Asymmetric Synthesis of 3-Allyloxindoles and 3-Allenyloxindoles by Scandium(III)-catalyzed Claisen Rearrangement Reactions

Zeng-Wei Lai[1,2], Chuan Liu[1], Hongbin Sun[2]*, and Shu-Li You[1]*

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

[2]*State Key Laboratory of Natural Medicines and Center of Drug Discovery, China Pharmaceutical University, 24 T ongjia Xiang, Nanjing 210009, China.*

* E-mail: slyou@sioc.ac.cn, or hbsun2000@yahoo.com; Tel.: telephone number ((optional)); Fax: (+86) 21-54925087

Received ((will be filled in by the editorial staff)); accepted ((will be filled in by the editorial staff)); published online XXXX, 2013.
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/cjoc.2013xxxxx or from the author. ((Please delete if not appropriate.)).
Dedicated to … on the Occasion of … ((optional))

Scandium-catalyzed asymmetric Claisen rearrangement reactions of 2-allyloxyindoles and 2-propargyloxyindoles provide a novel approach to diverse 3-allyloxindoles and 3-allenyloxindoles in excellent yields (up to 99%) and enantioselectivity (up to 99% ee) under mild reaction conditions. The scandium catalyst was derived from $Sc(OTf)_3$ and Pybox ligand.

Keywords allene, asymmetric catalysis, Pybox, rearrangement, scandium

Introduction

The oxindoles that incorporate a quaternary stereocenter at the C3 position exist widely in natural products[1] and bioactive compounds[2] (Figure 1) which show significant pharmaceutical properties. Therefore, these motifs have attracted considerable attention and have served as key intermediates for the synthesis of indole alkaloids.[3] The catalytic asymmetric construction of a quaternary stereocenter is one of the most challenging and dynamic research fields in modern organic synthesis.[4] Hence, the enantioselective synthesis of 3,3'-disubstituted oxindoles bearing a tetrasubstituted stereogenic center has been the most prevailing synthetic subject in the past few years,[5] and dozens of methods (nucleophilic addition to isatins,[6] direct functionalization of oxindoles,[7] Heck reaction,[8] cyanoamidation,[9] arylation,[10] acyl migration[11]) have been developed to construct different kinds of 3,3'-disubstituted oxindole motifs including all-carbon and heteroatom-containing substituents. Although significant advances have been achieved, there are only two examples of asymmetric synthesis of 3-ester-3-allyloxindoles.[12,13]

In 2006, Trost and Brennan utilized the Pd-catalyzed asymmetric allylic alkylation reaction to yield 3-ester-3-allyloxindoles, however, the substrates required a multi-step synthesis. In 2000, Booker-Milburn, Fedouloff and their coworkers developed a Claisen rearrangement of 2-allyloxyindoles and 2-propargyloxyindoles to synthesize 3-allyloxindoles and 3-allenyloxindoles respectively.[14] In 2008, Kozlowski and coworkers accomplished an asymmetric version with good enantioselectivity employing the $[Pd(^tBu\text{-}Phox)](SbF_6)_2$ complex as Lewis acid catalyst.[13a,b] As a substantial extension of the work, they reported the same reaction using a substoichiometric Cu(II)-Box catalysts, but only moderate enantioselectivities were obtained.[13c] Despite the elegance of Kozlowski's approach, two precious metals (Ag and Pd) are needed and special care (in the dark) should be taken during the preparation of the catalyst. Based on the known Lewis acid mediated

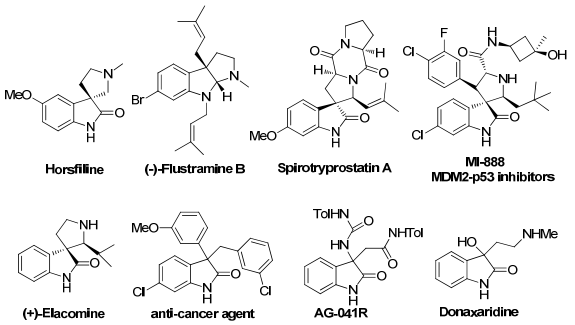


Figure 1. Selected natural products and bioactive compounds (The core structure or synthetic intermediate of these indole alkaloids is the 3,3'-disubstituted oxindole motif).

activation of Claisen rearrangements,[15] we envisaged that $Sc(OTf)_3$-Box complex, prepared easily, might be a suitable catalyst. Herein, we report a highly enantioselective synthesis of 3-allyl oxindoles and 3-allenyl oxindoles *via* scandium-catalyzed Claisen rearrangement reactions of 2-allyloxyindoles and

2-propargyloxyindoles, respectively.

Experimental

General Procedure for Asymmetric Rearrangement Reaction of Allyloxy- and Propargyloxy Indoles:

To a flame-dried Schlenk tube were added 4Å MS (200 mg), $Sc(OTf)_3$ (22.1 mg, 0.045 mmol), **L7** (19.5 mg, 0.0495 mmol) and DCE (2 mL). After stirring the suspension at rt for 1 h, a solution of **1a** (36.8 mg, 0.15 mmol) in DCE (1 mL) was added. The mixture was stirred at rt for 12 h prior to quenching with saturated $NaHCO_3$ (5 mL) and extracting with EtOAc (3 x 10 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (PE/EtOAc=30:1) to afford **2a** as a white solid (33.9 mg, 92% yield).

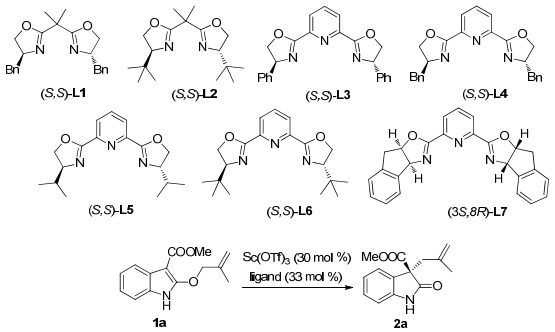
General Procedure for Asymmetric Rearrangement Reaction of Propargyloxy Indoles:

To a flame-dried Schlenk tube were added 4Å MS (200 mg), $Sc(OTf)_3$ (3.69 mg, 0.0075 mmol), **L7** (3.24 mg, 0.008 mmol) and DCE (2 mL). After stirring the suspension at rt for 1 h, a solution of **3g** (45.8 mg, 0.15 mmol) in DCE (1 mL) was added. The mixture was stirred at rt for 60 min prior to quenching with saturated $NaHCO_3$ (5 mL) and extracting with EtOAc (3 x 10 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (PE/ EtOAc =30:1) to **4g** as a white solid (43.9 mg, 96% yield).

Results and Discussion

At the outset, we utilized the well-developed Sc-complex including $Sc(OTf)_3$ and the Box ligand as catalyst[16] and chose **1a** as a substrate to investigate the reaction conditions (Table 1). In the presence of 30 mol % $Sc(OTf)_3$, 33 mol % **L1** and 4 Å molecular sieves (MS) in DCE at room temperature, the reaction proceeded smoothly to afford the desired rearrangement product **2a** in 50% yield within 48 hours but with no enantioselective control (entry 1, Table 1). To improve the enantioselectivity of the reaction, various chiral ligands were tested. As illustrated in Table 1, ligands **L2** and **L6** could be used to promote the reaction with moderate conversions, but with poor enantioselective control. With ligands **L3**, **L4** and **L5**, the reaction occurred smoothly with moderate enantioselectivity (13-47% ee, entries 3-5, Table 1). To our great delight, when inda-pybox (**L7**) was employed, the reaction gave the best enantioselectivity (86% ee, entry 7, Table 1). With **L7** as the optimal ligand, we examined molecular sieves as the additive and found that 4 Å MS was the best (entries 7-9, Table 1). Next, various solvents were used, and DCE gave the best result (entries 10-12, Table 1). Varying the reaction temperature to 0 °C and 50 °C led to decreased yields and enantioselectivity (entries 13-14, Table 1). Lowering the catalyst loading led to a decline in both yield and enantioselectivity (51% yield, 80% ee, entry 15, Table 1). Interestingly, we found that substrate concentration could also affect the reactivity and enantioselectivity significantly (entries 16-18, Table 1). Finally, the best conditions were obtained as the following: **1a** in DCE (0.05 M), 30 mol % of $Sc(OTf)_3$, 33 mol % of **L7**, 200 mg 4Å MS at rt. Under the optimization conditions, product **2a** was obtained in 92% yield and 91% ee (entry 17, Table 1). The absolute configuration of the product was assigned as (*R*) by comparing the sign of the optical rotation with that reported in the literature. [13a]

Table 1 Optimization of the reaction conditions.[a]



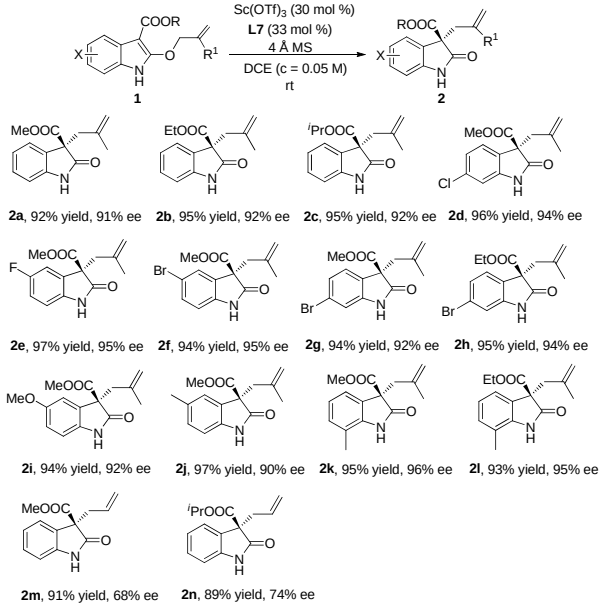
entry	ligand	additive	temp (°C)	time (h)	sol. con.(M)	yield (%)[b]	ee (%)[c]
1	**L1**	4Å MS	rt	48	DCE 0.017	50	0
2	**L2**	4Å MS	rt	48	DCE 0.017	52	2
3	**L3**	4Å MS	rt	15	DCE 0.017	85	47
4	**L4**	4Å MS	rt	48	DCE 0.017	51	31
5	**L5**	4Å MS	rt	48	DCE 0.017	50	13
6	**L6**	4Å MS	rt	48	DCE 0.017	57	2
7	**L7**	4Å MS	rt	24	DCE 0.017	78	86
8	**L7**	3Å MS	rt	24	DCE 0.017	75	79
9	**L7**	5Å MS	rt	24	DCE 0.017	73	77
10	**L7**	4Å MS	rt	14	DCM 0.017	70	76
11	**L7**	4Å MS	rt	48	toluene 0.017	25	31
12	**L7**	4Å MS	rt	24	$CHCl_3$ 0.017	60	33
13	**L7**	4Å MS	50	16	DCE 0.017	80	60
14	**L7**	4Å MS	0	48	DCE 0.017	15	82
15[d]	**L7**	4Å MS	rt	24	DCE 0.017	51	80
16	**L7**	4Å MS	rt	24	DCE 0.033	85	89
17	**L7**	**4ÅMS**	**rt**	**10**	**DCE 0.05**	**92**	**91**
18	**L7**	4 Å MS	rt	24	DCE 0.067	71	85

[a] Reagents and conditions: 0.15 mmol **1a**, 30 mol % $Sc(OTf)_3$, 33 mol % ligand, 200 mg additive. [b] Isolated yield. [c] Determined by HPLC analysis. [d] With 20 mol % $Sc(OTf)_3$ and 22 mol % **L7**.

Under the above optimized reaction conditions, the substrate scope was explored to examine the generality of the rearrangement process. As summarized in Scheme 1, the method was general for different kinds of 2-allyloxyindoles (89-97% yield, 68-96% ee). Substrates bearing various substituents on the different positions of the indole core (5-F, 5-Br, 5-MeO, 5-Me, 6-Cl, 6-Br, 7-Me), regardless of their electronic nature,

were well tolerated, providing the corresponding rearrangement products in excellent yields and ee values (93-97% yield, 90-96% ee). With respect to the C3 ester group, excellent enantioselectivities were obtained regardless of the size of the ester (methyl, ethyl and isopropyl ester). Notably, enantioselectivities were decreased when the methyl group at the allyl C2' position was replaced with an H atom (**2m** and **2n**, 68% ee and 74% ee, respectively).

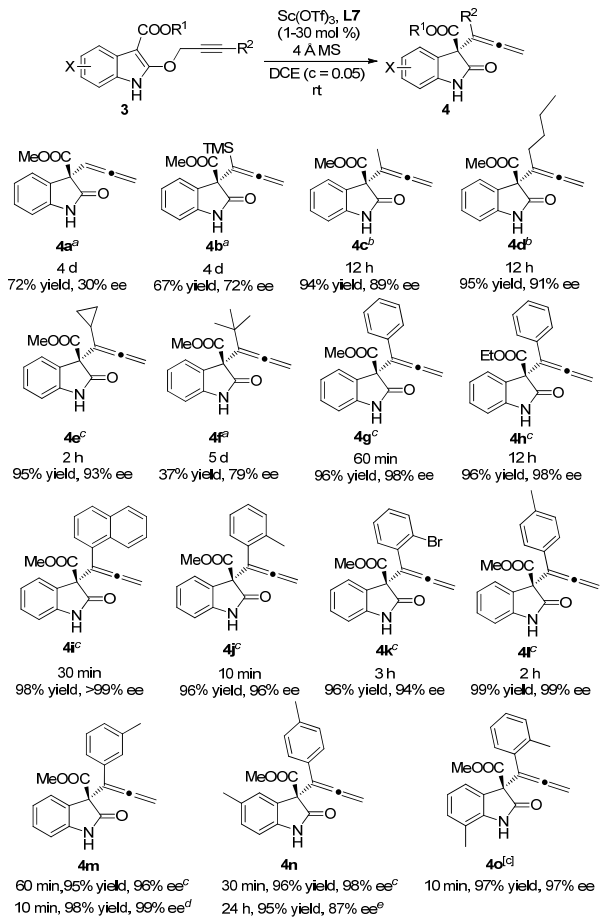
Scheme 1. Substrate scope for asymmetric rearrangement of allyloxyindoles. [a]



[a] All reactions were performed on a 0.15 mmol scale of **1** with $Sc(OTf)_3$ (0.045 mmol), **L7** (0.0495 mmol), 4 Å MS (200 mg), 3 mL DCE (0.05 M) at room temperature for 12 h. The yields are those of the isolated products and the ee values were determined by HPLC analysis.

Allenes have been demonstrated as extremely important intermediates in organic synthesis.[17,18] To further broaden the application of the catalytic system, 2-propargyloxyindole substrates were also tested to afford the corresponding 3-allenyloxindole products (Scheme 2). Under the above reaction conditions, the substrates with H- and TMS-substituted alkyne displayed low reactivity. However, moderate conversions and ee values were obtained even after several days at 40 °C (**4a**, **4b**, 67-72% yield, 30-72% ee). In general, the enantioselectivity and reactivity steadily increased as the size of the alkyl groups at R^2 increased (**4c**-**4e**, 89% ee to 93% ee). However, the substrate bearing a *t*-Bu substituent resulted in a slightly lower enantioselectivity (**4f**, 79% ee). To be noted, substrate (**3e**) with the cyclopropyl substituent displayed the best reactivity, along with rapid conversion (2 h) under low catalyst loading (from 30 mol % to 5 mol %). For the aryl-substituted alkynes, with methyl or bromide group at the different positions of the indole core or phenyl ring were well tolerated. In all cases, the reactions proceeded rapidly to afford 3-allenyloxindole products in excellent yields and enantioselectivity (95-99% yield, 94-99% ee) within 10 min to 12 h. It is worthy mentioned that the catalyst loading could be reduced to 5 mol% from the original 30 mol%. Particularly, the rearrangement reaction of substrate **4n** afforded the desired product in 95% yield and 87% ee even with only 1 mol% catalyst.

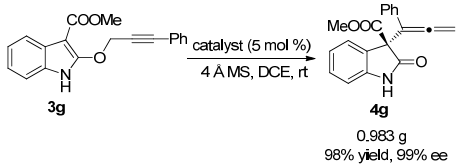
Scheme 2. Substrate scope for asymmetric rearrangement of propargyloxy-substituted indoles. [a]



[a] All reactions were performed on a 0.15 mmol scale of **3**, 4 Å MS (200 mg), 3 mL DCE (0.05 M). [a] 30 mol % $Sc(OTf)_3$, 33 mol % **L7**, 40 °C. [b] 30 mol % $Sc(OTf)_3$, 33 mol % **L7**, rt. [c] 5 mol % $Sc(OTf)_3$, 5.5 mol % **L7**, rt. [d] 20 mol % $Sc(OTf)_3$, 22 mol % **L7**, rt. [e] 1 mol % $Sc(OTf)_3$, 1.1 mol % **L7**, rt.

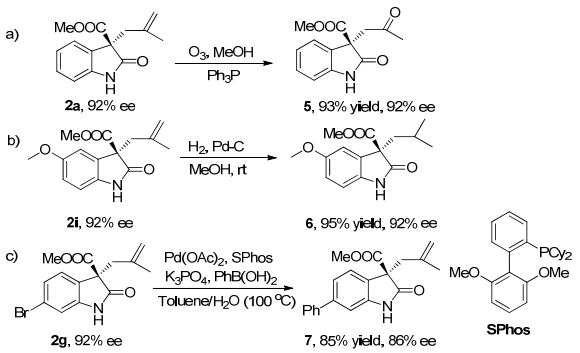
To evaluate the practicality of the catalytic process, a gram-scale reaction was carried out. As shown in Scheme 3, product **4g** could be obtained in 98% yield and 99% ee.

Scheme 3. A gram-scale synthesis of 4g.



Several transformations were carried out to demonstrate the utility of the 3-allyloxindoles products. For example, oxidative cleavage of the double bond of **2a** with ozone afforded **5**, furnishing a carbonyl functional group (Scheme 4, a). The enantioenriched product **2i** was converted into **6** after Pd/C mediated hydrogenation reaction (Scheme 4, b). The bromo-containing product **2g** underwent the Suzuki coupling reaction with $PhB(OH)_2$ in the presence of 5 mol % $Pd(OAc)_2$, 10 mol % SPhos and 2 equiv of K_3PO_4 (Scheme 4, c).

Scheme 4. Transformation of the rearrangement products.



Conclusions

In conclusion, an efficient enantioselective synthesis of 3-allyloxindole and 3-allenyloxindole *via* scandium-catalyzed Claisen rearrangement of 2-allyloxyindole and 2-propargyloxyindole derivatives, respectively, has been developed. The notable features of these reactions include simple operational procedure, mild reaction conditions, high reactivity and enantioselectivity, and broad functional group compatibility. Moreover, the enantioenriched rearrangement products can be used as versatile precursors to construct useful chiral building blocks. Further application of the products obtained here is underway in our laboratory.

Acknowledgement ((optional))

We thank the National Key R&D Program of China (2016YFA0202900), National Basic Research Program of China (2015CB856600), the NSFC (21332009, 21421091), Program of Shanghai Subject Chief Scientist (16XD1404300), and the CAS (XDB20000000, QYZDY-SSW-SLH012) for generous financial support.

References

[1] For selected natural products: (a) Carle, J. S.; Christophersen, C. *J. Am. Chem. Soc.* **1979**, *101*, 4012. (b) Jossang, A.; Jossang, P.; Hadi, H. A.; Sevenet, T.; Bodo, B. *J. Org. Chem*. **1991**, *56*, 6527. (c) Cui, C.-B.; Kakeya, H.; Osada, H. *Tetrahedron* **1996**, *52*, 12651. (d) Toyota, M.; Ihara, M. *Nat. Prod. Rep*. **1998**, 327. (e) Hibino, S.; Choshi, T. *Nat. Prod. Rep*. **2001**, *18*, 66. (f) Kato, H.; Yoshida, T.; Tokue, T.; Nojiri, Y.; Hirota, H.; Ohta, T.; Williams, R. M.; Tsukamoto, S. *Angew. Chem., Int. Ed*. **2007**, *46*, 2254.

[2] For selected drug candidates: (a) Bignan, G. C.; Battista, K.; Connolly, P. J.; Orsini, M. J.; Liu, J.; Middleton, S. A.; Reitz, A. B. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 5022. (b) Ding, K.; Lu, Y.; Nikolovska-Coleska, Z.; Qiu, S.; Ding, Y.; Gao, W.; Stuckey, J.; Krajewski, K.; Roller, P. P.; Tomita, Y.; Parrish, D. A.; Deschamps, J. R.; Wang, S. *J. Am. Chem. Soc*, **2005**, *127*, 10130. (c) Ding, K.; Lu, Y.; Nikolovska-Coleska, Z.; Wang, G.; Qiu, S.; Shangary, S.; Gao, W.; Qin, D.; Stuckey, J.; Krajewski, K.; Roller, P. P.; Wang, S. *J. Med. Chem*. **2006**, *49*, 3432. (d) Franz, A. K.; Dreyfuss, P. D.; Schreiber, S. L. *J. Am. Chem. Soc*. **2007**, *129*, 1020. (e) Fensome, A.; Adams, W. R.; Adams, A. L.; Berrodin, T. J.; Cohen, J.; Huselton, C.; Illenberger, A.; Kern, J. C.; Hudak, V. A.; Marella, M. A;. Melenski, E. G.; McComas, C. C.; Mugford, C. A.; Slayden, O. D.; Yudt, M.; Zhang, Z.; Zhang, P.; Zhu, Y.; Winneker, R. C.; Wrobel, J. E. *J. Med. Chem*. **2008**, *51*, 1861. (f) Antonchick, A. P.; Gerding-Reimers, C.; Catarinella, M.; Schürmann, M.; Preut, H.; Ziegler, S.; Rauh, D.; Waldmann, H. *Nat. Chem*. **2010**, *2*, 735. (g) Zhao, Y.; Yu, S.; Sun, W.; Liu, L.; Lu, J.; McEachern, D.; Shargary, S.; Bernard, D.; Li, X.; Zhao, T.; Zou, P.; Sun, D.; Wang. S. *J. Med. Chem*. **2013**, *56*, 5553. (h) 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. (i) Wang, S.; Jiang, Y.; Wu, S.; Dong, G.; Miao, Z.; Zhang, W.; Sheng, C. *Org. Lett*. **2016**, *18*, 1028. (j) Gollner, D.; Rudolph, D.; Arnhof, H.; Bauer, M.; Blake, S.; Boehmelt, G.; Cockroft, X.-L.; Dahmann, G.; Ettmayer, P.; Gerstberger, T.; Oezguer, J. K.; Kessler, D.; Kofink, C.; Rajarter, J.; Rinnenthal, J.; Savchenko, A.; Schnitzer, R.; Weinstabl, H.; Czernilofsky, U. W.; Wunberg, T.; McConnell, D. B. *J. Med. Chem*. **2016**, *59*, 10147.

[3] For reviews, see: (a) Marti, C.; Carreira, E. M. *Eur. J. Org. Chem*. **2003**, 2209. (b) Galliford, C. V.; Scheidt, K. A. *Angew. Chem., Int. Ed*. **2007**, *46*, 8748. (c) Trost, B. M.; Brennan, M. K. *Synthesis*, **2009**, 3003.

[4] For reviews on the catalytic asymmetric construction of all-carbon quaternary centers, see: (a) Fuji, K. *Chem. Rev*. **1993**, *93*, 2037. (b) Corey, E. J.; Guzman-Perez, A. *Angew. Chem., Int. Ed*. **1998**, *37*, 388. (c) Christoffers, J.; Mann, A.; *Angew. Chem., Int. Ed*. **2001**, *40*, 4591. (d) Denissova, I.; Barriault, L. *Tetrahedron* **2003**, *59*, 10105. (e) Trost, B. M.; Jiang, C. *Synthesis* **2006**, 369. (f) Mohr, J. T.; Stoltz, B. M. *Chem. Asian J.* **2007**, *2*, 1476. (g) Hawner, C.; Alexakis, A. *Chem. Commun*. **2010**, *46*, 7295. (h) Das, J. P.; Marek, I. *Chem. Commun*. **2011**, *47*, 4593. (i) Shimizu, M. *Angew. Chem., Int. Ed*. **2011,** *50*, 5998. (j) Wang, B.; Tu, Y. Q. *Acc. Chem. Res*. **2011**, *44*, 1207.

[5] For reviews, see: (a) Zhou, F.; Liu, Y.-L.; Zhou, J. *Adv. Synth. Catal*. **2010**, *352*, 1381. (b) Shen, K.; Liu, X.; Lin, L.; Feng, X. *Chem. Sci*. **2012**, *3*, 327. (c) Ball-Jones, N. R.; Badillo, J. J.; Franz, A. K. *Org. Biomol. Chem*. **2012**, *10*, 5165. (d) Dalpozzo, R.; Bartolib, G.; Bencivenni, G. *Chem. Soc. Rev*. **2012**, *41*, 7247. (e) Cheng, D.; Ishihara, Y.; Tan, B.; Barbas, C. F. ш. *ACS Catal.* **2014**, *4*, 743.

[6] For selected recent examples, see: (a) Chauhan, P.; Chimni, S. S. *Chem. Eur. J*. **2010**, *16*, 7709. (b) Hanhan, N. V.; Sahin, A. H.; Chang, T. W.; Fettinger J. C.; Franz, A. K. *Angew. Chem., Int. Ed*. **2010**, *49*, 744. (c) Gutierrez, E. G.; Wong, G. J.; Sahin, A. H.; Franz, A. K. *Org. Lett*. **2011**, *13*, 5754. (D) Cao, Z.-Y.; Zhang, Y.; Ji, C.-B.; Zhou, J. *Org. Lett*. **2011**, *13*, 6398. (d) Hanhan, N. V.; Tang, Y. C.; Tran, N. T.; Franz, A. K. *Org. Lett*. **2012**, *14*, 2218. (e) Kuang, Y.; Lu, Y.; Tang, Y.; Liu, X.; Lin, L. Feng, X. *Org. Lett*. **2014**, *16*, 4244. (f) Zhuang, Y.; He, Y.; Zhou, Z.; Xia, W.; Cheng, C.; Wang, M.; Chen, B. Zhou, Z.; Pang, J.; Qiu, L. *J. Org. Chem*. **2015**, *80*, 6968. (g) Xu, N.; Gu, D.-W.; Zi, J.; Wu, X.-Y.; Guo, X.-X. *Org. Lett*. **2016**, *18*, 2439.

[7] (a) Han, Y.-Y.; Wu, Z.-J.; Chen, W.-B.; Du, X.-L.; Zhang, X.-M.; Yuan, W.-C. *Org. Lett*. **2011**, *13*, 5064. (b) Li, J.; Cai, Y.; Chen, W.; Liu, X.; Lin L.; Feng, X. *J. Org. Chem*. **2012**, *77*, 9148. (c) Yang, Y.; Moinodeen, F.; Chin, W.; Ma, T.; Jiang, Z.; Tan, C. H. *Org. Lett*. **2012**, *14*, 4762. (d) Guo, J.; Dong, S.; Zhang, Y.; Kuang, Y.; Liu, X.; Lin, L.; Feng, X. *Angew. Chem., Int. Ed*. **2013**, *52*, 10245. (e) Dou, X.; Zhou, B.; Yao, W.; Zhong, F.; Jiang, C.; Lu, Y. *Org. Lett*. **2013**, *19*, 4920. (f) Zhong, F.; Dou, X.; Han, X.; Yao,

W.; Zhu, Q.; Meng, Y.; Lu, Y. *Angew. Chem., Int. Ed*. **2013**, *52*, 943. (g) Wang, Z.; Zhang, Z.; Yao, Q.; Liu, X.; Cai, Y.; Lin, L.; Feng, X. *Chem. Eur. J*. **2013**, *19*, 8591. (h) Zhang, H.; Hong, L.; Kang, H.; Wang, R. *J. Am. Chem. Soc*. **2013**, *135*, 14098. (i) Zhou, P.; Cai, Y.; Lin, L.; Lian, X.; Xia, Y.; Liu, X.; Feng, X. *Adv. Synth. Catal*. **2015**, *357*, 912. (j) Wang, Y.-M.; Zhang, H.-H.; Li, C.; Fan, T.; Shi, F. *Chem. Commun*. **2016**, *52*, 1804. (k) Yamamoto, K.; Qureshi, Z.; Tsoung, J.; Pisella, G.; Lautens, M. *Org. Lett*. **2016**, 18, 4954. (l) Chen, J.; Wen, X.; Wang, Y.; Du, F.; Cai, L.; Peng, Y. *Org. Lett*. **2016**, *18*, 4336. (m) Zhu, L.; Chen, Q.; Shen, D.; Zhang, W.; Shen, C.; Zeng, X.; Zhong, G. *Org. Lett*. **2016**, *18*, 2387. (n) Zhao, K.; Zhi, Y.; Wang, A.; Enders, D. *ACS Catal*. **2016**, *6*, 657. (o) Jumde, R. P.; Mandoli, A. *ACS Catal*. **2016**, *6*, 4281. (p) Guo, J.; Liu, Y.; Li, X.; Liu, X.; Lin, L.; Feng, X. *Chem. Sci*. **2016**, *7*, 2717. (q) Wang, L.; Li, S.; Blümel, M.; Philipps, A.; Wang, A.; Puttreddy, R.; Rissanen, K.; Enders, D. *Angew. Chem., Int. Ed.* **2016**, *55,* 11110. (r) Zhao, K.; Zhi, Y.; Shu, T.; Valkonen, A.; Rissanen, K.; Enders, D. *Angew. Chem., Int. Ed.* **2016**, *55,* 12104. (s) Uraguchi, D.; Torii, M.; Ooi, T. *ACS Catal*. **2017**, *7*, 2765. (t) Zhu, G.; Wei, Q.; Chen, H.; Zhang, Y.; Shen, W.; Qu, J.; Wang, B. *Org. Lett*. **2017**, *19*, 1862. (u) Guo, W.; Liu, Y.; Li, C. *Org. Lett*. **2017**, *19*, 1044. (v) Cheng, G.; Lu, X.; Ge, L.; Chen, J.; Gao, W.; Wu, X.; Zhao, G. *Org. Chem. Front*. **2017**, *4*, 101. (w) Chen, X.-Y.; Chen, K.-Q.; Sun, D.-Q.; Ye, S. *Chem. Sci*. **2017**, *8*, 1936. (x) Zhu, G.; Bao, G.; Li, Y.; Sun, W.; Li, J.; Hong, L.; Wang, R. *Angew. Chem., Int. Ed.* **2017**, *56*, 5332.

[8] For selected examples, see: (a) Ashimori, A.; Matsuura, T.; Overman, L. E.; Poon, D. J. *J. Org. Chem*. **1993**, *58*, 6949. (b) Matsuura, T.; Overman, L. E.; Poon, D. J. *J. Am. Chem. Soc*. **1998**, *120*, 6500. (c) Dounay, A. B.; Hatanaka, K.; Kodanko, J. J.; Oestreich, M.; Overman, L. E.; Pfeifer, L. A.; Weiss, M. M. *J. Am. Chem. Soc.* **2003**, *125*, 6261. (d) Pinto, A.; Jia, Y.; Neuville, L.; Zhu, J. *Chem. Eur. J*. **2007**, *13*, 961. (e) Fan, J.-H.; Wei, W.-T.; Zhou, M.-B.; Song, R.-J.; Li, J.-H. *Angew. Chem. Int., Ed.* **2014**, *53*, 6650. (f) Kong, W.; Wang, Q.; Zhu, J. *Angew. Chem., Int. Ed.* **2016**, *55*, 9714.

[9] (a) Yasui, Y.; Kamisaki, H.; Takemoto, Y. *Org. Lett*. **2008**, *10*, 3303. (b) Reddy, V. J.; Douglas, C. J. *Org. Lett*. **2010**, *12*, 952.

[10] For selected examples, see: (a) Glorius, F.; Altenhoff, G.; Goddard R.; Lehmann, C. *Chem. Commun*. **2002**, 2704. (b) Arao, T.; Kondo, K.; Aoyama, T. *Tetrahedron Lett*. **2006**, *47*, 1417. (c) Kündig, E. P.; Seidel, T. M.; Jia, Y.; Bernardinelli, G. *Angew. Chem., Int. Ed*. **2007**, *46*, 8484. (d) Jia, Y.-X.; Hillgren, J. M.; Watson, E. L.; Marsden, S. P.; Kündig, E. P. *Chem. Commun*. **2008**, 4040. (e) Tomita, D.; Yamatsugu, K.; Kanai, M.; Shibasaki, M.; *J. Am. Chem. Soc*. **2009**, *131*, 6946.

[11] (a) Black, T. H.; Arrivo, S. M.; Schumm, J. S.; Knobeloch, J. M. *J. Chem. Soc. Chem. Commun*. **1986**, 1524. (b) Black, T. H.; Arrivo, S. M.; Schumm, J. S.; Knobeloch, J. M. *J. Org. Chem*. **1987**, *52*, 5425. (c) Hills, I. D.; Fu, G. C. *Angew. Chem., Int. Ed*. **2003**, *42*, 3839. (d) Duffey, T. A.; Shaw, S. A.; Vedejs, E. *J. Am. Chem. Soc*. **2009**, *131*, 14.

[12] Trost, B. M.; Brennan, M. K. *Org. Lett*. **2006**, *8*, 2027.

[13] (a) Linton, E. C.; Kozlowski, M. C. *J. Am. Chem. Soc*. **2008**, *130*, 16162. (b) Cao, T.; Deitch, J.; Linton, E. C.; Kozlowski, M. C. *Angew. Chem., Int. Ed*. **2012**, *51*, 2448. (c) Cao, T.; Linton, E. C.; Deitch, J.; Berritt, S.; Kozlowski, M. C. *J. Org. Chem*. **2012,** *77,* 11034.

[14] Booker-Milburn, K. I.; Fedouloff, M.; Paknoham, S. J.; Strachan, J. B.; Melville, J. L.; Voyle, M. *Tetrahedron Lett*. **2000**, *41*, 4657.

[15] (a) Maruoka, K.; Banno, H.; Yamamoto, H. *J. Am. Chem. Soc*. **1990**, *112*, 316. (b) Trost, B. M.; Schroeder, G. M. *J. Am. Chem. Soc*. **2000**, *122*, 3785. (c) Abraam, L.; Czerwonka, R.; Hiersemann, M. *Angew. Chem., Int. Ed*. **2001**, *40*, 4700. (d) Kaden, S.; Hiersemann, M. *Synlett* **2002**, 1999. (e) Abraham, L.; Körner, M.; Hiersemann, M. *Tetrahedron Lett*. **2004**, *45*, 3647. (f) Marié, J.-C.; Xiong, Y.; Min, G. K.; Yeager, A. R.; Taniguchi, T.; Berova, N.; Schaus, S. E.; Jr, J. A. P. *J. Org. Chem*. **2010**, *75*, 4584. (g) Jaschinski, T.; Hiersemann, M. *Org. Lett*. **2012**, *14*, 4114. (h) Becker, J.; Butt, L.; Kiedrowski, V.; Mischler, E.; Quentin, F.; Hiersemann, M. *J. Org. Chem*. **2014**, *79*, 3040.

[16] For selected examples using Sc(III)-Box in asymmetric catalysis, see: (a) Liang, G.; Trauner, D. *J. Am. Chem. Soc*. **2004**, *126*, 9544. (b) Evans, D. A.; Fandrick, K. R.; Song, H.-J.; Scheidt, K. A.; Xu, R. *J. Am. Chem. Soc*. **2007**, *129*, 10029. (c) Zhao, Y.-J.; Li, B.; Tan, L.-J. S.; Shen, Z.-L.; Loh, T.-P. *J. Am. Chem. Soc*. **2010**, *132*, 10242.

[17] For selected reviews, see: (a) Hoffmann-Röder, A.; Krause, N. *Angew. Chem., Int. Ed*. **2004**, *43*, 1196. (b) Zimmer, R.; Dinesh, C.; Nandanan, E.; Khan, F. *Chem. Rev*. **2000**, *100*, 3067. (c) Ma, S. *Chem. Rev*. **2005**, *105*, 2829. (d) Ma, S. *Acc. Chem. Res.* **2009**, *42*, 1679. (e) Rivera-Fuentes, P.; Diederich, F. *Angew. Chem., Int. Ed*. **2012**, *51*, 2818. (f) Yu, S.; Ma, S. *Chem. Commun*. **2011**, *47*, 5384. (g) Ye, J.; Ma, S. *Org. Chem. Front*. **2014**, *1*, 1210.

[18] For selected recent examples of synthesis of chiral allenes, see: (a) Wang, Y.; Ma, S. *Adv. Synth. Catal*. **2013**, *355*, 741. (b) Wang, Y.; Zhang, W.; Ma, S. *J. Am. Chem. Soc*. **2013**, *135*, 11517. (c) Huang, X.; Xue, C.; Fu, C.; Ma, S. *Org. Chem. Front*. **2015**, *2*, 1040. (d) Kuang, J.; Tang, X.; Ma, S. *Org. Chem. Front*. **2015**, *2*, 470. (e) Wu, S.; Huang, X.; Wu, W.; Li, P.; Fu, C.; Ma, S. *Nature Commun*. **2015**, *6*, 7946. (f) Poh, J.-S.; Makai, S.; Keutz, T.; Tran, D. N.; Battilocchio, C.; Pasau, P.; Ley, S. V. *Angew. Chem., Int. Ed*. **2017**, *56*, 1864.

Entry for the Table of Contents

Page No.

Asymmetric Synthesis of 3-Allyloxindoles and 3-Allenyloxindoles by Scandium(III)-catalyzed Claisen Rearrangement Reactions

Zeng-Wei Lai, Chuan Liu, Hongbin Sun*, and Shu-Li You*