma, D. *J. Am. Chem. Soc.* **2006**, *128*, 16050.

(3) Zhou, F.; Cai, Q. *Beilstein J. Org. Chem.* **2015**, *11*, 2600.

(4) For early examples of biaryl compounds synthesis via chiral substrate-induced copper-catalyzed asymmetric Ullmann coupling, see: (a) Stavrakov, G.; Keller, M.; Breit, B. *Eur. J. Org. Chem.* **2007**, *2007*, 5726. (b) Gorobets, E.; McDonald, R.; Keay, B. A. *Org. Lett.* **2006**, *8*, 1483. (c) Meyers, A. I.; Nelson, T. D.; Moorlag, H.; Rawson, D. J.; Meier, A. *Tetrahedron* **2004**, *60*, 4459. (d) Spring, D. R.; Krishnan, S.; Schreiber, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 5656.

DOI: 10.1021/acs.orglett.9b01373
Org. Lett. XXXX, XXX, XXX−XXX

(e) Lipshutz, B. H.; Kayser, F.; Liu, Z.-P. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1842. (f) Nelson, T. D.; Meyers, A. I. *J. Org. Chem.* **1994**, *59*, 2655. (g) Rawal, V. H.; Florjancic, A. S.; Singh, S. P. *Tetrahedron Lett.* **1994**, *35*, 8985.

(5) For examples of copper-catalyzed oxidative asymmetric C-arylation with arylboronic acids, see: (a) Querard, P.; Perepichka, I.; Zysman-Colman, E.; Li, C.-J. *Beilstein J. Org. Chem.* **2016**, *12*, 2636. (b) Baslé, O.; Li, C.-J. *Org. Lett.* **2008**, *10*, 3661.

(6) For selected examples of enantioselective C-arylation by Pd or Ni-catalyzed coupling of aryl halide with anion equivalents, see: (a) Zhu, Y.; Buchwald, S. L. *J. Am. Chem. Soc.* **2014**, *136*, 4500. (b) Taylor, A. M.; Altman, R. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2009**, *131*, 9900. (c) Hamada, T.; Chieffi, A.; Ahman, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 1261. (d) Ahman, J.; Wolfe, J. P.; Troutman, M. V.; Palucki, M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 1918. (e) Ge, S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2011**, *133*, 16330. (f) Liao, X.; Weng, Z.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 195. (g) Huang, Z.; Liu, Z.; Zhou, J. *J. Am. Chem. Soc.* **2011**, *133*, 15882. (h) Jiao, Z.; Chee, K. W.; Zhou, J. *J. Am. Chem. Soc.* **2016**, *138*, 16240. (i) Zhu, C.; Wang, D.; Zhao, Y.; Sun, W.-Y.; Shi, Z. *J. Am. Chem. Soc.* **2017**, *139*, 16486. (j) Liu, R.-R.; Li, B.-L.; Lu, J.; Shen, C.; Gao, J.-R.; Jia, Y.-X. *J. Am. Chem. Soc.* **2016**, *138*, 5198.

(7) For selected reviews and examples of transition metal-catalyzed enantioselective C-arylation through C−H functionalization, see: (a) Saint-Denis, T. G.; Zhu, R.-Y.; Chen, G.; Wu, Q.-F.; Yu, J.-Q. *Science* **2018**, *359*, No. eaao4798. (b) Newton, C. G.; Wang, S.-G.; Oliveira, C. C.; Cramer, N. *Chem. Rev.* **2017**, *117*, 8908. (c) Tong, H.-R.; Zheng, S.; Li, X.; Deng, Z.; Wang, H.; He, G.; Peng, Q.; Chen, G. *ACS Catal.* **2018**, *8*, 11502. (d) Yan, S.-Y.; Han, Y.-Q.; Yao, Q.-J.; Nie, X.-L.; Liu, L.; Shi, B.-F. *Angew. Chem., Int. Ed.* **2018**, *57*, 9093. (e) Chen, G.; Gong, W.; Zhuang, Z.; Andrä, M. S.; Chen, Y.-Q.; Hong, X.; Yang, Y.-F.; Liu, T.; Houk, K. N.; Yu, J.-Q. *Science* **2016**, *353*, 1023. (f) Yan, S.-B.; Zhang, S.; Duan, W.-L. *Org. Lett.* **2015**, *17*, 2458.

(8) (a) Galliford, C. V.; Scheidt, K. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 8748. (b) Aho, J. E.; Pihko, P. M.; Rissa, T. K. *Chem. Rev.* **2005**, *105*, 4406. (c) Minkin, V. I. *Chem. Rev.* **2004**, *104*, 2751.

(9) For selected examples, see: (a) Namjoshi, O. A.; Cook, J. M. *Alkaloids* **2016**, *76*, 63. (b) Bhaskar, G.; Arun, Y.; Balachandran, C.; Saikumar, C.; Perumal, P. T. *Eur. J. Med. Chem.* **2012**, *51*, 79. (c) Miller, K. A.; Tsukamoto, S.; Williams, R. M. *Nat. Chem.* **2009**, *1*, 63. (d) Hanhan, N. V.; Ball-Jones, N. R.; Tran, N. T.; Franz, A. K. *Angew. Chem., Int. Ed.* **2012**, *51*, 989. (e) Ye, N.; Chen, H. Y.; Wold, E. A.; Shi, P. Y.; Zhou, J. *ACS Infect. Dis.* **2016**, *2*, 382. (f) Sampson, P. B.; Liu, Y.; Forrest, B.; Cumming, G.; Li, S.-W.; Patel, N. K.; Edwards, L.; Laufer, R.; Feher, M.; Ban, F.; et al. *J. Med. Chem.* **2015**, *58*, 147. (g) Zhao, Y.; Liu, L.; Sun, W.; Lu, J.; McEachern, D.; Li, X.; Yu, S.; Bernard, D.; Ochsenbein, P.; Ferey, V.; Carry, J.-C.; Deschamps, J. R.; Sun, D.; Wang, S. *J. Am. Chem. Soc.* **2013**, *135*, 7223.

(10) For selected reviews, see: (a) Carreira, E. M.; Fessard, T. C. *Chem. Rev.* **2014**, *114*, 8257. (b) Volla, C. M. R.; Atodiresei, L.; Rueping, M. *Chem. Rev.* **2014**, *114*, 2390. (c) Cheng, D.; Ishihara, Y.; Tan, B.; Barbas, C. F., III *ACS Catal.* **2014**, *4*, 743. (d) Franz, A. K.; Hanhan, N. V.; Ball-Jones, N. R. *ACS Catal.* **2013**, *3*, 540. (e) Rios, R. *Chem. Soc. Rev.* **2012**, *41*, 1060.

(11) For selected examples, see: (a) Zhang, L.-L.; Zhang, J.-W.; Xiang, S.-H.; Guo, Z.; Tan, B. *Org. Lett.* **2018**, *20*, 6022. (b) Jayakumar, S.; Louven, K.; Strohmann, C.; Kumar, K. *Angew. Chem., Int. Ed.* **2017**, *56*, 15945. (c) Huang, J.-R.; Sohail, M.; Taniguchi, T.; Monde, K.; Tanaka, F. *Angew. Chem., Int. Ed.* **2017**, *56*, 5853. (d) Zhang, L.; Lu, H.; Xu, G.-Q.; Wang, Z.-Y.; Xu, P.-F. *J. Org. Chem.* **2017**, *82*, 5782. (e) Wu, M.-Y.; He, W.-W.; Liu, X.-Y.; Tan, B. *Angew. Chem., Int. Ed.* **2015**, *54*, 9409. (f) Xu, J.; Shao, L.-D.; Li, D.; Deng, X.; Liu, Y.-C.; Zhao, Q.-S.; Xia, C. *J. Am. Chem. Soc.* **2014**, *136*, 17962. (g) Trost, B. M.; Bringley, D. A.; Zhang, T.; Cramer, N. *J. Am. Chem. Soc.* **2013**, *135*, 16720. (h) Dugal-Tessier, J. D.; O'Bryan, E. A.; Schroeder, T. B. H.; Cohen, D. T.; Scheidt, K. A. *Angew. Chem., Int. Ed.* **2012**, *51*, 4963. (i) Hande, S. M.; Nakajima, M.; Kamisaki, H.; Tsukano, C.; Takemoto, Y. *Org. Lett.* **2011**, *13*, 1828. (j) Tan, B.; Candeias, N. R.; Barbas, C. F., III *Nat. Chem.* **2011**, *3*, 473. (k) Jiang, X.; Cao, Y.; Wang, Y.; Liu, L.; Shen, F.; Wang, R. *J. Am. Chem. Soc.* **2010**, *132*, 15328. (l) Jiang, K.; Jia, Z.-J.; Yin, X.; Wu, L.; Chen, Y.-C. *Org. Lett.* **2010**, *12*, 2766. (m) Shintani, R.; Hayashi, S.-Y.; Murakami, M.; Takeda, M.; Hayashi, T. *Org. Lett.* **2009**, *11*, 3754. (n) Trost, B. M.; Cramer, N.; Silverman, S. M. *J. Am. Chem. Soc.* **2007**, *129*, 12396. (o) Lo, M. M.-C.; Neumann, C. S.; Nagayama, S.; Perlstein, E. O.; Schreiber, S. L. *J. Am. Chem. Soc.* **2004**, *126*, 16077.

(12) Wang, J.; Yuan, Y.; Xiong, R.; Zhang-Negrerie, D.; Du, Y.; Zhao, K. *Org. Lett.* **2012**, *14*, 2210.

(13) For a recent work to form racemic spirocyclic *bis*-oxindoles, see: Sun, J.; Li, G.; Zhang, G.; Cong, Y.; An, X.; Zhang-Negrerie, D.; Du, Y. *Adv. Synth. Catal.* **2018**, *360*, 2476.

(14) Wu, H.; He, Y.-P.; Xu, L.; Zhang, D.-Y.; Gong, L.-Z. *Angew. Chem., Int. Ed.* **2014**, *53*, 3466.

(15) For selected reviews about iodine reagents-mediated reactions, see: (a) Cai, Q.; Ma, H. *Huaxue Xuebao* **2019**, *77*, 213. (b) Flores, A.; Cots, E.; Bergès, J.; Muñiz, K. *Adv. Synth. Catal.* **2019**, *361*, 2. (c) Yoshimura, A.; Zhdankin, V. V. *Chem. Rev.* **2016**, *116*, 3328. (d) Harned, A. M. *Tetrahedron Lett.* **2014**, *55*, 4681. (e) Romero, R. M.; Wöste, T. H.; Muñiz, K. *Chem. - Asian J.* **2014**, *9*, 972. (f) Singh, F. V.; Wirth, T. *Chem. - Asian J.* **2014**, *9*, 950. (g) Parra, A.; Reboredo, S. *Chem. - Eur. J.* **2013**, *19*, 17244. (h) Liang, H.; Ciufolini, M. A. *Angew. Chem., Int. Ed.* **2011**, *50*, 11849. (i) Duan, Y.; Jiang, S.; Han, Y.; Sun, B.; Zhang, C. *Youji Huaxue* **2016**, *36*, 1973.

(16) Zhou, F.; Liu, J.; Cai, Q. *Synlett* **2016**, *27*, 664.

(17) (a) Liu, J.; Tian, Y.; Shi, J.; Zhang, S.; Cai, Q. *Angew. Chem., Int. Ed.* **2015**, *54*, 10917. (b) Yang, W.; Liu, Y.; Zhang, S.; Cai, Q. *Angew. Chem., Int. Ed.* **2015**, *54*, 8805. (c) Zhou, F.; Guo, J.; Liu, J.; Ding, K.; Yu, S.; Cai, Q. *J. Am. Chem. Soc.* **2012**, *134*, 14326. (d) Liu, J.; Yan, J.; Qin, D.; Cai, Q. *Synthesis* **2014**, *46*, 1917.

(18) See the Supporting Information.

(19) Calculations were conducted with B3LYP-D3/[6-31G(d), Lanl2dz+d or f, I (ξ(d) = 0.289) and Cu (ξ(f) = 3.525)] (BSI). Single-point energy was calculated by using the SMD solvation model (dichloromethane) at the B3LYP-D3/[6-311++G**; Def2TZVP for Cu and I] (BSII). All calculations were performed with Gaussian 16 (Frisch, M. J., et al. *Gaussian 16*; Gaussian, Inc., Wallingford, CT, 2009). (More details are included in the Supporting Information.)

(20) Hickman, A. J.; Sanford, M. S. *Nature* **2012**, *484*, 177.

(21) Liu, L.; Xi, Z. *Chin. J. Chem.* **2018**, *36*, 1213.

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Org. Lett. XXXX, XXX, XXX−XXX