CHEMISTRY
A European Journal

A Journal of
ChemPubSoc Europe

Accepted Article

Title: Palladium(0)-Catalyzed Intermolecular Asymmetric Cascade Dearomatization Reaction of Indoles with Propargyl Carbonate

Authors: Lu Ding, Run-Duo Gao, and Shuli You

To be cited as: *Chem. Eur. J.* 10.1002/chem.201900425

Link to VoR: http://dx.doi.org/10.1002/chem.201900425

Supported by
ACES

WILEY-VCH

10.1002/chem.201900425

WILEY-VCH

Palladium(0)-Catalyzed Intermolecular Asymmetric Cascade Dearomatization Reaction of Indoles with Propargyl Carbonate

Lu Ding,[b] Run-Duo Gao,[a] and Shu-Li You*[a,b,c]

Abstract: An intermolecular asymmetric cascade dearomatization reaction of indole derivatives with propargyl carbonate was developed. The challenges on the chemoselectivity between carbon nucleophile and nitrogen nucleophile, and the enantioselective control during the formation of an all-carbon quaternary stereogenic center were well addressed by a Pd catalytic system derived from the Feringa ligand. A series of enantioenriched multiple substituted fused indolenines were provided in good yields (71-86%) with excellent enantioselectivity (91-96% ee) and chemoselectivity (**3**/**4** >19:1 in most cases).

Fused indolenines are important structural cores of natural products and frequently appear in biologically active molecules (Figure 1).[1] Accordingly, extensive efforts have been devoted to develop efficient methods for the construction of these scaffolds in a highly chemo- and enantio-selective manner. In this regard, the recently emerging catalytic asymmetric dearomatization (CADA) reactions provide a large array of methods allowing efficient accesses to fused indolenines from readily available indole derivatives.[2] Notably, transition-metal-catalyzed allylic dearomatization reactions of indoles have witnessed significant progresses in the past decade.[3,4,5]

Recently, we realized the construction of fused indolenine skeletons in a cascade fashion.[6] In 2014, the Rawal group and we independently reported an intermolecular cascade dearomatization reaction of indole-based bisnucleophiles with propargyl carbonate, leading to a series of spiroindolenines and spiroindolines. Moderate enantioselectivity (≤ 77% ee) was achieved for limited substrates (Scheme 1, eq 1).[6a,7,8] Rawal and coworkers found that the indole N-H moiety could participate in the cyclization process when the nucleophilic side chain was decorated at the C2 position of the C3 methyl substituted indole (Scheme 1, eq 2).[7,9] Herein, we report a chemo- and enantioselective synthesis of multi substituted fused indolenines by Pd-catalyzed cascade dearomatization of indoles bearing a nucleophile at the C2 position with propargyl carbonate (Scheme 1, eq 3).

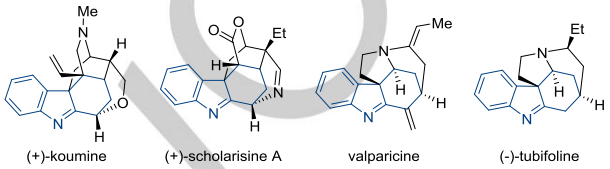
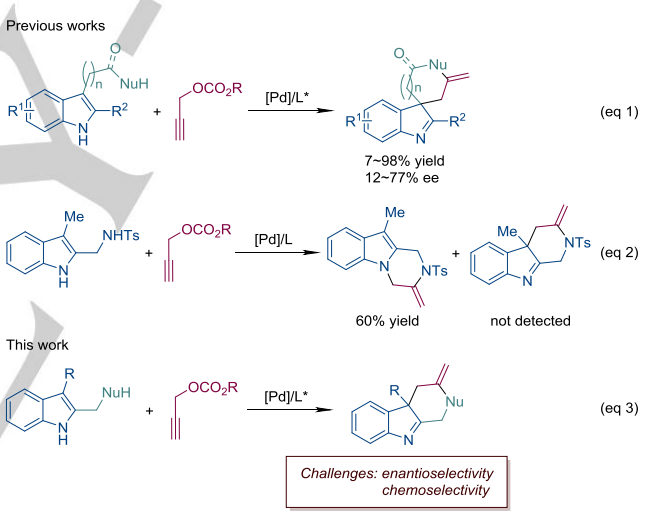


Figure 1. Selected Natural Products Containing Multiple Substituted Fused Indolenine Scaffolds.



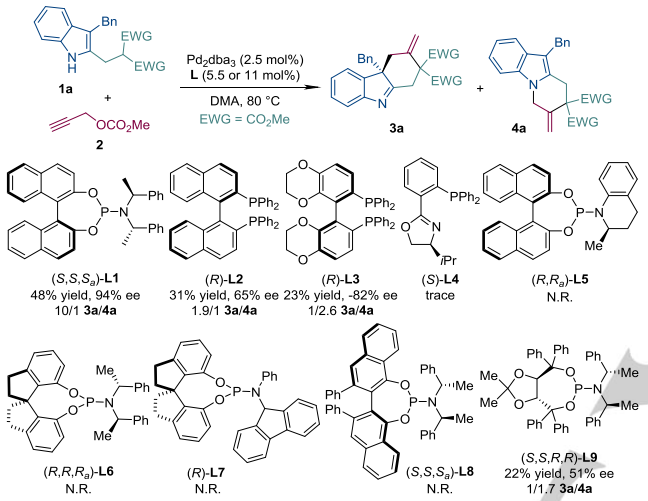
Scheme 1. Palladium-Catalyzed Intermolecular Cascade Reaction between Indole Derivatives and Propargyl Carbonate.

We began our studies by examining the reaction of dimethyl 2-((3-benzyl-1*H*-indol-2-yl)methyl)malonate (**1a**) with methyl prop-2-yn-1-yl carbonate (**2**) in DMA in the presence of Pd catalyst derived from Pd_2dba_3. Firstly, several commercially available chiral phosphorus ligands were tested (Scheme 2). The desired product **3a** was obtained in moderate yields when Feringa ligand (*S,S,S*$_a$)-**L1**, BINAP (*R*)-**L2**, or Synphos (*R*)-**L3** were used. However, Pd complex derived from PHOX ligand (*S*)-**L4** could hardly promote this reaction. It is worth noting that the reaction with **L1** led to **3a** in excellent enantioselectivity and good chemoselectivity (94% ee, 10/1 **3a**/**4a**). Encouraged by these results, phosphoramidite ligands **L5**-**L9** were investigated, however, no better results were obtained. Next, further optimization of the reaction conditions was carried out using **L1** (Table 1). Reactions in varied solvents such as DMF, DCM and THF afforded comparable yields and enantioselectivity albeit with lower **3a**/**4a** ratios (entries 2-4), while MeOH and PhMe led to almost no reaction

[a] Dr. R.-D. Gao, Prof. Dr. S.-L. You
State Key Laboratory of Organometallic Chemistry
Shanghai Institute of Organic Chemistry
University of Chinese Academy of Sciences
Chinese Academy of Sciences
345 Lingling Lu, Shanghai 200032 (China)
E-mail: slyou@sioc.ac.cn
Homepage: http://shuliyou.sioc.ac.cn/
[b] L. Ding, Prof. Dr. S.-L. You
School of Physical Science and Technology, ShanghaiTech University, 100 Haike Road, Shanghai 201210 (China)
[c] Prof. Dr. S.-L. You
Collaborative Innovation Center of Chemical Science and Engineering, Tianjin 300072 (China)

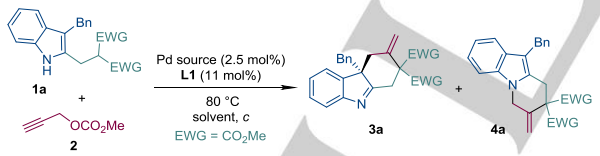
Supporting information for this article is given via a link at the end of the document.

(entries 5-6). Further evaluation of the concentration (entries 7-11) of **1a** revealed that *c* = 0.2 mol/L was optimal in terms of yield (entry 8). $Pd_2(4\text{-OMe-dba})_3$ was a better palladium source than Pd_2dba_3 and $[Pd(allyl)Cl]_2$ (entries 12-13).[10] Furthermore, some additives were tested. To our delight, both of the yield and **3a**/**4a** ratio were improved remarkably when 4 Å molecular sieves were used (82% yield, 95% ee, >19/1 **3a**/**4a**, entry 15). Finally, the optimized reaction conditions were established as the following: $Pd_2(4\text{-OMe-dba})_3$ (2.5 mol%), **L1** (11 mol%), 4 Å MS (100 mg) in DMA (1 mL) at 80 °C (entry 15). To be noted, **4a** can not be converted to **3a** under the optimized conditions, suggesting the formation of C-N is likely an irreversible process here.



Scheme 2. Investigation of the ligands. Reaction conditions: **1a** (0.2 mmol), **2** (0.26 mmol), Pd_2dba_3 (0.005 mmol), and **L** (0.011 or 0.022 mmol) in DMA (3.0 mL) at 80 °C. The ratios of **3a**/**4a** were determined by ^{1}H NMR analysis of the crude reaction mixture. The ee values were determined by HPLC analysis.

Table 1. Investigation of the Reaction Conditions[a]

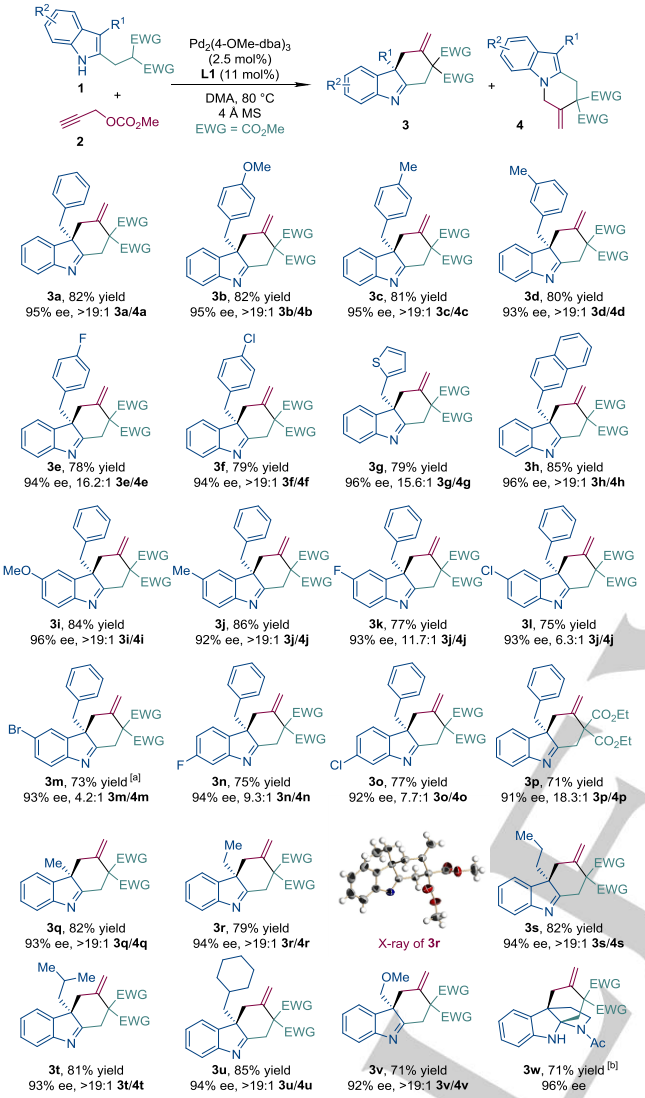


entry	[Pd]	solvent	*c* (mol/L)	**3a**/**4a**[b]	yield (%)[c]	ee (%)[d]
1	Pd_2dba_3	DMA	0.067	10/1	48	94
2	Pd_2dba_3	DMF	0.067	4.8/1	46	93
3	Pd_2dba_3	DCM	0.067	2.6/1	51	94
4	Pd_2dba_3	THF	0.067	1.2/1	47	93
5	Pd_2dba_3	MeOH	0.067		trace	
6	Pd_2dba_3	PhMe	0.067		N.R.	
7	Pd_2dba_3	DMA	0.4	8.1/1	60	94
8	Pd_2dba_3	DMA	0.2	8.6/1	73	92
9	Pd_2dba_3	DMA	0.1	8.3/1	58	92
10	Pd_2dba_3	DMA	0.05	6/1	39	93
11	Pd_2dba_3	DMA	0.033	5.4/1	34	94
12	$[Pd(allyl)Cl]_2$	DMA	0.2		N.R.	
13[e]	$Pd_2(4\text{-OMe-dba})_3$	DMA	0.2	10.4/1	75	94
14[f]	$Pd_2(4\text{-OMe-dba})_3$	DMA	0.2	8.6/1	84	93
15[g]	$Pd_2(4\text{-OMe-dba})_3$	DMA	0.2	>19/1	82	95
16[h]	$Pd_2(4\text{-OMe-dba})_3$	DMA	0.2	11.3/1	73	94
17[i]	$Pd_2(4\text{-OMe-dba})_3$	DMA	0.2		complex	

[a] Reaction conditions: **1a** (0.2 mmol), **2** (0.26 mmol), Pd source (0.005 mmol), and **L1** (0.022 mmol) in solvent at 80 °C. [b] Determined by ^{1}H NMR analysis of the crude reaction mixture. [c] Isolated yield of **3a**. [d] Determined by HPLC analysis. [e] 4-OMe-dba: di(4-methoxybenzylidene)acetone. [f] 3 Å MS (100 mg) was added. [g] 4 Å MS (100 mg) was added. [h] 5 Å MS (100 mg) was added. [i] Cs_2CO_3 (0.2 mmol) was added.

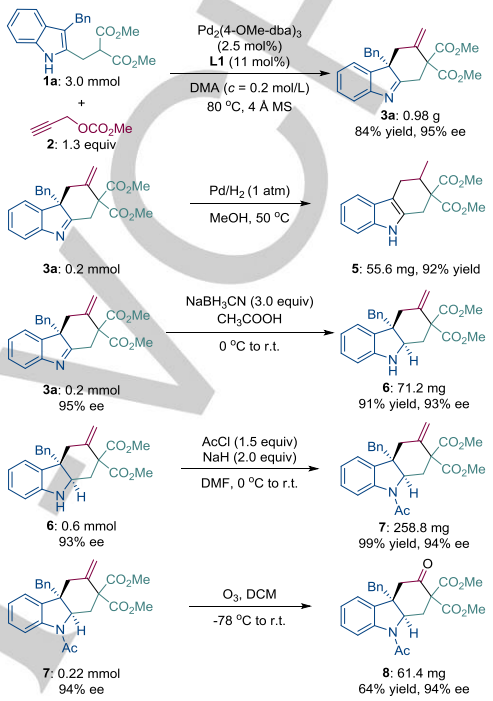
With the optimized conditions in hands, we then explored the substrate scope of this reaction (Scheme 3). Firstly, substrates with different substituents on the benzyl group were examined. Both electron-donating groups (**3b**: 4-OMe, **3c**: 4-Me, **3d**: 3-Me) and electron-withdrawing groups (**3e**: 4-F, **3f**: 4-Cl) were found to be well tolerated. The corresponding products were obtained in good to excellent yields, with excellent chemo- and enantioselectivities (**3b**-**3f**, 78-82% yields, 16.2:1 ~ >19:1 **3**/**4**, 93-95% ee). When the benzyl group was changed to 2-thienyl or 2-naphthyl, the desired products could also be obtained in gratifying results (**3g**: 79% yield, 15.6:1 **3g**/**4g**, 96% ee, **3h**: 85% yield, >19:1 **3h**/**4h**, 96% ee). Next, substrates with different substituents on the indole ring were investigated. The dearomatized products were afforded in excellent yields, chemo- and enantioselectivities when an electron-donating group (**3i**: 5-OMe, **3j**: 5-Me) was installed on the indole ring (**3i**: 84% yield, >19:1 **3i**/**4i**, 96% ee, **3j**: 86% yield, >19:1 **3j**/**4j**, 92% ee). Remarkably, when an electron-withdrawing group was introduced on the indole ring (**3k**: 5-F, **3l**: 5-Cl, **3m**: 5-Br, **3n**: 6-F, **3o**: 6-Cl), good to excellent yields, C/N ratios and excellent enantioselectivity were obtained (**3k-3o**: 73-77% yields, 4.2:1 ~ 11.7:1 **3**/**4**, 92-94% ee). Notably, the formation of allylic amination products was more favorable when stronger electron-withdrawing group was introduced (from 5-F to 5-Br, 6-F to 6-Cl). These are probably due to the increased acidity of the indole N-H and more easily formed N nucleophiles caused by the electron-withdrawing substituent. When EWG group on substrate **1** was changed from methyl carbonate to ethyl carbonate, the desired product could also be obtained in good results (**3p**: 71% yield, 18.3:1 **3p**/**4p**, 91% ee). Furthermore, when an aliphatic group was installed at the C3 position, all substrates could be well tolerated (**3q-3v**: 71-85% yields, >19:1 **3**/**4** in all cases, 92-94% ee). The structure and absolute configuration of product **3r** were confirmed by an X-ray crystallographic analysis of an enantiopure example (See the Support-

ing Information for details). Moreover, substrate **1w** bearing a nucleophilic chain at the C3 position underwent the reaction smoothly, affording the bridged indoline **3w** in 71% yield and 96% ee.

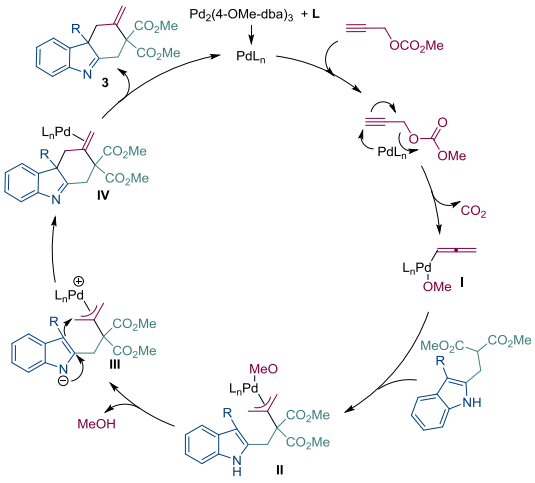


Scheme 3. Substrate Scope. Reaction conditions: **1** (0.2 mmol), **2** (0.26 mmol), $Pd_2(4\text{-OMe-dba})_3$ (0.005 mmol), **L1** (0.022 mmol), and 4 Å MS (100 mg) in DMA (1.0 mL) at 80 °C. The ratios of **3**/**4** were determined by ^1H NMR analysis of the crude reaction mixture. The ee values were determined by HPLC analysis. [a] **4m** was isolated in 14% yield. [b] After **1w** was disappeared, $TsOH\cdot H_2O$ (0.02 mmol) was added at room temperature.

To demonstrate the utility of the current method, a gram-scale reaction and several transformations of the product were carried out (Scheme 4). The asymmetric cascade dearomatization reaction of **1a** with **2** on a 3.0 mmol scale provided product **3a** in 84% yield and 95% ee. Under Pd/C hydrogenation conditions, the exocyclic double bond of product **3a** was reduced and the benzyl group was also removed at the same time likely due to the driving force of aromatization, giving **5** in 92% yield. The imine moiety in **3a** could be reduced by $NaBH_3CN$ in acetic acid to afford **6** in 91% yield. The relative configuration of **6** was determined by NOE analysis (For details, see the Supporting Information). Treatment of **6** with acetyl chloride and NaH produced **7** in quantitative yield. Finally, the double bond in **7** was oxidized with ozone to give ketone **8** in 64% yield.



Scheme 4. Gram-Scale Reaction and Product Transformations



Scheme 5. A Plausible Catalytic Cycle

A proposed catalytic cycle is depicted in Scheme 5. The propargyl carbonate is activated by Pd(0) to give intermediate **I**. Then the nucleophilic side chain attacks intermediate **I** to generate π-allyl palladium species **II**. Upon the deprotonation of indole N-H, the C3 position of indole in **III** attacks π-allyl palladium

moiety to deliver **IV**. Finally, product **3** is provided upon the liberation of palladium catalyst.

In conclusion, we have achieved an efficient palladium(0)-catalyzed intermolecular asymmetric cascade dearomatization reaction of indole derivatives with propargyl carbonate. A series of multiple substituted fused indolenines were obtained in good to excellent yields, excellent chemo- and enantio-selectivities. This method features mild reaction conditions and broad substrate scope. Further studies on the reaction mechanism are currently underway in our laboratory.

Acknowledgements

We thank the National Key R&D Program of China (2016YFA0202900), the National Basic Research Program of China (2015CB856600), NSFC (21572252, 21821002), Program of Shanghai Subject Chief Scientist (16XD1404300), and the CAS (XDB20000000, QYZDY-SSW-SLH012) for generous financial support.

Keywords: allylic • asymmetric catalysis • cascade • dearomatization • indole • palladium

[1] a) S. Takano, K. Ogasawara in The Alkaloids: Chemistry and Pharmacology, Vol. 36, **1989**, Chapter 5, pp. 225-251; b) P. M. Dewick, Medicinal Natural Products: A Biosynthetic Approach, 2nd ed., Wiley, New York, **2002**; c) Modern Alkaloids (Eds.: E. Fattorusso, O. T. Scafati), Wiley-VCH, Weinheim, **2008**.

[2] For recent reviews on catalytic asymmetric dearomatization reactions, see: a) A. R. Pape, K. P. Kaliappan, E. P. Kündig, *Chem. Rev*. **2000**, *100*, 2917; b) S. Quideau, L. Pouységu, D. Deffieux, *Synlett* **2008**, 467; c) L. Pouységu, D. Deffieux, S. Quideau, *Tetrahedron* **2010**, *66*, 2235; d) L. Pouységu, T. Sylla, T. Garnier, L. B. Rojas, J. Charris, D. Deffieux, S. Quideau, *Tetrahedron* **2010**, *66*, 5908; e) S. P. Roche, Jr. J. A. Porco, *Angew. Chem. Int. Ed.* **2011**, *50*, 4068; *Angew. Chem.* **2011**, *123*, 4154; f) C.-X. Zhuo, W. Zhang, S.-L. You, *Angew. Chem. Int. Ed*. **2012**, *51*, 12662; *Angew. Chem.* **2012**, *124*, 12834; g) D.-S. Wang, Q.-A. Chen, S.-M. Lu, Y.-G. Zhou, *Chem. Rev*. **2012**, *112*, 2557; h) C.-X. Zhuo, C. Zheng, S.-L. You, *Acc. Chem. Res*. **2014**, *47*, 2558; i) R. Dalpozzo, *Chem. Soc. Rev.* **2015**, *44*, 742; j) C. Zheng, S.-L. You, *Chem* **2016**, *1*, 830; k) W.-T. Wu, L. Zhang, S.-L. You, *Chem. Soc. Rev.* **2016**, *45*, 1570; l) W.-T. Wu, L. Zhang, S.-L. You, *Acta Chim. Sinica* **2017**, *75*, 419; m) J.-B. Chen, Y.-X. Jia, *Org. Biomol. Chem.* **2017**, *15*, 3550. For a book, see: n) S.-L. You, *Asymmetric Dearomatization Reactions*. Wiley-VCH, Weinheim, **2016**.

[3] For selected transition-metal-catalyzed asymmetric dearomatization reaction of indoles, see: a) L. M. Repka, J. Ni, S. E. Reisman, *J. Am. Chem. Soc*. **2010**, *132*, 14418; b) Y. Lian, H. M. L. Davis, *J. Am. Chem. Soc*. **2010**, *132*, 440; c) J. E. Spangler, H. M. L. Davies, *J. Am. Chem. Soc*. **2013**, *135*, 6802; d) H. Xiong, H. Xu, S. Liao, Z. Xie, Y. Tang, *J. Am. Chem. Soc*. **2013**, *135*, 7851; e) L. Han, C. Liu, W. Zhang, X.-X. Shi, S.-L. You, *Chem. Commun*. **2014**, *50*, 1231; f) W. Shao, H. Li, C. Liu, C.-J. Liu, S.-L. You, *Angew. Chem. Int. Ed*. **2015**, *54*, 7684; *Angew. Chem.* **2015**, *127*, 7794; g) L. Han, W. Zhang, X.-X. Shi, S.-L. You, *Adv. Synth. Catal*. **2015**, *357*, 3064; h) X. Zhao, X. Liu, Q. Xiong, H. Mei, B. Ma, L. Lin, X. Feng, *Chem. Commun*. **2015**, *51*, 16076; i) X. Zhao, X. Liu, H. Mei, J. Guo, L. Lin, X. Feng, *Angew. Chem. Int. Ed*. **2015**, *54*, 4032; *Angew. Chem.* **2015**, *127*, 4104; j) C. Shen, R.-R. Liu, R.-J. Fan, Y.-L. Li, T.-F. Xu, J.-R. Gao, Y.-X. Jia, *J. Am. Chem. Soc*. **2015**, *137*, 4936; k) W. Zi, H. Wu, F. D. Toste, *J. Am. Chem. Soc.* **2015**, *137,* 3225; l) C. Liu, J.-C. Yi, X.-W. Liang, R.-Q. Xu, L.-X. Dai, S.-L. You, *Chem. Eur. J.* **2016**, *22*, 10813; m) C. Liu, J.-C. Yi, Z.-B. Zheng, Y. Tang, L.-X. Dai, S.-L. You, *Angew. Chem. Int. Ed.* **2016**, *55*, 751; *Angew. Chem.* **2016**, *128*, 761; n) W. Shao, S.-L. You, *Chem. Eur. J.* **2017**, *23*, 12489; o) V. Pirovano, M. Borri, G. Abbiati, S. Rizzato, E. Rossi, *Adv. Synth. Catal*. **2017**, *359*, 1912; p) H. Xu, Y.-P. Li, Y. Cai, G.-P. Wang, S.-F. Zhu, Q.-L. Zhou, *J. Am. Chem. Soc.* **2017**, *139*, 7697; q) Z. L. Niemeyer, S. Pindi, D. A. Khrakovsky, C. N. Kuzniewski, C. M. Hong, L. A. Joyce, M. S. Sigman, F. D. Toste, *J. Am. Chem. Soc.* **2017**, *139*, 12943; r) X. Qin, M. W. Y. Lee, J. S. Zhou, *Angew. Chem. Int. Ed.* **2017**, *56*, 12723; *Angew. Chem.* **2017**, *129*, 12897; s) G. Xu, L. Chen, J. Sun, *Org. Lett.* **2018**, *20*, 3408; t) R.-X. Liang, R.-Z. Yang, R.-R. Liu, Y.-X. Jia, *Org. Chem. Front*. **2018**, *5*, 1840; u) Z. Wang, H. Ji, W.-M. He, Y. Xiong, G. Zhang, *Synthesis* **2018**, DOI: 10.1055/s-0037-1609753; v) X. Li, B. Zhou, R.-Z. Yang, F.-M. Yang, R.-X. Liang, R.-R. Liu, Y.-X. Jia, *J. Am. Chem. Soc.* **2018**, *140*, 13945; w) L. Chen, J.-J. Shen, Q. Gao, S. Xu, *Chem. Sci*. **2018**, *9*, 5855; x) G. Xu, L. Chen, J. Sun, *Org. Lett.* **2018**, *20*, 3408.

[4] For selected intermolecular allylic dearomatization reactions of indoles, see: (a) X. Zhang, Z.-P. Yang, C. Liu, S.-L. You, *Chem. Sci*. **2013**, *4*, 3239; b) Y. Liu, H. Du, *Org. Lett*. **2013**, *15*, 740; c) X. Zhang, L. Han, S.-L. You, *Chem. Sci*. **2014**, *5*, 1059; d) J. Ruchti, E. M. Carreira, *J. Am. Chem. Soc*. **2014**, *136*, 16756; e) P. Dhankher, L. Benhamou, T. D. Sheppard, *Chem. Eur. J.* **2014**, *20*, 13375; f) X. Zhang, W.-B. Liu, H.-F. Tu, S.-L. You, *Chem. Sci*. **2015**, *6*, 4525; g) H. Zhang, R.-B. Hu, N. Liu, S.-X. Li, S.-D. Yang, *Org. Lett.* **2016**, *18*, 28; h) S. Gao, Z. Wu, X. Fang, A. Lin, H. Yao, *Org. Lett*. **2016**, *18*, 3906; i) R.-D. Gao, Q.-L. Xu, B. Zhang, Y. Gu, L.-X. Dai, S.-L. You, *Chem. Eur. J*. **2016**, *22*, 11601; j) E. Manoni, A. De Nisi, M. Bandini, *Pure Appl. Chem*. **2016**, *88*, 207; k) S. Panda, J. M. Ready, *J. Am. Chem. Soc*. **2017**, *139*, 6038; l) Y. S. Gee, D. J. Rivinoja, S. M. Wales, M. G. Gardiner, J. H. Ryan, C. J. T. Hyland, *J. Org. Chem.* **2017**, *82*, 13517; m) D. J. Rivinoja, Y. S. Gee, M. G. Gardiner, J. H. Ryan, C. J. T. Hyland, *ACS Catal.* **2017**, *7*, 1053; n) M. Laugeois, J. Ling, C. Férard, V. Michelet, V. Ratovelomanana-Vidal, M. R. Vitale, *Org. Lett*. **2017**, *19*, 2266; o) R.-D. Gao, L. Ding, L.-X. Dai, S.-L. You, *Org. Lett*. **2018**, *20*, 748; p) H.-F. Tu, X. Zhang, C. Zheng, M. Zhu, S.-L. You, *Nature Catal*. **2018**, *1*, 601; q) Q. Cheng, F. Zhang, Y. Cai, Y.-L. Guo, S.-L.You, *Angew. Chem. Int. Ed*. **2018**, *57*, 2134; *Angew. Chem.* **2018**, *130*, 2156; r) J.-Q. Zhang, F. Tong, B.-B. Sun, W.-T. Fan, J.-B. Chen, D. Hu, X.-W. Wang, *J. Org. Chem.* **2018**, *83*, 2882; s) M. Sun, Z.-Q. Zhu, L. Gu, X. Wan, G.-J. Mei, F. Shi, *J. Org. Chem.* **2018**, *83*, 2341; t) J.-J. Suo, W. Liu, J. Du, C.-H. Ding, X.-L. Hou, *Chem. Asian J.* **2018**, *13*, 959; u) X.-W. Liang, Y. Cai, S.-L. You, *Chin. J. Chem.* **2018**, *36*, 925; v) S. Panda, J. M. Ready, *J. Am. Chem. Soc*. **2018**, *140*, 13242.

[5] For selected intramolecular allylic dearomatization reactions of indoles, see: a) Q.-F. Wu, H. He, W.-B. Liu, S.-L. You, *J. Am. Chem. Soc*. **2010**, *132*, 11418; b) Q.-F. Wu, C. Zheng, S.-L. You, *Angew. Chem. Int. Ed.* **2012**, *51*, 1680; *Angew. Chem.* **2012**, *124*, 1712; c) T. Nemoto, Z. Zhao, T. Yokosaka, Y. Suzuki, R. Wu, Y. Hamada, *Angew. Chem. Int. Ed.* **2013**, *52*, 2217; *Angew. Chem.* **2013**, *125*, 2273; d) Q.-L. Xu, L.-X. Dai, S.-L. You, *Chem. Sci.* **2013**, *4*, 97; e) T. D. Montgomery, Y. Zhu, N. Kagawa, V. H. Rawal, *Org. Lett*. **2013**, *15*, 1140; f) X. Zhang, W.-B. Liu, Q.-F. Wu, S.-L. You, *Org. Lett*. **2013**, *15*, 3746; g) J. Chen, M. J. Cook, *Org. Lett*. **2013**, *15*, 1088; h) T. M. Kaiser, J. Yang, *Eur. J. Org. Chem.* **2013**, 3983; i) C.-X. Zhuo, Y. Zhou, Q. Cheng, L. Huang, S.-L. You, *Angew. Chem. Int. Ed.* **2015**, *54*, 14146; *Angew. Chem.* **2015**, *127*, 14352; j) S.-Z. Jiang, X.-Y. Zeng, X. Liang, T. Lei, K. Wei, Y.-R. Yang, *Angew. Chem. Int. Ed*. **2016**, *55*, 4044; *Angew. Chem*. **2016**, *128*, 4112; k) Z.-X. Zhang, S.-C. Chen, L. Jiao, *Angew. Chem. Int. Ed.* **2016**, *55*, 8090; *Angew. Chem.* **2016**, *128*, 8222; l) Q.-F. Wu, C. Zheng, C.-X. Zhuo, S.-L. You, *Chem. Sci.* **2016**, *7*, 4453; m) J. T. R. Liddon, A. K. Clarke, R. J. K. Taylor, W. P. Unsworth, *Org. Lett*. **2016**, *18*, 6328; n) Y. Wang, C. Zheng, S.-L. You, *Angew. Chem. Int. Ed.* **2017**, *56*, 15093; *Angew. Chem*. **2017**, *129*, 15289.

[6] a) R.-D. Gao, C. Liu, L.-X. Dai, W. Zhang, S.-L. You, *Org. Lett*. **2014**, *16*, 3919; b) R.-D. Gao, Q.-L. Xu, L.-X. Dai, S.-L. You, *Org. Biomol. Chem.* **2016**, 8044.

[7] T. D. Montgomery, A. E. Nibbs, Y. Zhu, V. H. Rawal, *Org. Lett*. **2014**, *16*, 3480.

[8] A. E. Nibbs, T. D. Montgomery, Y. Zhu, V. H. Rawal, *J. Org. Chem*. **2015**, *80*, 4928.

[9] For selected examples of the N-functionalization of indoles: a) B. M. Trost, M. Osipov, G. Dong, *J. Am. Chem. Soc.* **2010**, *132*, 15800; b) A. Ueno, Y. Kayaki, T. Ikariya, *Organometallics* **2014**, *33*, 4479; c) J. Lee, J. H. Choi, S. Shin, J.-N. Heo, H. J. Lim, *Synthesis* **2015,** *47*, 3301; d) B. M. Trost, E. Gnanamani, C.-I. Hung, *Angew. Chem. Int. Ed.* **2017**, *56*, 10451; *Angew. Chem.* **2017**, *129*, 10587; e) M. Chen, J. Sun, *Angew. Chem. Int. Ed.* **2017**, *56*, 4583; *Angew. Chem*. **2017**, *129*, 4654.

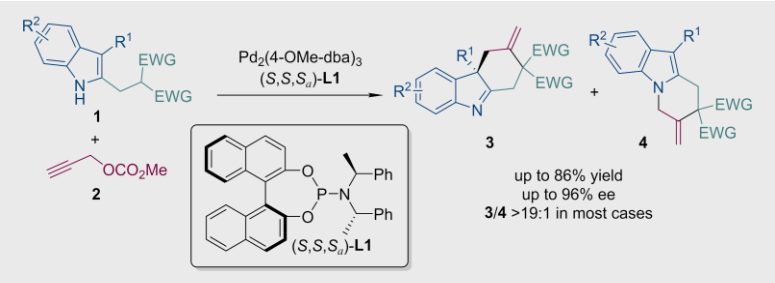
[10] a) C. Amatore, A. Jutand, *Coord. Chem. Rev*. **1998**, *178*, 511; b) I. J. S. Fairlamb, A. R. Kapdi, A. F. Lee, G. P. McGlacken, F. Weissburger, A. H. M. De Vries, L. Schmieder-Van De Vondervoort, *Chem. Eur. J*. **2006**, *12*, 8750; c) A. T. Parsons, M. J. Campbell, J. S. Johnson, *Org. Lett.* **2008**, *10*, 2541.

[11] For details, see the Supporting Information.

10.1002/chem.201900425

WILEY-VCH

COMMUNICATION



*Lu Ding, Run-Duo Gao, and Shu-Li You**

Page No. – Page No.

Palladium(0)-Catalyzed Intermolecular Asymmetric Cascade Dearomatization Reaction of Indoles with Propargyl Carbonate

An intermolecular asymmetric cascade dearomatization reaction of indole derivatives with propargyl carbonate was developed. The challenges on the chemoselectivity between carbon nucleophile and nitrogen nucleophile, and the enantioselective control during the formation of an all-carbon quaternary stereogenic center were well addressed by a Pd catalytic system derived from the Feringa ligand. A series of enantioenriched multiple substituted fused indole-nines were provided in good yields (71-86%) with excellent enantioselectivity (91-96% ee) and chemoselectivity (**3**/**4** >19:1 in most cases).