Advanced Synthesis & Catalysis

DOI: 10.1002/adsc.201401007

Rhodium-Catalyzed Direct C7 Alkynylation of Indolines

Ning Jin,[a] Changduo Pan,[a] Honglin Zhang,[a] Pan Xu,[a] Yixiang Cheng,[a] and Chengjian Zhu[a,b,*]

[a] State Key Laboratory of Coordination Chemistry, School of Chemistry and Chemical Engineering, Nanjing University, Nanjing, 210093, People's Republic of China
E-mail: cjzhu@nju.edu.cn
[b] State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Shanghai, 200032, People's Republic of China

Received: October 23, 2014; Revised: January 26, 2015; Published online: ■■ ■■, 0000

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201401007.

Abstract: An efficient rhodium(III)-catalyzed direct C7 alkynylation of indoline C–H bonds with the alkynylated hypervalent iodine reagents has been developed. This reaction proceeds smoothly under mild conditions over a wide structural scope with high site-selectivity and excellent functional-group tolerance. *N*-Acetyl as well as other *N*-acyls served as effective directing groups (DG). This procedure allows for the synthesis of a variety of 7-alkynyl-substituted indolines in good to excellent yield. More significantly, C7-alkynylated indoles through further transformations have been successfully accessed.

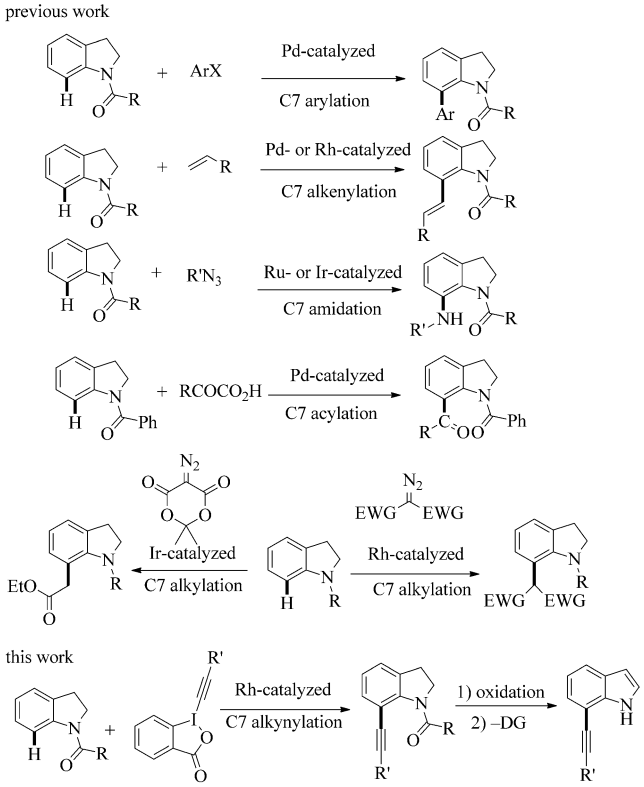
Keywords: alkynylation; C–H activation; indolines; iodine; rhodium

Alkynes are important building blocks in synthetic organic chemistry and material sciences since the alkyne moiety has been recognized as a versatile functional group for facile conversion into a multitude of functionalities or various useful molecules.[1] In this regard, the discovery of novel and reliable methods for the introduction of alkynyl functionality has attracted much attention. Over the past few decades, with the surge in research on C–H activation, rhodium-catalyzed direct functionalization of C–H bonds has emerged as a straightforward and highly efficient tool for the construction of C–E bonds (E = C, N, O, or S).[2] However, rhodium-catalyzed direct C–H bond alkynylation has hung behind. Notably, in 1996, Zhdankin first introduced the alkynylated hypervalent iodine reagent 1-[(triisopropylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (TIPS-EBX).[3] Since then, Waser developed several Au- and Pd-catalyzed direct alkynylations of heterocycles and enolates by using TIPS-EBX under very mild conditions.[4] Very recently, in 2014, Li,[5] Loh,[6] Glorius,[7] and Chang[8] independently reported the rhodium-catalyzed alkynylation of C–H bonds with TIPS-EBX.

The indoline nucleus is a prominent structural motif found in numerous natural products and bioactive compounds.[9] Particularly, C7-substituted indoline scaffolds are found in many pharmaceutical agents.[10] Thus, the direct C–H bond functionalization of indolines at the C7 position through chelation-assisted C–H activation is synthetically attractive but relatively rare. In the past years, considerable efforts have been made to achieve direct C–H bond arylation[11] or alkenylation[12] of indolines at the C7 position (Scheme 1).

Inspired by this, our group focused on the synthesis of indole and indoline derivatives via C–H activation,[13] and recently, we have reported a Ru-catalyzed C7 amidation of indolines with sulfonyl azides.[14] Later, Chang also disclosed an Ir-catalyzed C7 amidation of indolines by using organic azides.[15] Shortly afterwards, Kim developed a facile method for the decarboxylative C7 acylation of indolines with α-oxocarboxylic acids.[16] Most recently, Zhou described C7 alkylation of indolines by Rh and Ir catalysis.[17] However, to the best of our knowledge, the C7 alkynylation of indolines has not been reported. Herein, we described a rhodium-catalyzed direct C7 alkynylation of indolines with the alkynylated hypervalent iodine compounds.

At the outset, we first investigated the reaction of *N*-acetylindoline (**1a**) with TIPS-EBX (**2a**) in the presence of 5 mol% $[RhCp^*Cl_2]_2$ and 20 mol% $AgNTf_2$ in DCE under an Ar atmosphere at 50 °C for 16 h. To our delight, the alkynylation product **3a** was obtained in 82% yield (Table 1, entry 1). Among different solvents screened, DCM turned out to have the best efficiency, giving the alkynylation product **3a** in 85% isolated yield, while THF exhibited negative re-

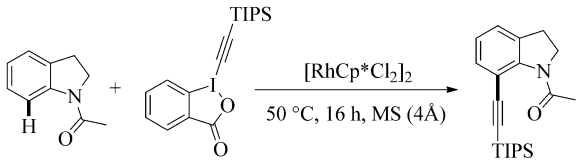


Scheme 1. Direct C–H bond functionalizations of indolines at the C7 position.

sults, and MeCN was ineffective in this reaction (Table 1, entries 2–4). On the other hand, lower amounts of product were formed with $[RuCl_2(p\text{-cymene})]_2$ (Table 1, entry 5). Meanwhile, various additives were also tested, and it was found that $AgSbF_6$, AgOTf and $Zn(OTf)_2$ were also active to provide **3a** selectively, but with lower yields than $AgNTf_2$ (Table 1, entries 7–9). In addition, the additive CsOAc was found to be ineffective in this coupling reaction (Table 1, entry 10). This alkynylation reaction was also sensitive to temperature. Raising the reaction temperature reduced the yield of product **3a** (Table 1, entry 11). Furthermore, screening of the loading of rhodium catalyst and silver salt indicated that 5 mol% $[RhCp^*Cl_2]_2$ and 20 mol% of $AgNTf_2$ were optimal (Table 1, entries 12–14). In controlled experiments, the alkynylation product **3a** was not observed in absence of either $[RhCp^*Cl_2]_2$ or $AgNTf_2$, which implied that a cationic Rh^{III} species was required for this coupling process (Table 1, entries 15 and 16).

With the optimized reaction conditions in hand, we began to examine the substrate scope for this novel protocol. As shown in Table 2, the C7 alkynylation of *N*-acetyl indolines proceeded well to give the desired products in good yields irrespective of various substitution patterns on the aromatic ring (**3a**–**3h**). It should be mentioned that halogen substituted

Table 1. Screening conditions for the Rh-catalyzed alkynylation[a]

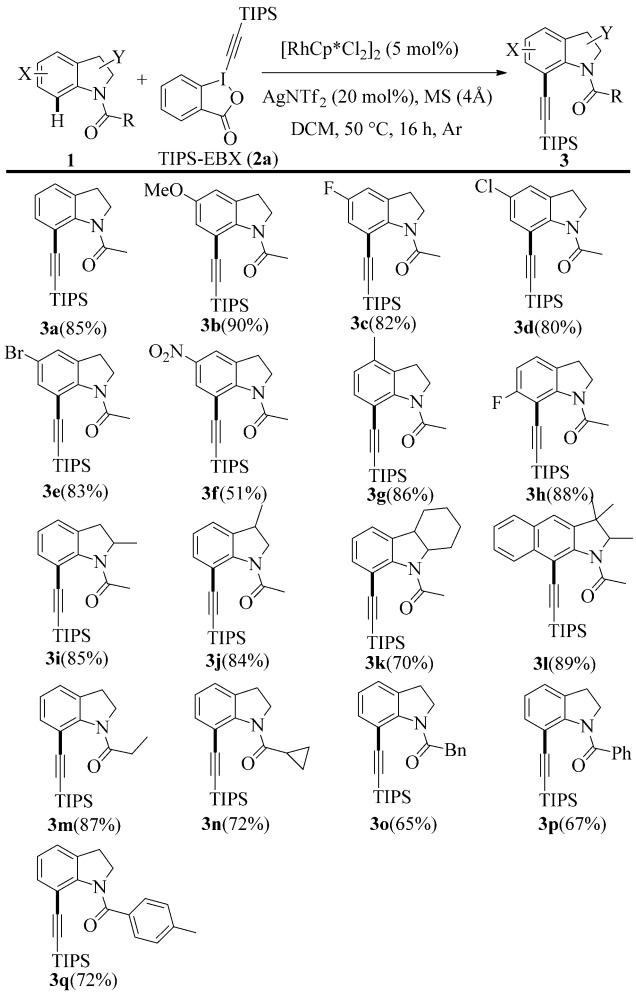


1a TIPS-EBX (**2a**) **3a**

Entry	Catalyst (mol%)	Additive (mol%)	Solvent	T [°C]	Yield [%][b]
1	$[RhCp^*Cl_2]_2$(5)	$AgNTf_2$(20)	DCE	50	82
2	$[RhCp^*Cl_2]_2$ (5)	$AgNTf_2$(20)	THF	50	61
3	$[RhCp^*Cl_2]_2$ (5)	$AgNTf_2$(20)	MeCN	50	trace
4	$[RhCp^*Cl_2]_2$ (5)	$AgNTf_2$(20)	DCM	50	85
5	$[RuCl_2(p\text{-cymene})]_2$ (5)	$AgNTf_2$(20)	DCM	50	59
7	$[RhCp^*Cl_2]_2$ (5)	$AgSbF_6$(20)	DCM	50	80
8	$[RhCp^*Cl_2]_2$ (5)	AgOTf(20)	DCM	50	60
9	$[RhCp^*Cl_2]_2$ (5)	$Zn(OTf)_2$(20)	DCM	50	22
10	$[RhCp^*Cl_2]_2$ (5)	CsOAc(20)	DCM	50	0
11	$[RhCp^*Cl_2]_2$ (5)	$AgNTf_2$(20)	DCM	80	64
12	$[RhCp^*Cl_2]_2$ (2.5)	$AgNTf_2$(10)	DCM	50	65
13	$[RhCp^*Cl_2]_2$(2.5)	$AgNTf_2$(20)	DCM	50	69
14	$[RhCp^*Cl_2]_2$ (5)	$AgNTf_2$(40)	DCM	50	83
15	$[RhCp^*Cl_2]_2$ (0)	$AgNTf_2$(20)	DCM	50	0
16	$[RhCp^*Cl_2]_2$ (5)	$AgNTf_2$(0)	DCM	50	0

[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), $[RhCp^*Cl_2]_2$ (5 mol%), $AgNTf_2$ (20 mol%), 4 Å molecular sieves (100 mg), solvent (0.5 mL), under Ar at 50 °C for 16 h.
[b] Isolated yield.

Table 2. Scope of indolines[a]

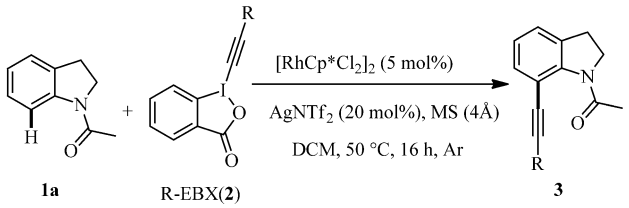


[a] Reaction conditions: **1** (0.1 mmol), **2a** (0.15 mmol), $[RhCp^*Cl_2]_2$ (5 mol%), $AgNTf_2$ (20 mol%), 4 Å molecular sieves (100 mg), solvent (0.5 mL), under Ar at 50 °C for 16 h.

N-acetyl indolines at C5 and C6 position were well-tolerated, and the bromo moiety of **3e** was kept intact in the reaction course, thus providing a handle for further transformations. This reaction also displayed high reactivity with C2- or C3-substituted indolines, affording the corresponding products (**3i–3l**) in high yields. Moreover, different directing groups (DG) have been investigated under the optimal reaction conditions. To our delight, indolines bearing a series of *N*-acyl groups were compatible with the reaction, giving the corresponding products (**3m–3q**) in good yields. However, the present reaction did not proceed when Boc- or Cbz-protecting groups were employed as a directing group.

Next, we further explored the scope of the alkynylated hypervalent iodine. TMS-EBX, TES-EBX, TBMS-EBX, Ph-EBX and ^{t}Bu-EBX were tested using **2a** as the model substrate (Table 3). To our delight, TMS-EBX, TES-EBX and TBMS-EBX were suitable for the alkynylation reaction, albeit the corresponding products were obtained in moderate yields (**3r–3t**). Here the reason is that TIPS-EBX has more steric protection for the stability of product. However, when Ph-EBX and ^{t}Bu-EBX were used, the reaction failed to give the desired product **3u** and **3v.**

Table 3. Scope of the alkynylated hypervalent iodines[a]



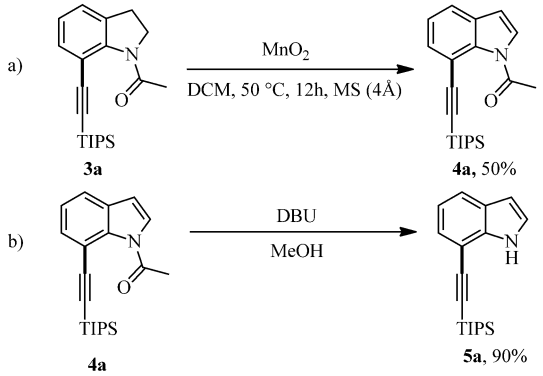
Entry	Product **3**	R	Yield[%][b]
1	**3a**	TIPS	85
2	**3r**	TMS	37
3	**3s**	TES	45
4	**3t**	TBDMS	52
5	**3u**	Ph	Nd
6	**3v**	^{t}Bu	Nd

[a] Reaction conditions: **1a** (0.1 mmol), **2** (0.15 mmol), $[RhCp^*Cl_2]_2$ (5 mol%), $AgNTf_2$ (20 mol%), 4 Å molecular sieves (100 mg), solvent (0.5 mL), under Ar at 50 °C for 16 h.

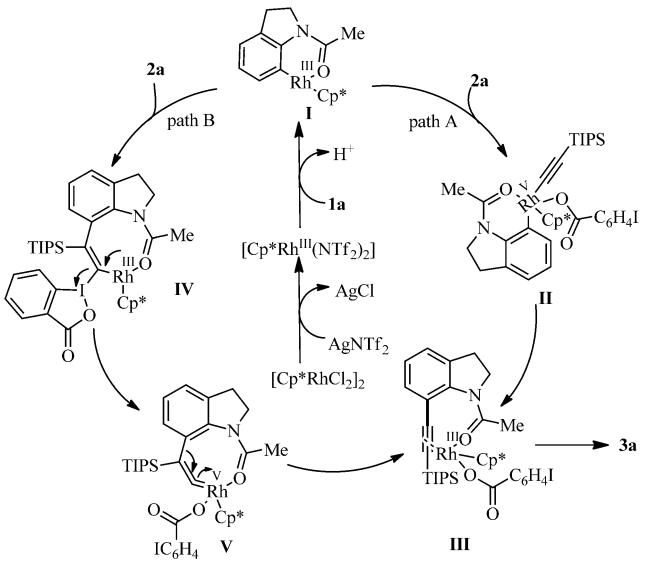
[b] Isolated yield.

Finally, in order to show the further synthetic utility of our products, we provided a method to access C7-alkynyl-substituted indoles (Scheme 2). Dehydrogenation of **3a** was performed well with the MnO_2 oxidant,[18] which gave **4a** in 50% yield. Then, using a well-known method,[19] we were able to remove the directing group of **4a** with DBU, which generated the C7-alkynylated indoles **5a** in 90% yield.

Accordingly, a plausible mechanism for this reaction has been outlined in Scheme 3. Initially, treatment of $[RhCp^*Cl_2]_2$ with $AgNTf_2$ generates the



Scheme 2. Dehydrogenation and removal of the directing group.



Scheme 3. Proposed mechanism.

active cationic Rh^{III} catalyst.[20] This active Rh^{III} catalyst coordinates to the substrate **1a**, which affords the rhodacycle intermediate **I** via a C-H activation. Subsequently, direct oxidative addition of the alkynylated hypervalent iodine reagents **2a** allows generation of the Rh^{V} alkynyl intermediate **II** (Path A).[5] Then, reductive elimination of intermediate **II** delivers the Rh^{III} alkyne intermediate **III**. Alternatively, rhodacyclic intermediate **I** may undergo regioselective migratory insertion into the alkyne unit to generate an alkenyl-rhodacycle **IV** (Path B). The following α-elimination of 2-iodobenzoic acid of **IV** occurs to produce a Rh^{III} vinylidene intermediate **V.** Then, a concerted or stepwise 1,2-aryl migration and elimination allows generation of the same intermediate **III.**[6,7] Finally, alkyne dissociation from **III** furnishes the alkynylated product **3a** together with an active Rh^{III} benzoate catalyst, which may undergo a C–H activation with **1a** to regenerate intermediate **I**.

In conclusion, we have developed the first rhodium-catalyzed direct C7 alkynylation of indoline C–H bonds with the alkynylated hypervalent iodine reagent as the alkynyl source. This present reaction is applicable to a variety of substrates under mild conditions with the features of high site-selectivity and excellent functional-group tolerance. Furthermore, this protocol provides an efficient approach for the synthesis of a range of 7-alkynyl-substituted indolines, which are valuable for further transformations. More importantly, we have successfully disclosed a reliable method to access C7-alkynylated indoles.

Experimental Section

Typical Experimental Procedure for Rh-Catalyzed Alkynylation of Indolines:

Under Ar atmosphere, a mixture of *N*-acetyindoline (0.1 mmol), TIPS-EBX (0.15 mmol), $[RhCp^*Cl_2]_2$ (5 mol%), $AgNTf_2$ (20 mol%), 4 Å molecular sieves (100 mg), and DCM (0.5 mL) was stirred in a sealed tube at 50 °C for 16 h. After cooling to room temperature, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (*n*-hexane/ethyl acetate) on silica gel to give the product.

Procedure for Dehydrogenation of 3a:

A mixture of the product **3a** (34.1 mg, 0.1 mmol), MnO_2 (173.9 mg, 2 mmol), 4 Å molecular sieves (100 mg) in DCM (2 mL) was stirred in a sealed tube at 50 °C for 12 h. After cooling to room temperature, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (*n*-hexane/ethyl acetate) on silica gel to give the product **4a** (17 mg, 50 %).

Procedure for Removal of the Directing Group of 4a:

To a solution of the product **4a** (34.0 mg, 0.1 mmol) in methanol (0.5 mL) was added DBU (30.2 mg, 0.2 mmol), and the mixture was refluxed in a sealed tube for 16 h. After cooling to room temperature, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (*n*-hexane/ethyl acetate) on silica gel to give the product **5a** (26.7 mg, 90 %).

Acknowledgements

We thank the National Natural Science Foundation of China (No. 21372114, 21172106, 21474048, and 51173078), the National Basic Research Program of China (2010CB923303) and the Research Fund for the Doctoral Program of Higher Education of China (20120091110010) for financial support.

References

[1] a) P. Siemsen, R. C. Livingston, F. Diederich, *Angew. Chem.* **2000**, *112*, 2740; *Angew. Chem. Int. Ed.* **2000**, *39*, 2632; b) E. Negishi, L. Anastasia, *Chem. Rev.* **2003**, *103*, 1979; c) F. Diederich, P. J. Stang, R. R. Tykwinsky (Eds.), *Acetylene Chemistry: Chemistry Biology and Material Science*, Wiley-VCH, Weinheim, **2005**; d) S. Toyota, *Chem. Rev.* **2010**, *110*, 5398; e) S. Diez-Gonzalez, *Catal. Sci. Technol.* **2011**, *1*, 166; f) J. P. Brand, J. Waser, *Chem. Soc. Rev.* **2012**, *41*, 4165; g) R. Chinchilla, C. Najera, *Chem. Rev.* **2014**, *114*, 1783.

[2] For selected recent reviews, and communications on rhodium-catalyzed C–H bond functionalization: a) D. A. Colby, A. S. Tsai, R. G. Bergman, J. A. Ellman, *Acc. Chem. Res.* **2011**, *45*, 814; b) G. Song, F. Wang, X. Li, *Chem. Soc. Rev.* **2012**, *41*, 3651; c) F. W. Patureau, J. Wencel-Delord, F. Glorius, *Aldrichimica*

Acta. **2012**, *45*, 31; d) S. Chen, J. Yu, Y. Jiang, F. Chen, J. Cheng, *Org. Lett.* **2013**, *15*, 4754; e) X. Li, S. Yu, F. Wang, B. Wan, X. Yu, *Angew. Chem.* **2013**, *125*, 2637; *Angew. Chem. Int. Ed.* **2013**, *52*, 2577; f) N. Kuhl, N. Schröder, F. Glorius, *Adv. Synth. Catal.* **2014**, *356*, 1443; g) Y. Yang, W. Hou, L. Qin, J. Du, H. Feng, B. Zhou, Y. Li, *Chem. Eur. J.* **2014**, *20*, 416; h) T. Zhang, Z. Qi, X. Zhang, L. Wu, X. Li, *Chem. Eur. J.* **2014**, *20*, 3283; i) K. Wu, Z. Fan, Y. Xue, Q. Yao, A. Zhang, *Org. Lett.* **2014**, *16*, 42; j) X Zhang, W. Si, M. Bao, N. Asao, Y. Yamamoto, T. Jin, *Org. Lett.* **2014**, *16*, 4830.

[3] a) V. V. Zhdankin, C. J. Kuehl, A. P. Krasutsky, J. T. Bolz, A. J. Simonsen, *J. Org. Chem.* **1996**, *61*, 6547; b) V. V. Zhdankin, P. J. Stang, *Tetrahdedron* **1998**, *54*, 10927; c) V. V. Zhdankin, P. J. Stang, *Chem. Rev.* **2008**, *108*, 5299.

[4] a) J. P. Brand, J. Charpentier, J. Waser, *Angew. Chem.* **2009**, *121*, 9510; *Angew. Chem. Int. Ed.* **2009**, *48*, 9346; b) J. P. Brand, J. Waser, *Angew. Chem.* **2010**, *122*, 7462; *Angew. Chem. Int. Ed.* **2010**, *49*, 7304; c) D. Fernandez Gonzalez, J. P. Brand, J. Waser, *Chem. Eur. J.* **2010**, *16*, 9457; d) S. Nicolai, S. Erard, D. Fernandez Gonzalez, J. Waser, *Org. Lett.* **2010**, *12*, 384; e) J. P. Brand, C. Chevalley, J. Waser, *Beilstein J. Org. Chem.* **2011**, *7*, 565; f) J. P. Brand, J. Waser, *Org. Lett.* **2012**, *14*, 744; g) D. Fernandez Gonzalez, J. P. Brand, R. Mondiere, J. Waser, *Adv. Synth. Catal.* **2013**, *355*, 1631; h) R. Frei, J. Waser, *J. Am. Chem. Soc.* **2013**, *135*, 9620; i) Y. Li, J. P. Brand, J. Waser, *Angew. Chem.* **2013**, *125*, 6875; *Angew. Chem. Int. Ed.* **2013**, *52*, 6743; j) Y. Li, J. Waser, *Beilstein J. Org. Chem.* **2013**, *9*, 1763; k) G. L. Tolnai, S. Ganss, J. P. Brand, J. Waser, *Org. Lett.* **2013**, *15*, 112.

[5] a) F. Xie, Z. Qi, S. Yu, X. Li, *J. Am. Chem. Soc.* **2014**, *136*, 4780; b) X. Zhang, Z. Qi, J. Gao, X. Li, *Org. Biomol. Chem.* **2014**, *12*, 9329.

[6] a) C. Feng, T.-P. Loh, *Angew. Chem.* **2014**, *126*, 2760; *Angew. Chem. Int. Ed.* **2014**, *53*, 2722; b) C. Feng, D. Feng, T.-P. Loh, *Chem. Commun.* **2014**, *50*, 9865.

[7] K. D. Collins, F. Lied, F. Glorius, *Chem. Commun.* **2014**, *50*, 4459.

[8] J. Jeong, P. Patel, H. Hwang, S. Chang, *Org. Lett.* **2014**, *16*, 4598.

[9] a) D. L. Boger, C. W. Boyce, R. M. Garbaccio, J. A. Goldberg, *Chem. Rev.* **1997**, *97*, 787; b) D. A. Horton, G. T. Bourne, M. L. Smythe, *Chem. Rev.* **2003**, *103*, 893; c) J. M. Ontoria, S. Di Marco, I. Conte, M. E. Di Francesco, C. Gardelli, U. Koch, V. G. Matassa, M. Poma, C. Steinkuhler, C. Volpari, S. Harper, *J. Med. Chem.* **2004**, *47*, 6443; d) M. G. Bell, D. L. Gernert, T. A. Grese, M. D. Belvo, P. S. Borromeo, S. A. Kelley, J. H. Kennedy, S. P. Kolis, P. A. Lander, R. Richey, V. S. Sharp, G. A. Stephenson, J. D. Williams, H. Yu, K. M. Zimmerman, M. I. Steinberg, P. K. Jadhav, *J. Med. Chem.* ***2007***, *50*, 6443; e) B. M. Trost, M. K. Brennan, *Synthesis* **2009**, 3003.

[10] a) S. P. Govek, L. E. Overman, *J. Am. Chem. Soc.* **2001**, *123*, 9468; b) T. Owa, A. Yokoi, K. Yamazaki, K. Yoshimatsu, T. Yamori, T. Nagasu, *J. Med. Chem.* **200**2, 45, 4913; c) R. J. Keizer, M. K. Zamacona, M. Jansen, D. Critchley, J. Wanders, J. H. Beijnen, J. H. M. Schellens, A. D. R. Huitema, *Invest. New Drugs* **2009**, *27*, 140; d) Y. Ozawa, K. Kusano, T. Owa, A. Yokoi, M. Asada, K. Yoshimatsu, *Cancer Chemother. Pharmacol.* **2012**, *69*, 1353.

[11] For selected examples, see: a) D. Kalyani, N. R. Deprez, L. V. Desai, M. S. Sanford, *J. Am. Chem. Soc.* **2005**, *127*, 7330; b) Z. Shi, B. Li, X. Wan, J. Cheng, Z. Fang, B. Cao, C. Qin, Y. Wang, *Angew. Chem.* **2007**, *119*, 5650; *Angew. Chem. Int. Ed.* **2007**, *46*, 5554; c) T. Nishikata, A. R. Abela, S. Huang, B. H. Lipshutz, *J. Am. Chem. Soc.* **2010**, *132*, 4978; d) S. De, S. Ghosh, S. Bhunia, J. A. Sheikh, A. Bisai, *Org. Lett.* **2012**, *14*, 4466; e) L.-Y. Jiao, M. Oestreich, *Chem. Eur. J.* **2013**, *19*, 10845.

[12] For selected examples, see: a) L.-Y. Jiao, M. Oestreich, *Org. Lett.* **2013**, *15*, 5374; b) Z. Song, R. Samanta, A. P. Antonchick, *Org. Lett.* **2013**, *15*, 5662.

[13] For selected examples, see: a) J. Xie, Q. Xue, H. Jin, H. Li, Y. Cheng, C. Zhu, *Chem. Sci.* **2013**, *4*, 1281; b) C. Pan, H. Jin, X. Liu, Y. Cheng, C. Zhu, *Chem. Commun.* **2013**, *49*, 2933; c) P. Xu, J. Xie, Q. Xue, C. Pan, Y. Cheng, C. Zhu, *Chem. Eur. J.* **2013**, *19*, 14039; d) C. Pan, H. Jin, P. Xu, X. Liu, Y. Cheng, C. Zhu, *J. Org. Chem.* **2013**, *78*, 9494.

[14] C. Pan, A. Abdukader, J. Han, Y. Cheng, C. Zhu, *Chem. Eur. J.* **2014**, *20*, 3606.

[15] K. Shin, S. Chang, *J. Org. Chem.* **2014**, *79*, 12197.

[16] M. Kim, N. K. Mishra, J. Park, S. Han, Y. Shin, S. Sharma, Y. Lee, E.-K. Lee, J. H. Kwak, I. S. Kim, *Chem. Commun.* **2014**, *50*, 14249.

[17] W. Ai, X. Yang, Y. Wu, X. Wang, Y. Li, Y. Yang, B, Zhou, *Chem. Eur. J.* **2014**, *20*, 17653.

[18] For selected oxidation of indoline to indole using MnO_2, see: a) Y. S. Lo, D. A. Walsh Jr, W. J. Welstead, R. P. Mays, E. K. Rose, D. H. Causey, R. L. Duncan, *J. Heterocycl. Chem.* **1980**, *17*, 1663; b) T. Chandra, S. Zou, K. L. Brown, *Tetrahedron Lett.* **2004**, *45*, 7783.

[19] M. Chakrabarty, N. Ghosh, S. Khasnobis, M. Chakrabarty, *Synth. Commun.* **2002**, *32*, 265.

[20] a) J. Kim, J. Kim, S. Chang, *Chem. Eur. J.* **2013**, *19*, 7328; b) J. Ryu, J. Kwak, K. Shin, D. Lee, S. Chang, *J. Am. Chem. Soc.* **2013**, *135*, 12861; c) H. Kim, K. Shin, S. Chang, *J. Am. Chem. Soc.* **2014**, *136*, 5904.

6 Rhodium-Catalyzed Direct C7 Alkynylation of Indolines

Adv. Synth. Catal. **2015**, *357*, 1 – 6

Ning Jin, Changduo Pan, Honglin Zhang, Pan Xu, Yixiang Cheng, Chengjian Zhu*