Organic LETTERS

Letter

pubs.acs.org/OrgLett

Zn-Catalyzed Diastereo- and Enantioselective Cascade Reaction of 3-Isothiocyanato Oxindoles and 3-Nitroindoles: Stereocontrolled Syntheses of Polycyclic Spirooxindoles

Jian-Qiang Zhao,[†,§] Zhi-Jun Wu,[‡] Ming-Qiang Zhou,[†] Xiao-Ying Xu,[*,†] Xiao-Mei Zhang,[†] and Wei-Cheng Yuan[*,†]

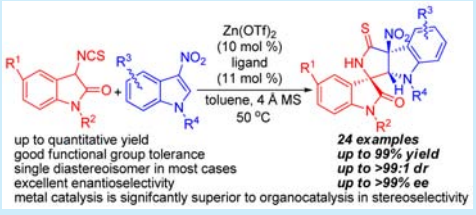
[†]National Engineering Research Center of Chiral Drugs, Chengdu Institute of Organic Chemistry, Chinese Academy of Sciences, Chengdu 610041, China

[‡]Chengdu Institute of Biology, Chinese Academy of Sciences, Chengdu 610041, China

[§]University of Chinese Academy of Sciences, Beijing 100049, China

Supporting Information

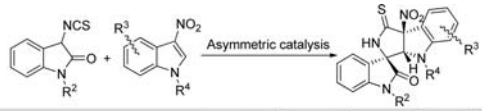
ABSTRACT: A catalytic asymmetric Michael/cyclization cascade reaction of 3-isothiocyanato oxindoles and 3-nitroindoles has been disclosed with a chiral $Zn(OTf)_2$/diphenylamine-linked bis(oxazoline) complex as the catalyst. A range of enantioenriched polycyclic spirooxindole derivatives containing three contiguous stereocenters were efficiently constructed in quantitative yields with excellent diastereo- and enantioselectivities. Importantly, the metal catalytic strategy in this work is significantly superior to the previous organocatalytic method in the diastereo- and enantioselectivities for almost all of the examined cases.



The spirooxindole scaffold defines the characteristic structural core of a large family of alkaloids and unnatural biologically active compounds.[1] Inspired by these important motifs, a great number of asymmetric methods for the construction of structurally diverse chiral spirooxindoles have been investigated over the past decade.[2] Thereinto, numerous structurally and stereochemically rich polycyclic spirooxindoles could be rapidly generated via a cascade process in a single step.[1−3] Moreover, some of these complex molecules also have been proven to possess definite pertinence with certain biological properties and pharmacological activities.[4] Accordingly, the development of efficient methods for the asymmetric synthesis of spirooxindoles will be important in the design and discovery of medicinally significant compounds. In particular, finding a simple and efficient approach to access the structurally diverse spirooxindoles with excellent stereocontrol is in high demand.

The synthesis of spirooxindole compounds with multiple stereocenters generally remains a significant challenge in organic chemistry. In continuation of our investigation in preparing various spirooxindoles,[5] a highly organocatalyzed asymmetric Michael/cyclization cascade reaction between 3-isothiocyanato oxindoles and 3-nitroindoles for the construction of polycyclic spirooxindoles was recently reported by us.[6] However, in that study, the stereoselectivity of the reaction was found to tolerate minor variations in the substituents of the N1-position with respect to 3-isothiocyanato oxindoles and 3-nitroindoles (Scheme 1). To remedy the deficiency in organocatalysis,[6] we turned our attention to explore a feasible catalytic system for the same reaction, hoping for good functional group tolerance. To our delight, the expected asymmetric Michael/cyclization cascade reaction could be efficiently realized with a chiral $Zn(OTf)_2$/diphenylamine-linked bis(oxazoline) complex as the catalyst. More importantly, a wide range of enantioenriched polycyclic spirooxindoles could be smoothly obtained with excellent results (95−99% yield, >99:1 dr for the most cases, up to >99% ee). Notably, the metal catalysis in this work is significantly superior to the organocatalytic method in the stereoselectivity for almost all of the examined cases (Scheme 1). Herein we wish to report the highly efficient metal-catalyzed strategy for the asymmetric

Scheme 1. Asymmetric Reaction of 3-Isothiocyanato Oxindoles and 3-Nitroindoles with Different Catalytic System



	our previous work organocatalysis	*this work* metal catalysis
R^4 = Ts, Bs; R^2 = Me	82:18~>99:1 dr 59~96% ee	93:7~>99:1 dr 91~99% ee
R^4 = Ms, Ns, Cbz, Boc, CO_2Et; R^2 = Me	50:50~91:9 dr 31~83% ee	>99:1 dr 98~>99% ee
R^4 = Ts; R^2 = Et, Bn, Ph	79:21~86:14 dr 36~40% ee	85:15~>99:1 dr 92~98% ee

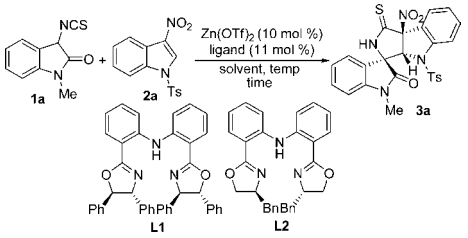
Received: August 29, 2015
Published: September 28, 2015

DOI: 10.1021/acs.orglett.5b02489
Org. Lett. 2015, 17, 5020−5023

reaction of 3-isothiocyanato oxindoles[7] and 3-nitroindoles[8] with good functional group tolerance.

We began our study by using the reaction of **1a** and **2a** for optimizing the reaction conditions. As shown in Table 1, in the presence of $Zn(OTf)_2$ (10 mol %) and ligand **L1** (11 mol %) bearing *trans*-diphenyl substitution on the oxazoline rings, the reaction could furnish spirooxindole **3a** in 94% yield with 98:2 dr and 80% ee at room temperature within 24 h (entry 1). With the $Zn(OTf)_2$/**L1** complex as the catalyst, the screening of solvents revealed that toluene was the best (entry 5 vs entires 2−4). Enhancing the ratio of **2a** to **1a** from 1:1 to 1.1:1 gave rise to an improved yield and excellent stereoselectivity (>99:1 dr, 97% ee) (entry 6). Decreasing the temperature to 0 °C caused the reaction to furnish **3a** in 75% yield with 94:6 dr and 79% ee, and a much longer reaction time was needed (entry 7). In contrast, a slightly improved reactivity and yield could be observed under 50 °C, albeit the dr and ee values remained unchanged (entry 8). Adding 4 Å molecular sieves (MS) led to a set of excellent results (entry 9).[9] Another similar ligand **L2** containing benzyl substitution on the oxazoline rings was examined; **3a** could be smoothly obtained with excellent results but a little lower ee value than those obtained with **L1** (entry 10 vs 9). Decreasing the catalyst loading led to different levels of erosion on the enantioselectivity (entries 11−12).

Table 1. Conditions Optimization[a]



	ligand	solvent	temp (°C)	time (h)	yield (%)[b]	dr[c]	ee (%)[d]
1	**L1**	CH_2Cl_2	rt	24	94	98:2	80
2	**L1**	DCE	rt	24	81	93:7	58
3	**L1**	THF	rt	24	trace	–	–
4	**L1**	dioxane	rt	24	93	67:33	39
5	**L1**	toluene	rt	24	92	98:2	95
6	**L1**	toluene	rt	24	96	>99:1	97[e]
7	**L1**	toluene	0	72	75	94:6	79[e]
8	**L1**	toluene	50	8	99	>99:1	97[e]
9	**L1**	toluene	50	8	99	>99:1	99[e,f]
10	**L2**	toluene	50	8	98	>99:1	(+)98[e,f]
11	**L1**	toluene	50	12	99	99:1	95[e,f,g]
12	**L1**	toluene	50	15	98	92:8	56[e,f,h]

[a]Unless specified, the reactions were carried out with **1a** (0.1 mmol) and **2a** (0.1 mmol) in 1.0 mL of solvent for the indicated time. [b]Yield of isolated product as a mixture of diastereoisomers. [c]Determined by chiral HPLC. [d]Ee of the major diastereomer was determined by chiral HPLC analysis after the product reacting with CH_3I.[6,7a] [e]0.11 mmol of **2a** was used. [f]100 mg of 4 Å MS was used. [g]$Zn(OTf)_2$ (5 mol %) and **L1** (5.5 mol %) were used. [h]$Zn(OTf)_2$ (3 mol %) and **L1** (3.3 mol %) were used. DCE = 1,2-dichloroethane.

Having established the optimal reaction conditions, we next explored the scope of the asymmetric Michael/cyclization cascade reaction. As shown in Table 2, the high reactivity and excellent stereoselectivity tested by the $Zn(OTf)_2$/**L1** complex could be expanded to a broad range of 3-isothiocyanato oxindoles and 3-nitroindoles. First, the reaction proved to exhibit no significant bias toward both the electronic nature and the substitution pattern of the substituents on the phenyl ring of 3-nitroindoles, as demonstrated by affording the products **3b−j** in 95−99% yields with up to >99:1 dr and 99% ee (entries 1−9). More importantly, a series of 3-nitroindoles with different substituent groups on the N1-position also performed very well, delivering the products **3k−r** in excellent yields as well as dr and ee values (entries 10−17). Yet, 3-isothiocyanato oxindoles bearing different substituents, regardless of variation at the N1-position (**1b−d**) or at the phenyl ring (**1e−f**), were also very compatible with the standard reaction conditions and led to their respective products in high to excellent results (entries 18−22). And in one case among them, product **3u** could be formed in 96% yield with 85:15 dr and 92% ee with the $Zn(OTf)_2$/**L2** complex as the catalyst (entry 20).

With the above-mentioned satisfactory results in hand, we were interested in comparing the current developed metal catalytic system with our previously reported organocatalytic system for the same reaction. In light of the results summarized in Table 2, we were pleased to find that, in general, the reactions were able to proceed smoothly with the chiral $Zn(OTf)_2$/**L1** complex and afford the corresponding polycyclic spirooxindoles in quantitative yields with excellent stereoselectivities. For the cases of **3b−j** and **3v−w** except for **3h**, the stereoselectivities with the metal catalytic system are superior to the results achieved with the organocatalytic system (entries 1−6, 8−9, and 21−22). In addition, for the other examples of **3k−u**, the method in this work gives significantly improved stereoselectivities compared with those obtained using the organocatalytic method (entries 10−15, 17−20). Therefore, we can draw the conclusion that this well-developed metal catalytic system makes up for the deficiency of stereoselectivity with the organocatalytic system in our previous report.[6] When we used electron-donating 3-nitroindole **2s** as a substrate reacting with **1a**, unfortunately, the reaction did not take place (entry 23).

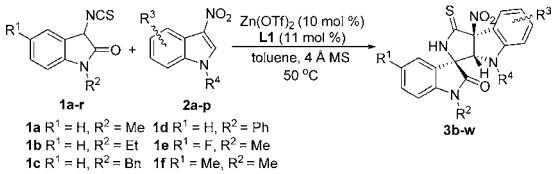
To gain insight into the reaction mechanism, comparative experiments were carried out with ligands **L2** and **L3** for the reaction of **1a** and **2a**. As shown in Scheme 2, **3a** could be obtained in 98% yield with >99:1 dr and 98% ee in the presence of **L2**. However, by replacing **L2** with ligand **L3**, the same reaction gave **3a** in 96% yield but with 77:23 dr and only 26% ee. By comparing these results and the structures of ligands **L2** and **L3**, we think that there is almost no H-bonding interaction between ligand **L3** and substrate **1a**, but it is probably between **L2** and **1a**. Therefore, it suggests that the NH proton of the diphenylamine moiety in the ligand is vital for excellent diastereo- and enantioselectivity.

The nonlinear effect[10] for the present catalytic system was also investigated with ligand **L1** in different enantiomeric purities. The relationship between the ee values of **3a** and ligand **L1** showed that a slightly positive nonlinear effect existed (Figure 1).[11] This observation suggested that minor oligomeric aggregates existed in the reaction system. Nevertheless, the catalytic composition was also attempted to be examined by using ESI-MS. A spectrum was obtained for a mixture of $Zn(OTf)_2$ and ligand **L1** in a 1:1.1 ratio. The MS peak at m/z 996.0804 (m/z calcd for $[\mathbf{L1} + Zn(OTf)_2 + Na]^+$ 996.0797) was observed.[11] These results revealed that the major monomeric complex $Zn(OTf)_2$/**L1** would function as the most active and effective catalytic intermediate.

Based on the above experimental observations, the absolute configuration of spirooxindole products, and the previous relevant reports,[7f,12,13] a possible transition state was tentatively

DOI: 10.1021/acs.orglett.5b02489
Org. Lett. 2015, 17, 5020−5023

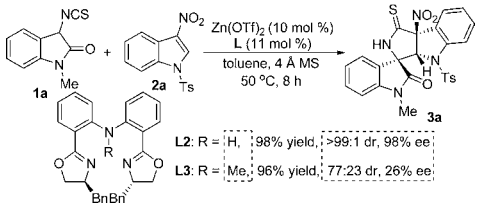
Table 2. Substrate Scope Examination[a]



					obtained in this work			with organocatalysis[e]	
entry	1	R^3/R^4	time (h)	3	yield (%)[b]	dr[c]	ee (%)[d]	dr[c]	ee (%)[d]
1	**1a**	5-Cl/Ts (**2b**)	9	**3b**	97	>99:1	98	>99:1	93
2	**1a**	5-Br/Ts (**2c**)	8	**3c**	98	>99:1	95	>99:1	93
3	**1a**	5-OMe/Ts (**2d**)	13	**3d**	96	>99:1	98	97:3	95
4	**1a**	5-OBn/Ts (**2e**)	9	**3e**	99	>99:1	98	97:3	93
5	**1a**	5-CN/Ts (**2f**)	8	**3f**	99	>99:1	99	82:18[f]	59[f]
6	**1a**	4-Cl/Ts (**2g**)	8	**3g**	99	95:5	95	97:3	90
7	**1a**	4-Br/Ts (**2h**)	9	**3h**	95	93:7	91	>99:1	94
8	**1a**	6-Cl/Ts (**2i**)	8	**3i**	99	>99:1	99	>99:1	93
9	**1a**	7-Me/Ts (**2j**)	9	**3j**	97	>99:1	98	97:3	96
10	**1a**	H/Bs (**2k**)	8	**3k**	98	>99:1	99	>99:1	95
11	**1a**	H/Ms (**2l**)	8	**3l**	97	>99:1	98	77:23	31
12	**1a**	H/Ns (**2m**)	8	**3m**	99	>99:1	99	91:9	72
13	**1a**	H/Ac (**2n**)	9	**3n**	99	>99:1	>99	50:50	80
14	**1a**	H/Cbz (**2o**)	9	**3o**	96	>99:1	>99	67:33	75
15	**1a**	H/CO_2Et (**2p**)	9	**3p**	98	>99:1	>99	66:34	83
16	**1a**	H/CO_2Me (**2q**)	10	**3q**	97	>99:1	>99		
17	**1a**	H/Boc (**2r**)	8	**3r**	97	>99:1	>99	55:45	77
18	**1b**	**2a**	8	**3s**	99	>99:1	98	84:16	40
19	**1c**	**2a**	8	**3t**	96	>99:1	94	86:14	39
20	**1d**	**2a**	8	**3u**	96	85:15	92[g]	79:21	36
21	**1e**	**2a**	8	**3v**	97	>99:1	99	96:4	92
22	**1f**	**2a**	8	**3w**	98	>99:1	97	>99:1	95
23	**1a**	H/Me (**2s**)	12	**3x**	nr	–	–		

[a]The reactions were carried out with **1** (0.1 mmol) and **2** (0.11 mmol) in 1.0 mL of toluene with 100 mg of 4 Å MS at 50 °C. [b]Isolated yield. [c]Determined by ^{1}H NMR analysis of crude reaction mixture. [d]Ee of major diastereomer was determined by chiral HPLC analysis after the product reacting with CH_3I.[6,7a] [e]The results refer to being obtained with organocatalysis in ref 6. [f]The result was obtained by using the standard reaction conditions reported in ref 6. [g]$Zn(OTf)_2$ (10 mol %) and **L2** (11 mol %) were used. For the abbreviations of Ts, Bs, Ms, Ns, Ac, Cbz, and Boc, see ref 6. nr = no reaction.

Scheme 2. Comparative Experiments with Ligands L2−3



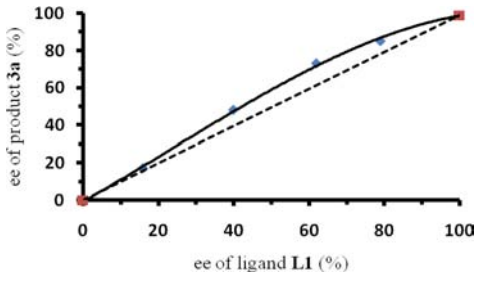


Figure 1. Investigation of nonlinear effect.

proposed. As shown in Figure 2, the 3-nitroindoles were activated by the Zn(II) core serving as a Lewis acid.[12] Concurrently, the 3-isothiocyanato oxindoles were directed by

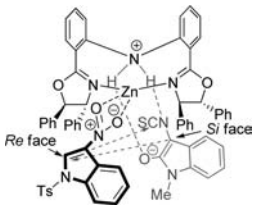


Figure 2. Proposed transition state.

the NH group serving as a Lewis base.[13] These imply that the catalyst plays a dual-functional role in the catalytic process.[7f] Thus, under the action of the $Zn(OTf)_2$/**L1** complex as catalyst, (1) the 2-position of 3-nitroindoles was attacked at the *Re* face by the activated 3-isothiocyanato oxindoles from the *Si* face. Subsequently, (2) the intramolecular cyclization leads to the formation of the polycyclic spirooxindole compounds.

In conclusion, we have developed a highly efficient Zn-catalyzed Michael/cyclization cascade reaction of 3-isothiocyanato oxindoles and 3-nitroindoles. With a chiral $Zn(OTf)_2$/diphenylamine-linked bis(oxazoline) complex as the catalyst, a wide range of enantioenriched spirooxindoles could be efficiently constructed in quantitative yields with excellent diastereo- and enantioselectivities. Importantly, the metal

DOI: 10.1021/acs.orglett.5b02489
Org. Lett. 2015, 17, 5020−5023

catalytic strategy in this work is significantly superior to the previous organocatalytic method in the diastereo- and enantioselectivities for almost all of the examined cases. This well-developed metal catalytic system makes up for the deficiency of stereoselectivity with the organocatalytic system in our previous report. A possible transition state model, characterized by the catalyst playing a dual-functional role, was also proposed. Further exploration of the catalytic system for other asymmetric syntheses of heterocyclic compounds is still in progress.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b02489.

Experimental details, characterization data for compounds, nonlinear effect experiment (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: xuxy@cioc.ac.cn.
*E-mail: yuanwc@cioc.ac.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful for financial support from NSFC (No. 21372217) and Sichuan Youth Science and Technology Foundation (2013JQ0021, 2015JQ0041).

■ REFERENCES

(1) For selected reviews, see: (a) Lin, H.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 36. (b) Marti, C.; Carreira, E. M. *Eur. J. Org. Chem.* **2003**, *2003*, 2209. (c) Galliford, C. V.; Scheidt, K. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 8748. (d) Trost, B. M.; Brennan, M. K. *Synthesis* **2009**, *2009*, 3003.

(2) For selected reviews, see: (a) Zhou, F.; Liu, Y.-L.; Zhou, J. *Adv. Synth. Catal.* **2010**, *352*, 1381. (b) Yu, J.; Shi, F.; Gong, L.-Z. *Acc. Chem. Res.* **2011**, *44*, 1156. (c) Rios, R. *Chem. Soc. Rev.* **2012**, *41*, 1060. (d) Ball-Jones, N. R.; Badillo, J. J.; Franz, A. K. *Org. Biomol. Chem.* **2012**, *10*, 5165. (e) Singh, G. S.; Desta, Z. Y. *Chem. Rev.* **2012**, *112*, 6104. (f) Dalpozzo, R.; Bartoli, G.; Bencivenni, G. *Chem. Soc. Rev.* **2012**, *41*, 7247. (g) Franz, A. K.; Hanhan, N. V.; Ball-Jones, N. R. *ACS Catal.* **2013**, *3*, 540. (h) Hong, L.; Wang, R. *Adv. Synth. Catal.* **2013**, *355*, 1023. (i) Cheng, D.; Ishihara, Y.; Tan, B.; Barbas, C. F., III. *ACS Catal.* **2014**, *4*, 743.

(3) For selected examples, see: (a) Tan, B.; Candeias, N. R.; Barbas, C. F., III. *Nat. Chem.* **2011**, *3*, 473. (b) Tan, B.; Candeias, N. R.; Barbas, C. F., III. *J. Am. Chem. Soc.* **2011**, *133*, 4672. (c) Tan, B.; Hernández-Torres, G.; Barbas, C. F., III. *J. Am. Chem. Soc.* **2011**, *133*, 12354. (d) Sun, W.-S.; Zhu, G.-M.; Wu, C.-Y.; Li, G.-F.; Hong, L.; Wang, R. *Angew. Chem., Int. Ed.* **2013**, *52*, 8633. (e) Liu, Y.-L.; Wang, X.; Zhao, Y.-L.; Zhu, F.; Zeng, X.-P.; Chen, L.; Wang, C.-H.; Zhao, X.-L.; Zhou, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 13735. (f) Yin, X.-P.; Zeng, X.-P.; Liu, Y.-L.; Liao, F.-M.; Yu, J.-S.; Zhou, F.; Zhou, J. *Angew. Chem., Int. Ed.* **2014**, *53*, 13740. (g) Wang, Y.; Shi, F.; Yao, X.-X.; Sun, M.; Dong, L.; Tu, S.-J. *Chem. - Eur. J.* **2014**, *20*, 15047. (h) Cao, Z.-Y.; Wang, X.-M.; Tan, C.; Zhao, X.-L.; Zhou, J.; Ding, K.-L. *J. Am. Chem. Soc.* **2013**, *135*, 8197. (i) Wang, Y.; Cao, Z.; Niu, Y.; Zhao, X.; Zhou, J. *Huaxue Xuebao* **2014**, *72*, 867. (j) Xie, M.; Wu, X.; Wang, G.; Lin, L.; Feng, X. *Huaxue Xuebao* **2014**, *72*, 856. (k) Cao, Z.-Y.; Zhou, J. *Org. Chem. Front.* **2015**, *2*, 849.

(4) For selected examples, see: (a) Overman, L. E.; Rosen, M. D. *Angew. Chem., Int. Ed.* **2000**, *39*, 4596. (b) Kumar, R. R.; Perumal, S.; Senthilkumar, P.; Yogeeswari, P.; Sriram, D. *J. Med. Chem.* **2008**, *51*, 5731. (c) Vintonyak, V. V.; Warburg, K.; Kruse, H.; Grimme, S.; Hübel, K.; Rauh, D.; Waldmann, H. *Angew. Chem., Int. Ed.* **2010**, *49*, 5902. (d) Antonchick, A. P.; Gerding-Reimers, C.; Catarinella, M.; Schürmann, M.; Preut, H.; Ziegler, S.; Rauh, D.; Waldmann, H. *Nat. Chem.* **2010**, *2*, 735.

(5) For selected examples of our group for the synthesis of spirooxindoles, see: (a) Chen, W.-B.; Wu, Z.-J.; Pei, Q.-L.; Cun, L.-F.; Zhang, X.-M.; Yuan, W.-C. *Org. Lett.* **2010**, *12*, 3132. (b) Han, Y.-Y.; Han, W.-Y.; Hou, X.; Zhang, X.-M.; Yuan, W.-C. *Org. Lett.* **2012**, *14*, 4054. (c) You, Y.; Cui, B.-D.; Zhou, M.-Q.; Zuo, J.; Zhao, J.-Q.; Xu, X.-Y.; Zhang, X.-M.; Yuan, W.-C. *J. Org. Chem.* **2015**, *80*, 5951.

(6) Zhao, J.-Q.; Zhou, M.-Q.; Wu, Z.-J.; Wang, Z.-H.; Yue, D.-F.; Xu, X.-Y.; Zhang, X.-M.; Yuan, W.-C. *Org. Lett.* **2015**, *17*, 2238.

(7) For selected examples on 3-isothiocyanato oxindoles in the synthesis of spirooxindole molecules, see: (a) Chen, W.-B.; Wu, Z.-J.; Hu, J.; Cun, L.-F.; Zhang, X.-M.; Yuan, W.-C. *Org. Lett.* **2011**, *13*, 2472. (b) Han, W.-Y.; Li, S.-W.; Wu, Z.-J.; Zhang, X.-M.; Yuan, W.-C. *Chem. - Eur. J.* **2013**, *19*, 5551. (c) Liu, X.-L.; Han, W.-Y.; Zhang, X.-M.; Yuan, W.-C. *Org. Lett.* **2013**, *15*, 1246. (d) Kato, S.; Yoshino, T.; Shibasaki, M.; Kanai, M.; Matsunaga, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 7007. (e) Wu, H.; Zhang, L.-L.; Tian, Z.-Q.; Huang, Y.-D.; Wang, Y.-M. *Chem. - Eur. J.* **2013**, *19*, 1747. (f) Tan, F.; Lu, L.-Q.; Yang, Q.-Q.; Guo, W.; Bian, Q.; Chen, J.-R.; Xiao, W.-J. *Chem. - Eur. J.* **2014**, *20*, 3415. (g) Wang, L.; Yang, D.; Li, D.; Wang, R. *Org. Lett.* **2015**, *17*, 3004. (h) Wang, L.; Yang, D.; Li, D.; Liu, X.; Zhao, Q.; Zhu, R.; Zhang, B.; Wang, R. *Org. Lett.* **2015**, *17*, 4260.

(8) For selected examples about the reactions of 3-nitroindoles, see: (a) Biolatto, B.; Kneeteman, M.; Paredes, E.; Mancini, P. M. E. *J. Org. Chem.* **2001**, *66*, 3906. (b) Chataigner, I.; Piettre, S. R. *Org. Lett.* **2007**, *9*, 4159. (c) Lee, S.; Diab, S.; Queval, P.; Sebban, M.; Chataigner, I.; Piettre, S. R. *Chem. - Eur. J.* **2013**, *19*, 7181. (d) Awata, A.; Arai, T. *Angew. Chem., Int. Ed.* **2014**, *53*, 10462.

(9) The absolute and relative stereochemistry of **3a** was determined by comparing the ^{1}H NMR, chiral HPLC, and optical rotation analysis with our previous report; see ref 6. Those of other products were assumed to have similar configurations as **3a**.

(10) (a) Guillaneux, D.; Zhao, S.-H.; Samuel, O.; Rainford, D.; Kagan, H. B. *J. Am. Chem. Soc.* **1994**, *116*, 9430. (b) Girard, C.; Kagan, H. B. *Angew. Chem., Int. Ed.* **1998**, *37*, 2922. (c) Satyanarayana, T.; Abraham, S.; Kagan, H. B. *Angew. Chem., Int. Ed.* **2009**, *48*, 456. (d) Wang, Z.; Yang, Z.; Chen, D.; Liu, X.; Lin, L.; Feng, X. *Angew. Chem., Int. Ed.* **2011**, *50*, 4928. (e) Li, J.; Lian, X.; Liu, X.; Lin, L.; Feng, X. *Chem. - Eur. J.* **2013**, *19*, 5134. (f) Zhou, Y.; Zhu, Y.; Lin, L.; Zhang, Y.; Zheng, J.; Liu, X.; Feng, X. *Chem. - Eur. J.* **2014**, *20*, 16753.

(11) For details, see the Supporting Information.

(12) (a) Du, D.-M.; Lu, S.-F.; Fang, T.; Xu, J.-X. *J. Org. Chem.* **2005**, *70*, 3712. (b) Lu, S.-F.; Du, D.-M.; Xu, J.-X. *Org. Lett.* **2006**, *8*, 2115. (c) Liu, H.; Lu, S.-F.; Xu, J.-X.; Du, D.-M. *Chem. - Asian J.* **2008**, *3*, 1111. (d) Jia, Y.; Yang, W.; Du, D.-M. *Org. Biomol. Chem.* **2012**, *10*, 4739. (e) Peng, J.-H.; Du, D.-M. *Eur. J. Org. Chem.* **2012**, *2012*, 4042. (f) Tan, F.; Xiao, C.; Cheng, H.-G.; Wu, W.; Ding, K.-R.; Xiao, W.-J. *Chem. - Asian J.* **2012**, *7*, 493.

(13) For selected reviews about the NH functional group in organometallic catalysis, see: (a) Ikariya, T.; Gridnev, I. D. *Chem. Rec.* **2009**, *9*, 106. (b) Zhao, B.; Han, Z.; Ding, K. *Angew. Chem., Int. Ed.* **2013**, *52*, 4744. For selected examples, see: (c) Gao, J.-X; Ikariya, T.; Noyori, R. *Organometallics* **1996**, *15*, 1087. (d) Jiang, Y.; Jiang, Q.; Zhang, X. *J. Am. Chem. Soc.* **1998**, *120*, 3817. (e) Ikariya, T.; Murata, K.; Noyori, R. *Org. Biomol. Chem.* **2006**, *4*, 393. (f) Zeng, W.; Chen, G.-Y.; Zhou, Y.-G.; Li, Y.-X. *J. Am. Chem. Soc.* **2007**, *129*, 750. (g) Wang, M.; Wang, C.-J.; Lin, Z. *Organometallics* **2012**, *31*, 7870.

DOI: 10.1021/acs.orglett.5b02489
Org. Lett. 2015, 17, 5020−5023