Advanced Synthesis & Catalysis

Accepted Article

Title: CuI-Catalyzed Selective 3-Alkylation of Indoles with N-Tosylhydrazones and the I2-Mediated Further Cyclization to Chromeno[2,3-b]indoles

Authors: Chun-Bao Miao, Yan-Fang Sun, He Wu, Xiaoqiang Sun, and Haitao Yang

To be cited as: *Adv. Synth. Catal.* 10.1002/adsc.201800206

Link to VoR: http://dx.doi.org/10.1002/adsc.201800206

10.1002/adsc.201800206

COMMUNICATION

DOI: 10.1002/adsc.201((will be filled in by the editorial staff))

CuI-Catalyzed Selective 3-Alkylation of Indoles with *N*-Tosylhydrazones and the I_2-Mediated Further Cyclization to Chromeno[2,3-*b*]indoles

Chun-Bao Miao,* Yan-Fang Sun, He Wu, Xiao-Qiang Sun, Hai-Tao Yang

Jiangsu Key Laboratory of Advanced Catalytic Materials and Technology, Advanced Catalysis and Green Manufacturing Collaborative Innovation Center, School of Petrochemical Engineering, Changzhou University, Changzhou 213164, China.
E-mail: estally@yahoo.com

Received: ((will be filled in by the editorial staff))

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201######.((Please delete if not appropriate))

Abstract. The CuI-catalyzed reaction of indoles with *N*-tosylhydrazones derived from the *ortho-/para*-hydroxybenzaldhydes affords selectively the *C*-3 alkylated products rather than the *N*-alkylated products. In addition, the I_2-mediated cyclization of the generated *C*-3 alkylated products allows the concise synthesis of chromeno[2,3-*b*]indole derivatives.

Keywords: indole; *N*-tosylhydrazone; CuI; iodine; chromeno[2,3-*b*]indole

N-tosylhydrazones, which can be easily prepared from aldehydes or ketones, have been widely used as the precursors of diazo compounds or carbenes. They have been used as versatile synthons in organic synthesis and various useful transformations through the transitionmetal-catalyzed or metal-free reactions of *N*-tosylhydrazones have been reported.[1] Carbene insertion into Y-H (Y = C,[2] N,[3] O,[4] S,[5] P,[6] B,[7] Si,[8] Sn[9]) bonds as one of the most important transformation in *N*-tosylhydrazone chemistry has widespread application in the construction of different types of C-Y bonds.

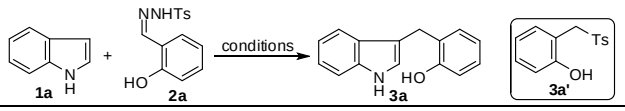
The indole core is a key building block found in various biologically active natural compounds and clinical drugs, which has attracted increasing attention in the direct functionalization of indoles for the synthesis of active indole derivatives.[10] Generally, the direct alkylation of indoles with alkyl/aryl halides always take place selectively at the *N*-position. The reaction of indoles with ester group stabilized carbene catalyzed by copper or rhodium catalyst can give N1, C2, or C3 substituted indoles depending on the substitution pattern of the original substrate.[11] The amide group stabilized carbene reacted with indoles catalyzed by rhodium only furnish the *N*–H insertion product.[12] Most recently, the non-stablized carbene generated from *N*-tosylhydrazones has also been used in the alkylation of indoles. Zhang *et al* reported the copper-catalyzed reductive cross coupling of *N*-tosylhydrazones with nonprotected indoles and the *N*-alkylated products were obtained exclusively through carbene insertion into N-H bond.[3e] Thus, the selective 3-alkylation of indoles with carbenes remains a great challenge.

It could be seen from the previously reported transformation of *N*-tosylhydrazones, they were easy to couple with various nucleophiles. As we know, the *C*-3 position of indoles also exhibited strong nucleophilicity, we wondered whether the regioselectivity of the reaction between indoles and *N*-tosylhydrazones could be reversed through the changes of the catalytic system or subtle structural tuning of the *N*-tosylhydrazones. When a hydroxyl group was introduced to the *ortho*-position of benzaldehyde-derived *N*-tosylhydrazone, to our delight, the reaction of **1a** with **2a** in the presence of catalytic amount of CuI (20 mol %) with K_2CO_3 (1.5 equiv) as the base under nitrogen atmosphere afforded the *C*-3 alkylated product **3a** selectively in 38% yield (Table 1, entry 1). There were many unreacted **1a** remaining in the reaction due to the considerable consumption of **2a** through its self-reaction. The **2a** could react with K_2CO_3 (or Cs_2CO_3) in the presence of CuI to give a complex mixture including salicylaldehyde, 4-methylbenzenesulfonamide, sulfone **3a'**,[13] and other unidentified products (See supporting information). Using Cs_2CO_3 instead of K_2CO_3 improved the yield to 49%, albeit still with many leftovers of **1a** (Table 1, entry 2). Pleasingly, when 1.6 equiv of **2a** and 2 equiv of Cs_2CO_3 were employed, full conversion of indole **1a** was observed, giving 72% yield of **3a** (Table 1, entry 3). Under air conditions, no desired product was formed (Table 1, entry 4). The influence of different solvents and copper salts were also examined. Using toluene and acetonitrile as the solvent gave very poor yield (Table 1, entries 5 and 6). DMSO gave comparative yield with that of 1,4-dioxane while DMF gave a slightly lower yield

10.1002/adsc.201800206

(Table 1, entries 7 and 8). Other copper salts such as $Cu(MeCN)_4BF_4$, $Cu(OAc)_2$, $CuCl_2$, $Cu(acac)_2$, and $Cu(ClO_4)_2$ exhibited a very low catalytic activity and CuX (X = Cl, Br) was inferior to the CuI (Table 1, entries 9-15). Using *t*-BuOLi, DBU, or DMAP as the base led to no formation of the desired product **3a** (Table 1, entries 16-18). When the amount of CuI was reduced to 0.1 or 0.05 equiv, a longer reaction time was needed and some indole **1a** remained, thus leading to a lower yield. In view of the operability, 1,4-dioxane was selected as the final solvent because it had a lower boiling point compared with DMSO.

Table 1. Surveying of the Reaction Conditions.[a]

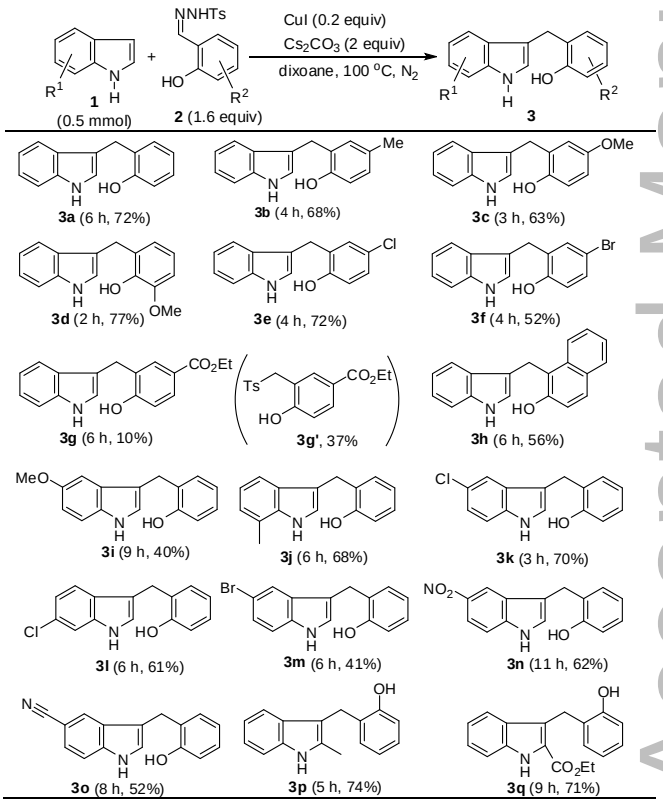


Entry	[Cu], Base	Solvent	Time (h)	Yield (%)
1[b]	CuI, K_2CO_3	1,4-dioxane	6	38
2[b]	CuI, Cs_2CO_3	1,4-dioxane	6	49
3	CuI, Cs_2CO_3	1,4-dioxane	6	72
4[c]	CuI, Cs_2CO_3	1,4-dioxane	6	0
5	CuI, Cs_2CO_3	toluene	12	16
6[d]	CuI, Cs_2CO_3	CH_3CN	12	12
7	CuI, Cs_2CO_3	DMSO	8	72
8	CuI, Cs_2CO_3	DMF	8	65
9	CuCl, Cs_2CO_3	1,4-dioxane	8	55
10	CuBr, Cs_2CO_3	1,4-dioxane	8	61
11	$Cu(MeCN)_4BF_4$, Cs_2CO_3	1,4-dioxane	12	17
12	$Cu(OAc)_2$, Cs_2CO_3	1,4-dioxane	18	18
13	$CuCl_2$, Cs_2CO_3	1,4-dioxane	18	10
14	$Cu(acac)_2$, Cs_2CO_3	1,4-dioxane	18	21
15	$Cu(ClO_4)_2$, Cs_2CO_3	1,4-dioxane	12	23
16	CuI, *t*-BuOLi	1,4-dioxane	12	0
17	CuI, DBU	1,4-dioxane	12	0
18	CuI, DMAP	1,4-dioxane	12	0
19[e]	CuI, Cs_2CO_3	1,4-dioxane	10	53
20[f]	CuI, Cs_2CO_3	1,4-dioxane	10	49

[a] Unless otherwise indication, the reaction was performed with 0.5 mmol of **1a**, 1.6 equiv of **2a**, 0.2 equiv of copper salt, 2 equiv of base, and 5 mL of solvent at 100 °C under nitrogen atmosphere. [b] **2a** (1 equiv), base (1.5 equiv). [c] Carried out under air condition. [d] Reacted at 80 °C. [e] 0.1 equiv of CuI was used. [f] 0.05 equiv of CuI was used.

Next, the general applicability of the CuI-catalyzed *C*-3 alkylation was assessed with respect to different substituted indoles **1** and *N*-tosylhyazones **2** (Table 2). As can be seen from table 2, this transformation displayed good functional group compatibility. For the hydrazones, most of the substrates gave moderate to good yield (**3a**–**f**). All the reactions of methyl-, methoxy-, chloro-, and bromosubstituted substrates **2** with indole **1a** yielded the corresponding products **3a**–**f** in 52%–77% yields. A strong electronic effect of the substituent was observed for substrates **2**. A moderate electron-withdrawing group on the phenyl ring of hydrazone (**2g**) led to dramatic descend of the yield (**3g**, 10%) due to the competitive self-reaction of **2g** to form sulfone **3g'** (37%).[13] No desired product was detected for the *N*-tosylhydrazone derived from 5-nitrosalicylaldehyde. *N*-Tosylhydrazone **2h** derived from 2-hydroxy-1-naphthaldehyde also delivered 56% yield of product **3h**. Differently substituted indoles with either electron-withdrawing or electron-donating group on the phenyl ring were well tolerated in the reaction to provide desired *C*-alkylated products **3i-o**. 2-Methyl or ester group substituted indole was also applicable to the reaction, providing the desired products **3p** or **3q** in 74% or 71% yield, respectively. Unfortunately, when the substrate was extended to the *N*-tosylhydrazone derived from 2-hydroxyacetophenone, no reaction occurred probably due to the steric hindrance. Moreover, it should be noted that the *N*-hydrogen atom of the indoles was essential to the present reaction and no desired product was obtained when it was replaced by a methyl, acetyl, or tosyl group.

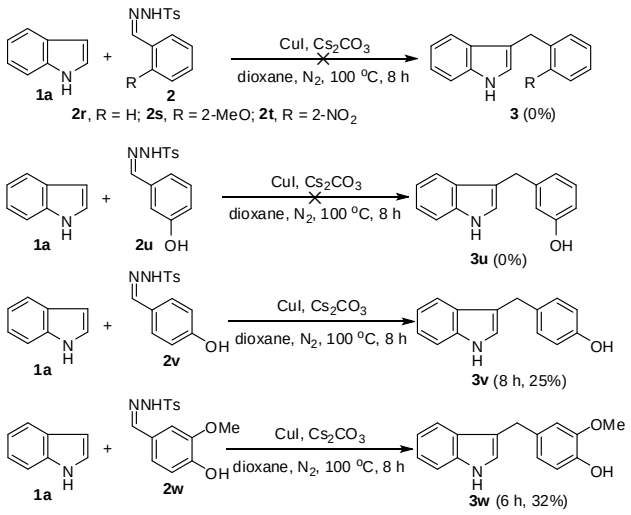
Table 2. Substrate Scope for the CuI-Catalyzed Reaction of *N*-Tosylhydrazones with Indoles.[a]



To ascertain the significance of the hydroxyl group, other hydrazones **2r**-**t** derived from benzaldehyde, 2-nitrobenzaldehyde, or 2-methoxybenzaldehyde were introduced to the reaction and no desired product was obtained (Scheme 1). The influence of the substituted position of the hydroxyl group was also evaluated. When the hydroxyl group was located at the *meta*-position, no anticipated product **3u** was formed.

10.1002/adsc.201800206

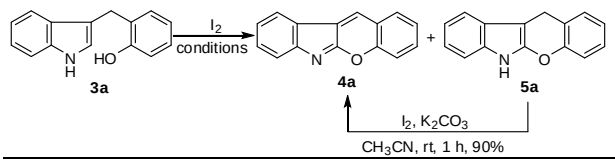
However, the *N*-tosylhydrazones **2v** and **2w** generated from 4-hydroxybenzaldehyde and 4-hydroxy-3-methoxybenzaldehyde could react with indole **1a** to afford 3-alkylated products **3v** and **3w**, respectively, albeit in a lower yield (Scheme 1). These results clearly demonstrated that the hydroxyl group and its location was critical to the present reaction.



Scheme 1. Reaction of **1a** with Different *N*-Tosylhydrazones.

Previously, we have focused on developing the I_2-mediated transformations.[14] In a continuous of our interesting in this area, we wondered whether the indole derivatives **3** could undergo a cycliazaiton triggered by iodine. Initially, the product **3a** was chosen to try the possibility (Table 3). The reaction of **3a** with 1 equiv of molecular iodine in the presence of 1 equiv of K_2CO_3 in acetonitrile proceeded smoothly at room temperature. Interestingly, two cyclization products chromeno[2,3-*b*]indole **4a** and 6,11-dihydrochromeno[2,3-*b*]indole **5a** were obtained in 36% and 19% yields, respectively, accompanied by a large amount of raw material surplus. Increasing the amount of iodine and K_2CO_3 to 2.5 equiv improved the yield of **4a** to 88% and only the traces of **5a** were observed (entry 3). Notably, treating **5a** with 1.2 equiv of I_2 and 1.2 equiv of K_2CO_3 resulted in the full conversion to **4a** in 90% yield. Other commonly used bases and solvents were also effective in this transformation (entries 4-10).

Table 3. Screening of the Cyclization Conditions.[a]

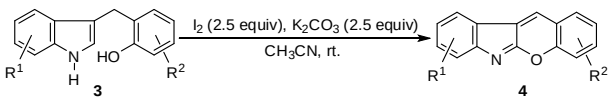


Entry	Base	Solvent	Ratio[b]	Time (h)	Yield (%)	
					4a	**5a**
1	K_2CO_3	CH_3CN	1:1:1	2	36	19
2	K_2CO_3	CH_3CN	1:2:2	2	73	7
3	K_2CO_3	CH_3CN	1:2.5:2.5	2	88	trace
4	K_2CO_3	CH_2Cl_2	1:2.5:2.5	2	74	trace
5	K_2CO_3	DMSO	1:2.5:2.5	2	63	trace
6	K_2CO_3	DMF	1:2.5:2.5	2	77	trace
7	K_2CO_3	EtOH	1:2.5:2.5	2	87	trace
8	K_2CO_3	THF	1:2.5:2.5	2	59	trace
9	DBU	CH_3CN	1:2.5:2.5	2	80	trace
10	DMAP	CH_3CN	1:2.5:2.5	2	86	trace

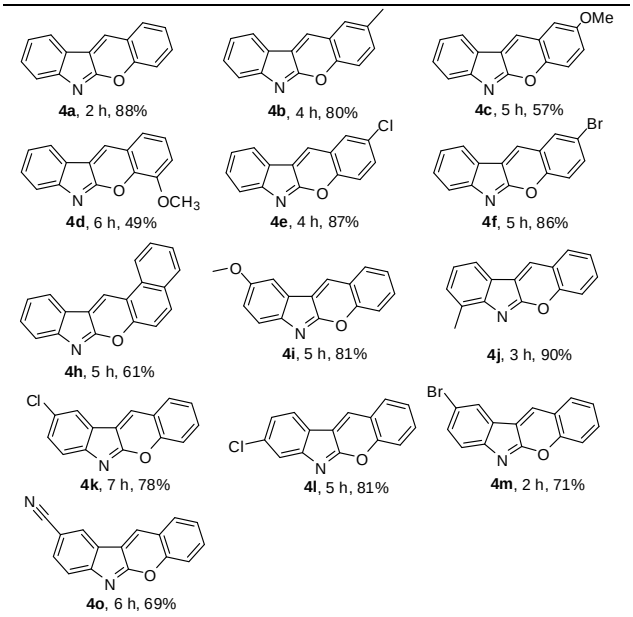
[a] All the reactions were carried out with 0.2 mmol of **3a** in 4 mL of solvent at room temperature for the designated time. [b] **3a**/I_2/additive.

Chromeno[2,3-*b*]indole is the core skeleton in the hyrtiazepine alkaloids hyrtimomine A and hyrtimomine B.[15] Until now, there are few reports on the synthesis of the chromeno[2,3-*b*]indole derivatives. The first report of the preparation came from the decomposition of the diazonium sulfate prepared from 3-*ortho*-aminobenzylidene-7-methyloxindole, affording 7-methylchromeno[2,3-*b*] indole as a byproduct.[16] Intramolecular cyclizations of the Knoevenagel adducts of oxindoles with 2-hydroxyacetophenones gave a very low yield of product.[17] The synthesis from 3-indolecarboxylates and phenols needed 3 step- reaction.[18] Liu and Zhu developed an efficient method for the synthesis of chromeno[2,3-*b*]indoles through the Pd-catalyzed cascade reaction of 2-bromoindoles with salicylaldehydes.[19] Nevertheless, the 2-bromoindoles were not easily available reagents. Most recently DDQ-mediated oxidative cyclization of 2,2-bisindolylmethylphenols was reported;[20] however, the use of excessive DDQ led to the formation of many organic wastes. Owing to the limited synthetic methods toward this nuclear, the biological character has been rarely investigated except the high antiproliferative activity against MV4-11, A549, and HCT116 cell lines.[18,21] Herein, a simple and efficient I_2-mediated cyclization of 3-(2-hydroxyl)-benzylindole for the synthesis of chromeno[2,3-*b*]indoles under mild conditions was developed. Various chromeno[2,3-*b*]indoles could be constructed in moderate to good yields under standard conditions (Table 4).

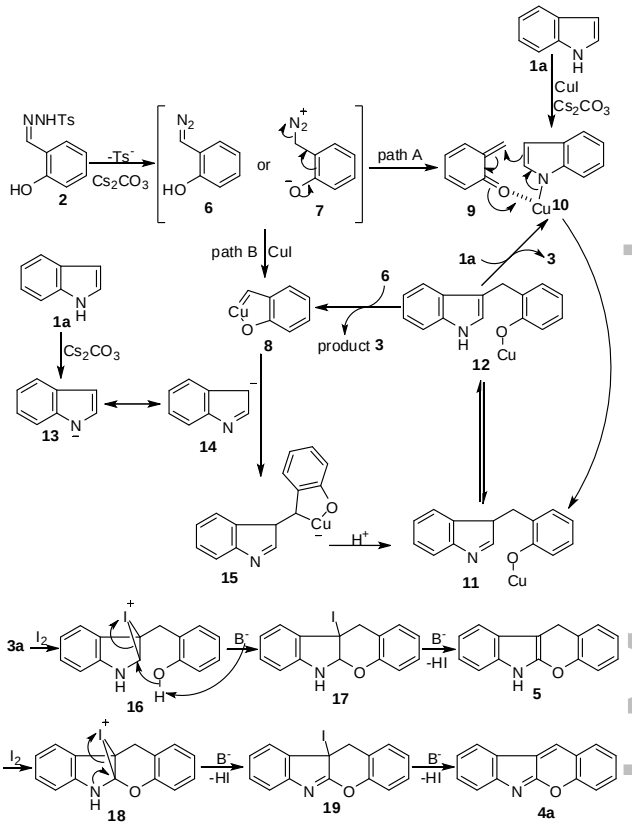
Table 4 Substrate Scope for the I_2-Mediated Cyclization of **3**.



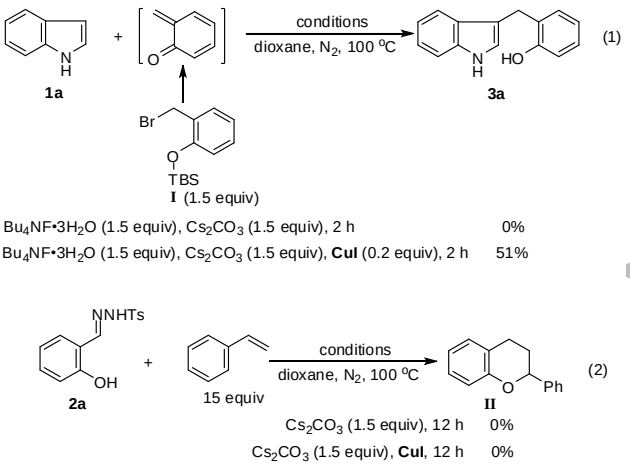
10.1002/adsc.201800206



The possible reaction mechanism for the *C*-3 alkylation of indole with *N*-tosylhydrazone was shown in Scheme 2. First, decomposition of the *N*-tosylhydrazone **2** in the presence of base generated the diazo compound **6** or **7**, which might react with CuI to give Cu(I) carbene complex **8** or produce *o*-quinone methide intermediate **9**. Indole **1a** reacted with CuI to generate complex **10**, which coordinated with **9** followed by intramolecular C-C bond formation to generate **11** (it was equal to **12**). Indole **1a** reacted with **12** to afford product **3** and regenerate complex **10** (path A). To confirm whether *o*-quinone methide **9** was generated in the transformation, several control experiments were performed (Scheme 3). TBS-protected 2-bromomethylphenol **I** has been usually used as a precursor of *o*-quinone methide *via* fluoride-induced desilylation.[22] However, the reaction of indole **1a** with 1.5 equiv of **I**, 1.5 equiv of TBAF, and 1.5 equiv of Cs_2CO_3 did not afford product **3a**. When 0.2 equiv of CuI was added, **3a** was obtained in 51% yield.[23] This demonstrated that *o*-quinone methide might be involved in the transformation. To further prove this, the reaction of **2a** with styrene (15 equiv) using Cs_2CO_3 as the base was carried out. However, no anticipated [4+2] product **II** was generated whether the CuI was added or not. This result contradicted with the formation of *o*-quinone methide because it was reported to react with styrene easily to form **II**.[24] Therefore, we proposed another possible reaction pathway (path B). Under the basic condition, indole was deprotonated to generate **13** (which was equal to **14**). The reaction of **14** with **8** gave **15** and the subsequent abstraction of proton afforded **11** (**12**). **12** reacted with **6** to give product **3** and regenerate Cu(I) cabene complex **8**. The Cs_2CO_3 gave a better result than the K_2CO_3 probably owing to the stronger basicity which is beneficial to the deprotonation of indoles. If the hydroxyl group was located at the *para*-position, the carbene complex **8** could not be formed and the direct C-H insertion to Cu(I) carbene (like **8**) would take place. Maybe this could explain the relative low yield for the reaction of indole **1a** with **2v** or **2w**. **3a** reacted with I_2 to generate the iodonium **16**, which underwent intramolecular attack by the hydroxyl group followed by dehydroiodination to give **5**. Further iodination of **5** *via* iodonium **18** provided **19**, which eliminated the hydrogen iodide under basic condition to afford chromeno[2,3-*b*] indole **4a**.



Scheme 2. Proposed Mechanism.



Scheme 3 Control Experiments.

In summary, the CuI-catalyzed reaction of indoles with *N*-tosylhydrazones for the selective *C*-3

alkylation was developed. Gratifyingly, there was no *N*-alkylated product being observed in the reaction. The *ortho*- or *para*- hydroxyl group was crucial to the reaction. In addition, we developed a simple method to synthesize the chromeno[2,3-*b*]indole derivatives through an I_2-mediated cyclization of the generated 3-(2-hydroxybenzyl)-indoles. This discovery might be of great importance on the selective construction of other polycyclic indole structures. A possible reaction mechanism for the two transformations was proposed.

Experimental Section

General information

^1H, ^{13}C NMR were recorded on 300 MHz (75 MHz for ^{13}C NMR) spectrometer. Melting points were determined on a micromelting point apparatus without corrections. Flash column chromatography was performed over silica gel (200−300 mesh). HRMS were obtained on an Thermo Scientific LTQ Orbitrap XL equipped with an ESI source (positive mode).

General Procedure for the Preparation of 3 through the CuI-Catalyzed Reaction of Indole with *N*-Tosylhydrazones

A test tube (Ø18 × 150 mm) was charged with indoles **1** (0.5 mmol), *N*-tosylhydrazones **2** (0.8 mmol), CuI (19.0 mg, 0.1 mmol), Cs_2CO_3 (325 mg, 1 mmol), and 1,4-dioxane (5 mL). The reaction tube was evacuated and backfilled with N_2 (3 times, balloon). The reaction mixture was stirred at 100 °C (oil bath temperature) under a N_2 balloon. After completion of the reaction as determined by TLC, the mixture was cooled to room temperature, diluted with dichloromethane, and quenched with $NH_3{\cdot}H_2O$. The reaction mixture was extracted with CH_2Cl_2 (20 mL × 3) and washed with brine. The organic phase was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*, and the residue was purified by column chromatography on silica gel eluted with ethyl acetate-petroleum ether to provide the corresponding products **3**.

The reaction of 3 with I_2 for the synthesis of 4

A test tube (Ø18 × 150 mm) was charged with **3** (0.2 mmol), I_2 (0.5 mmol), K_2CO_3 (0.5 mmol), and acetonitrile (4 mL). The reaction mixture was stirred at room temperature until the completion of the reaction as determined by TLC. The reaction mixture was quenched with 2 aqueous solution of $Na_2S_2O_3$ (100 mg / mL,), and then extracted with CH_2Cl_2 (20 mL × 3). The organic layer was dried over anhydrous Na_2SO_4, and then concentrated under reduced pressure. The residue was purified by column chromatography on silica gel eluted with ethyl acetate-toluene to provide **4**.

Acknowledgments

We are grateful for financial support from the Jiangsu Key Laboratory of Advanced Catalytic Materials and Technology (BM2012110) and Advanced Catalysis and Green Manufacturing Collaborative Innovation Center.

References

[1] a) J. Barluenga, C. Valdés, *Angew. Chem. Int. Ed.* **2011**, *50*, 7486–7500; (b) Q. Xiao, Y. Zhang, J. Wang, *Acc. Chem. Res.* **2012**, *46*, 236–247.

[2] a) Z. Liu, H. Tan, L. Wang, T. Fu, Y. Xia, Y. Zhang, J. Wang, *Angew. Chem. Int. Ed.* **2015**, *54*, 3056−3060; b) S. Xu, G. Wu, F. Ye, X. Wang, H. Li, X. Zhao, Y. Zhang, J. Wang, *Angew. Chem. Int. Ed.* **2015**, *54*, 4669−4672; c) Q. Zhou, S. Li, Y. Zhang, J. Wang, *Angew. Chem. Int. Ed.* **2017**, *56*, 16013−16017; d) X. Zhao, G. Wu, Y. Zhang, J. Wang, *J. Am. Chem. Soc.* **2011**, *133*, 3296–3299; e) F. Ye, X. Ma, Q. Xiao, H. Li, Y. Zhang, J. Wang, *J. Am. Chem. Soc.* **2012**, *134*, 5742−5745; f) A. Kishor, N. Jain, *Chem. Commun.* **2016**, *52*, 1831−1834; g) N. Krogsgaard-Larsen, B. Begtrup, M. M. Herth, J. Kehler, *Synthesis* **2010**, 4287−4299.

[3] a) J. Aziz, J.-D. Brion, A. Hamze, M. Alami, *Adv. Synth. Catal.* **2013**, *355*, 2417−2429; b) P. Xu, F.-L. Qi, F.-S. Han, Y.-H. Wang, *Chem. Asian J.* **2016**, *11*, 2030−2034; c) M. Roche, G. Frison, J.-D. Brion, O. Provot, A. Hamze, M. Alami, *J. Org. Chem.* **2013**, *78*, 8485−8495; d) X. Zeng, G. Cheng, J. Shen, X. Cui, *Org. Lett.* **2013**, *15*, 3022−3025; e) L. Ling, J. Cao, J. Hu, H. Zhang, *RSC Adv.* **2017**, *7*, 27974–27980.

[4] a) J. Barluenga, M. Tomás-Gamasa, F. Aznar, C. Valdés, *Angew. Chem. Int. Ed.* **2010**, *49*, 4993–4996; b) A.-H. García-Muñoz, M. Tomás-Gamasa, M. C. Pérez-Aguilar, E. Cuevas-Yañez, C. Valdés, *Eur. J. Org. Chem.* **2012**, 3925–3928.

[5] Q. Ding, B. Cao, J. Yuan, X. Liu, Y. Peng, *Org. Biomol. Chem.* **2011**, *9*, 748−751.

[6] Z.-S. Chen, Z.-Z. Zhou, H.-L. Hua, X.-H. Duan, J.-Y. Luo, J. Wang, P.-X. Zhou, Y.-M. Liang, *Tetrahedron* **2013**, *69*, 1065−1068.

[7] H. Li, L. Wang, Y. Zhang, J. Wang, *Angew. Chem. Int. Ed.* **2012**, *51*, 2943−2946.

[8] D. Chen, D.-X. Zhu, M.-H. Xu, *J. Am. Chem. Soc.* **2016**, *138*, 1498−1501.

[9] D. Qiu, S. Wang, H. Meng, S. Tang, T. Zhang, J. Wang, *J. Org. Chem.* **2017**, *82*, 624−632.

[10] a) B. U. W. Maes, *Topics in Heterocyclic Chemistry, Vol. 26*; G. W. Gribble, *Heterocyclic Scaffolds II: Reactions and Applications of Indoles*; Press: Springer, **2010**; Vol. 26; b) M. Shiri, *Chem. Rev.* **2012**, *112*, 3508.

[11] a) A. DeAngelis, V. W. Shurtleff, O. Dmitrenko, J. M. Fox, *J. Am. Chem. Soc.* **2011**, *133*, 1650–1653; b) M. B. Johansen, M. A. Kerr, *Org. Lett.* **2010**, *12*, 4956−4959; c) G. Özüuru, T. Schubach, M. M. K. Boysen, *Org. Lett.* **2012**, *14*, 4990−4993; d) R. Gibe, M. Kerr, *J. Org. Chem.* **2002**, *67*, 6247−6249; e) M. Delgado-Rebollo, A. Prieto, P. J. Pérez, *ChemCatChem* **2014**, *6*, 2047−2052.

[12] S. Muthusamy, P. Srinivasan, *Tetrahedron Lett.* **2005**, *46*, 1063−1066.

[13] X.-W. Feng, J. Wang, J. Zhang, J. Yang, N. Wang, X.-Q. Yu, *Org. Lett.* **2010**, *12*, 4408−4411.

[14] a) C.-B. Miao, M. Zhang, Z.-Y. Tian, H.-T. Xi, X.-Q. Sun, H.-T. Yang, *J. Org. Chem.* **2011**, *76*, 9809; (b)

C.-B. Miao, C.-P. Dong, M. Zhang, W.-L. Ren, Q. Meng, X.-Q. Sun, *J. Org. Chem.* **2013**, *78*, 4329; c) C.-B. Miao, Y.-H. Wang, M.-L. Xing, X.-W. Lu, X.-Q. Sun, H.-T. Yang, *J. Org. Chem.* **2013**, *78*, 11584−11589; d) C.-B. Miao, R. Liu, Y.-F. Sun, X.-Q. Sun, H.-T. Yang, *Tetrahedron Lett*. **2017**, *58*, 541−545.

[15] R. Momose, N. Tanaka, J. Fromont, J. Kobayashi, *Org*. *Lett*. **2013**, *15*, 2011-2013.

[16] R. A. Abramovitch, D. H. Hey, *J. Chem. Soc*. **1954**,1697−1703

[17] M. Nyerges, E. Gráczol-Fördos, T. Novák, G. Blaskó, I. Fejes, F. Perron-Sierra, *Heterocycles* **2013**, *87*, 2053−2069.

[18] W. Peng, M. Świtalska, L. Wang, Z. W. Mei, Y. Edazawa, C. Q. Pang, I. E.-T. El-Sayed, J. Wietrzyk, T. Inokuchi, Eur. *J. Med. Chem.* **2012**, *58*, 441−451.

[19] J. Liu, N. Liu, Y. Yue, Y. Wang, K. Chen, J. Zhang, S. Zhao, K. Zhuo, *Chem. Asian J.* **2017**, *12*, 401−404.

[20] C. Challa, J. Ravindran, M. M. Konai, S. Varughese, J. Jacob, B. S. P. Kumar, J. Haldar, R. S. Kankalapalli, *ACS Omega* **2017**, *2*, 5187−5195.

[21] Tsutomu, I.; Yui, H.; Toshitake, U. JP 2013173679 A.

[22] a) R. S. Lewis, C. J. Garza, A. T. Dang, T. K. Pedro, W. J. Chain, *Org. Lett.* **2015**, *17*, 2278−2281; b) K. X. Rodriguez, J. D. Vail, B. L. Ashfeld, *Org. Lett.* **2016**, *18*, 4514−4517; c) A. F. Barrero, J. F. Quílez de Moral, M. Mar Herrador, P. Arteaga, *Tetrahedron* **2006**, *62*, 6012−6017.

[23] The TBS-protected phenol **I** in dioxane was added dropwise to the reaction mixture.

[24] a) R. Rodriguez, R. M. Adlington, J. E. Moses, A. Cowley, J. E. Baldwin, *Org. Lett*. **2004**, *6*, 3617−3619; b) S. Nakamura, M. Uchiyama, T. Ohwada, *J. Am. Chem. Soc.* **2003**, *125*, 5282−5283.

10.1002/adsc.201800206

COMMUNICATION

CuI-Catalyzed Selective 3-Alkylation of Indoles with *N*-Tosylhydrazones and the I_2-Mediated Further Cyclization to Chromeno[2,3-*b*]indoles

Adv. Synth. Catal. **Year**, *Volume*, Page – Page

Chun-Bao Miao,* Yan-Fang Sun, He Wu, Xiao-Qiang Sun, Hai-Tao Yang