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Collective Synthesis of 3-Acylindoles, Indole-3-carboxylic Esters, Indole-3-sulfinic Acids, and 3-(Methylsulfonyl)indoles from Free (N−H) Indoles via Common *N*-Indolyl Triethylborate

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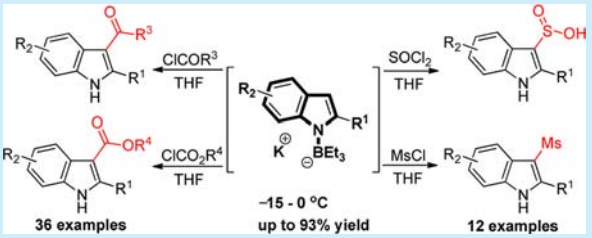
Supporting Information

ABSTRACT: A general and direct C3 functionalization of free (N−H) indoles with readily available electrophiles such as acid chlorides, chloroformates, thionyl chloride, and methylsulfonyl chloride via a common *N*-indolyl triethylborate intermediate is reported. The reaction proceeds smoothly under mild conditions in up to 93% yield. Indoles with substituents at the C2, C4, C5, C6, and C7 positions are well tolerated. The easy accessibility of a variety of important 3-acylindoles, indole-3-carboxylic esters, indole-3-sulfinic acids, and 3-(methylsulfonyl)indoles demonstrates the high degree of compatibility and practicability of this method.



Substituted indoles are versatile structural motifs in biologically active natural products and drug molecules[1] and have been considered as "privileged scaffolds" in drug discovery[2] since they are capable of binding many receptors with high affinity.[3] 3-Acylindoles and indole-3-carboxylic esters are among the most useful fragments because of their privileged core and their widespread applications in the synthesis of a broad range of useful indole derivatives (Figure 1).[4] 3-Sulfurindole-based compounds also exhibited excellent activities against HIV,[5] cancer,[6] CNS disorders,[7] heart disease,[8] etc. Synthetic methods for each of these C3-functionalized indoles have been intensely studied in the past.[9−11] Direct functionalization at the C3 position using various electrophiles is extremely attractive,[9,11] and other elegant cyclization strategies have been also developed via transition-metal-catalyzed or transition-metal-free reactions.[10] However, despite tremendous efforts to develop more efficient strategies in these areas, drawbacks, such as harsh conditions, side reactions, the need of expensive catalyst, and poor selectivity especially on unprotected indole substrates, are also obvious. A general and straightforward strategy to access all of these interesting skeletons via a common intermediate from free (N−H) indoles using readily available electrophiles remains highly desirable.

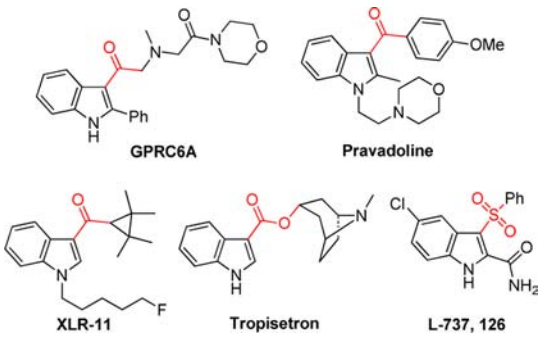


Figure 1. Examples of bioactive C3-functionalized compounds.

Functionalization at the C3 position of free (N−H) indoles is challenging because it often suffers from competing reactions at N1 and C2[12] due to the inherent reactivity of the aromatic system.[13] For the electron-rich indoles, other side reactions, such as polymerization and dimerization, also occur under acidic conditions.[9d,e] The use of *N*-protecting groups and metal indolides such as magnesium[9a] and zinc[9b,14] is generally the strategy for improving efficiency. However, the inefficient nature of the protecting groups and moderate nucleophilicity of these metal indolides made it necessary to develop more efficient approaches.

In 2013, Yang and co-workers reported that *N*-indoly triethylborate, prepared from potassium indole salt and triethylborane, was a useful reagent for dearomatizing C3-alkylation of 3-substituted indoles.[15] Similar effects have also been observed in palladium- and iridium-catalyzed C3 allylation and benzylation reactions of indoles with trialkylborane as the

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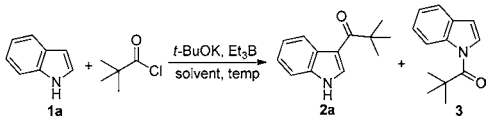
additive.[16] Based on these important precedents, we envisioned that *N*-indolyl triethylborate may be used as a nucleophile to react with readily available electrophilic carbonyl reagents regioselectively. Herein, we describe the extension of this method and report that not only acid chloride but also chloroformate, thionyl chloride, and methylsulfonyl chloride could react with *N*-indolyl triethylborate under mild conditions to provide a variety of C3 functionalized N−H indoles in high to excellent yield (up to 93% yield). Arylsulfinic acids (salts) are valuable functional groups since they could be easily converted to aryl sulfones,[17] sulfoxides,[18] and sulfides,[19] which have received much attention in drug discovery.[20] In this paper, we highlight our results on the collective synthesis of unprotected 3-acylindoles, indole-3-carboxylic esters, indole-3-sulfinic acids, and 3-(methylsulfonyl)indoles employing *N*-indolyl triethylborate as a common intermediate.

Our studies commenced with the acylation of indole **1a** with pivaloyl chloride under the established conditions (*t*-BuOK, Et_3B, 1,4-dioxane, rt).[15] Gratifyingly, the desired 3-trimethylacetylated indole **2a** was formed in 55% yield along with *N*-acylated product **3** in 30% yield (Table 1, entry 1). The solvents

Table 1. Optimization of C3 Acylation of Indole 1a



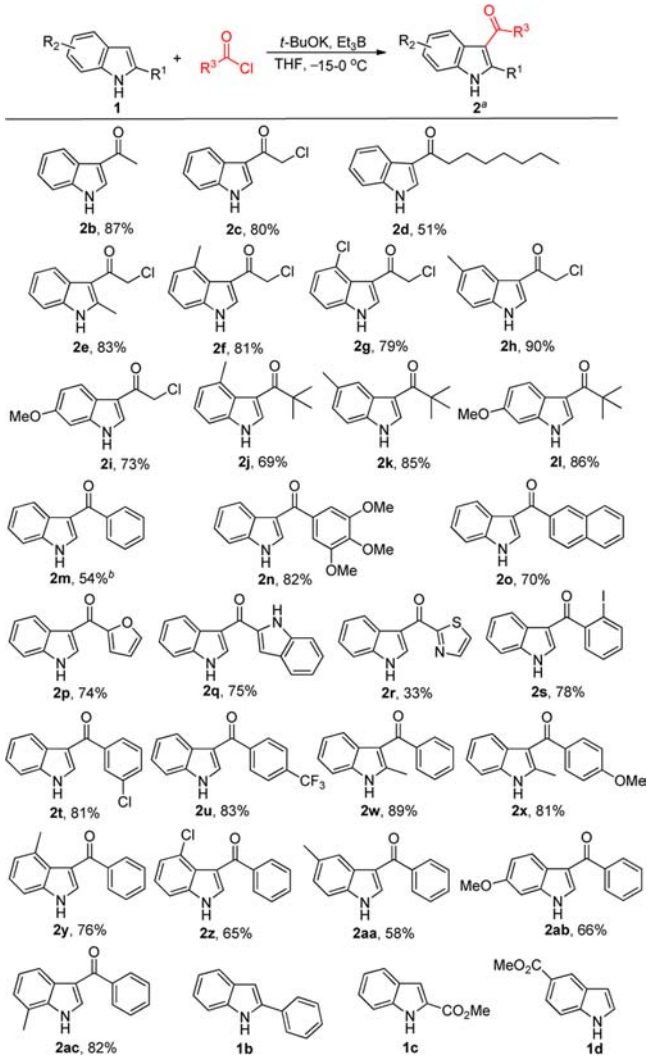
entry[a]	solvent	temp (°C)	time (h)	**2a**/**3** (%)
1	1,4-dioxane	25	12	55/30
2	THF	25	12	58/31
3	toluene	25	12	50/27
4	CH_2Cl_2	25	12	42/23
5	THF	0	16	80/12
6	THF	−15	24	91/trace
7[b]	THF	−15	4	0/89

[a]Reaction conditions: **1a** (0.5 mmol), *t*-BuOK (1.1 equiv), Et_3B (1.1 equiv), pivaloyl chloride (1.1 equiv) in 10 mL of solvent. [b]In the absence of Et_3B.

were briefly investigated, and THF was found to give a slightly higher combined yield (89%) with same ratio of **2a**/**3** (entry 2−4). Further screening revealed that the temperature has a crucial effect on the regioselectivity. When the reaction was conducted at 0 °C, **2a** was obtained in 80% yield and **3** in 12% yield (entry 5). When performed at −15 °C, the reaction gave the best result (entry 6), with a trace amount of **3** detected. A control experiment showed that **3** was generated exclusively in the absence of Et_3B (entry 7).

With the optimized conditions in hand, we first sought to explore the scope of C3 acylation reactions with aliphatic acyl chlorides at −15 °C. As shown in Scheme 1, the more reactive acetyl chloride and even chloroacetyl chloride could react smoothly with indole **1a** under the optimized conditions to give **2b** and **2c**, respectively, in high yield. Octanoyl chloride resulted in a relatively low yield of **2d** (51%). Because of the usefulness of the α-chlorine for further synthetic manipulations, chloroacetyl chloride was selected to test the scope of indole substrates. Substituents at the 2-, 4-, 5-, and 6-positions on the indole ring are well tolerated. Reactions of indoles substituted with methyl (**2e**, **2f**, and **2h**), methoxy (**2i**), and chloro (**2g**) groups all provided the corresponding 3-acylindoles in good to excellent yield (79−90%). No alkylated product was observed in any of the

Scheme 1. Acylation of Indoles with Aliphatic and Aromatic Acid Chlorides



[a]Reactions of 1 run on 0.5 mmol scale with 1.1 equiv of *t*-BuOK and 1.1 equiv of Et_3B. [b]Reactions were conducted at 0 °C when aromatic acid chlorides were used as electrophiles.

reactions. Notably, the dichloride substituents of compound **2g** may be used as handles to synthesize indoles of greater complexity.[21] Pivaloyl chloride and substituted indoles were also compatible reaction partners, with **2j**−**l** obtained in good yield.

Compared to aliphatic acyl chlorides, less reactive aromatic acyl chlorides needed higher temperature (0 °C) to complete the reaction. Benzoyl chloride offered a modest yield of **2m** (54%) after 24 h at 0 °C under otherwise identical conditions. Electron-rich aromatic acyl chlorides such as 3,4,5-trimethoxybenzoyl chloride, 2-naphthoyl chloride, and α-furoyl chloride afforded **2n**−**p** in 70−82% yield. 1*H*-Indole-2-carbonyl chloride was also compatible with this reaction system, giving **2q** in 75% yield. The thiazole-2-carboxyl chloride provided a low yield of **2r** (33%), a natural 3-acylindole alkaloid (namely indothiazinone) isolated in a culture of myxobacterial strain.[22] Aryl acyl chlorides bearing electron-withdrawing groups at the *ortho*, *meta*, and *para* positions gave **2s**−**u** in good yield. Indoles containing substituents at various positions (C2, C4, C5, C6, and C7) reacted to afford the desired **2w**−**ac** in 58−89% yield. Acylated

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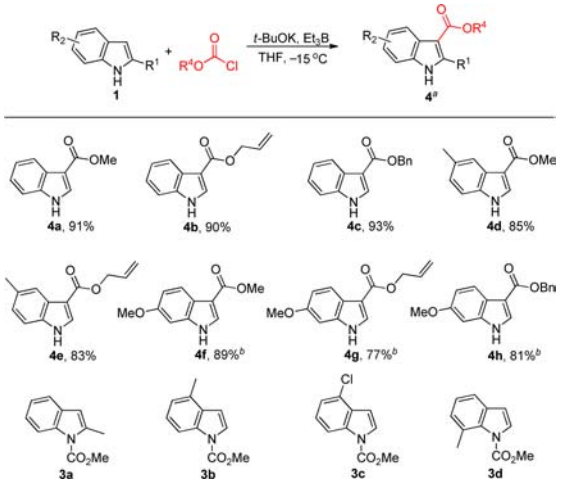
product **2x** could be easily transformed into the analgesic agent pravadoline (Figure 1) in one step according to reported method.[23] However, reactions of indole **1a** with phenylacetyl chloride or cinnamoyl chloride gave inseparable mixtures in both cases. N-Acylated product (not shown) was generated exclusively when 2-phenyl-substituted indole **1b** or indole-2-carboxylic acid methyl ester **1c** was used as the substrate, presumably because of the difficulty of the formation of *N*-indolyl triethylborate intermediate. Indole-5-carboxylic acid methyl ester **1d** was also an unsuitable substrate.

We next focused on the reaction of indoles with chloroformates with the expectation that indole-3-carboxylic esters (**4**, Scheme 2) would be formed. To our great delight, on

Scheme 2. Reactions of Indoles with Chloroformate

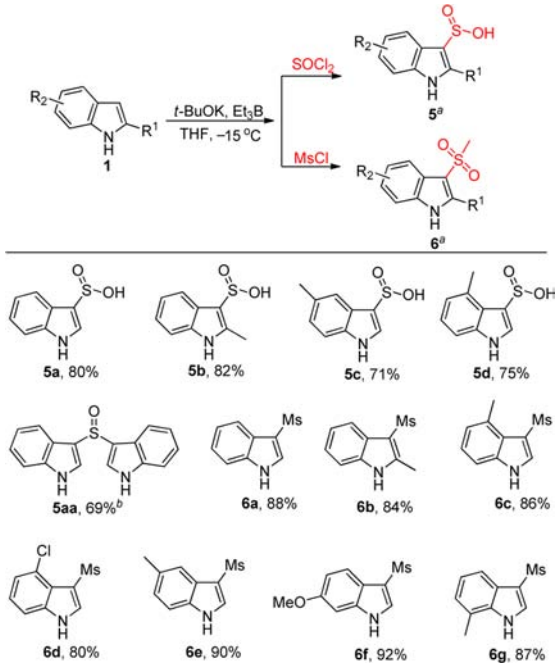


[a]Reaction conditions: **1** (0.5 mmol), *t*-BuOK (1.1 equiv), Et_3B (1.1 equiv), chloroformate (1.1 equiv) in 10 mL of THF. [b]Reaction was conducted at 0 °C.

treatment of the *N*-indolyl triethylborate of **1a** with methyl chloroformate, allyl chloroformate, and benzyl chloroformate, respectively, the esters **4a−c** were generated regioselectively in excellent yield (90−93%). 5-Methyl-1*H*-indole and 6-methoxy-1*H*-indole also showed good reactivity and regioselectivity in the formation of the desired products **4d−h**. Indoles bearing substituents at the C2, C4, or C7 position proved to be incompatible substrates and offered N-protected **3a−d** as the major products. Only a trace of the desired esters was obtained for these cases.

To further explore the reactivity (Scheme 3) of the *N*-indolyl triethylborate reagent, thionyl chloride was used to react with indole **1a**. After the reaction was quenched with aqueous ammonium chloride, indole-3-sulfinic acid **5a** was produced in 80% yield. C2-, C4-, and C5-methylated indoles also gave the desired sulfinic acid **5b−d** in high yield. It is important to note that when 0.5 equiv of thionyl chloride was used to react with indole **1a**, symmetric sulfoxide **5aa** was formed in 69% yield. This reaction demonstrates that arene sulfinyl chlorides are also suitable electrophiles. Encouraged by this result, we turned our attention to the sulfonylation reaction of indoles. Methylsulfonyl chloride was first examined, which reacted with various indoles smoothly to produce the 3-methylsulfonyl indoles **6a−g** in 80−92% yield. However, the arylsulfonyl chlorides including *p*-toluenesulfonyl chloride, 2-nitrobenzenesulfonyl chloride, and *p*-

Scheme 3. Reactions of Indoles with Thionyl Chloride or Methylsulfonyl Chloride



[a]Reaction conditions: **1** (0.5 mmol), *t*-BuOK (1.1 equiv), Et_3B (1.1 equiv), thionyl chloride or methylsulfonyl chloride (1.1 equiv) in 10 mL of THF. [b]0.5 equiv of $SOCl_2$ was used.

fluorobenzenesulfonyl chloride proved to be unsuitable electrophiles and gave complex mixtures.

In conclusion, we have demonstrated that *N*-indolyl triethylborate reacted with a series of electrophiles to regioselectively generate a wide range of C3-functionalized free (N−H) indoles that are important building blocks in medicinal and biological chemistry. 3-Acylindoles, indole-3-carboxylic esters, indole-3-sulfinic acids, and 3-methylsulfonyl indoles were easily produced in a direct and efficient manner utilizing *N*-indolyl triethylborate. Further investigation of the scope of the reaction is underway in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b01970.

Experimental procedures, product characterization, and ^1H and ^{13}C NMR spectra for all compounds (PDF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) (a) *Indoles*; Sundberg, R. J., Ed.; Academic: New York, 1996. (b) Casapullo, A.; Bifulco, G.; Bruno, I.; Riccio, R. *J. Nat. Prod.* **2000**, *63*, 447−451. (c) Humphrey, G. R.; Kuethe, J. T. *Chem. Rev.* **2006**, *106*, 2875−2911. (d) Smart, B. P.; Oslund, R. C.; Walsh, L. A.; Gelb, M. H. *J. Med. Chem.* **2006**, *49*, 2858−2860. (e) Bandini, M.; Eichholzer, A. *Angew. Chem., Int. Ed.* **2009**, *48*, 9608−9644. (f) Joucla, L.; Djakovitch, L. *Adv. Synth. Catal.* **2009**, *351*, 673−714. (g) Kochanowska-Karamyan, A. J.; Hamann, M. T. *Chem. Rev.* **2010**, *110*, 4489−4497. (h) Ishikura, M.; Abe, T.; Choshi, T.; Hibino, S. *Nat. Prod. Rep.* **2013**, *30*, 694−752. (i) Sun, Y.; Li, R.; Zhang, W.; Li, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 9201−9204. (j) Li, Y.; Zhu, S.; Li, J.; Li, A. *J. Am. Chem. Soc.* **2016**, *138*, 3982−3985.

(2) Horton, D. A.; Bourne, G. T.; Smythe, M. L. *Chem. Rev.* **2003**, *103*, 893−930.

(3) (a) Evans, B. E.; Rittle, K. E.; Bock, M. G.; Dipardo, R. M.; Freidinger, R. M.; Whitter, W. L.; Lundell, G. F.; Veber, D. F.; Anderson, P. S. *J. Med. Chem.* **1988**, *31*, 2235−2246. (b) Vasiljevik, T.; Franks, L. N.; Ford, B. M.; Douglas, J. T.; Prather, P. L.; Fantegrossi, W. E.; Prisinzano, T. E. *J. Med. Chem.* **2013**, *56*, 4537−4550.

(4) (a) Robinson, B. *Chem. Rev.* **1969**, *69*, 785−797. (b) Macor, J. E.; Blank, D. H.; Fox, C. B.; Lebel, L. A.; Newman, M. E.; Post, R. J.; Ryan, K.; Schmidt, A. W.; Schulz, D. W.; Koe, B. K. *J. Med. Chem.* **1994**, *37*, 2509−2512. (c) Lauchli, R.; Shea, K. J. *Org. Lett.* **2006**, *8*, 5287−5289. (d) Coldham, I.; Dobson, B. C.; Fletcher, S. R.; Franklin, A. I. *Eur. J. Org. Chem.* **2007**, *2007*, 2676−2686. (e) Chen, X.; Si, L.; Liu, D.; Proksch, P.; Zhang, L.; Zhou, D.; Lin, W. *Eur. J. Med. Chem.* **2015**, *93*, 182−195.

(5) Ragno, R.; Coluccia, A.; La Regina, G. L.; De Martino, G. D.; Piscitelli, F.; Lavecchia, A.; Novellino, E.; Bergamini, A.; Ciaprini, C.; Sinistro, A.; Maga, G.; Crespan, E.; Artico, M.; Silvestri, R. *J. Med. Chem.* **2006**, *49*, 3172−3184.

(6) De Martino, G. D.; La Regina, G. L.; Coluccia, A.; Edler, M. C.; Barbera, M. C.; Brancale, A.; Wilcox, E.; Hamel, E.; Artico, M.; Silvestri, R. *J. Med. Chem.* **2004**, *47*, 6120−6123.

(7) Bernotas, R.; Lenicek, S.; Antane, S.; Zhang, G. M.; Smith, D.; Coupet, J.; Harrison, B.; Schechter, L. E. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5499−5502.

(8) Funk, C. D. *Nat. Rev. Drug Discovery* **2005**, *4*, 664−672.

(9) For selected examples for the synthesis of 3-acylindoles, see: (a) Bergman, J.; Venemalm, L. *Tetrahedron Lett.* **1987**, *28*, 3741−3744. (b) Bergman, J.; Venemalm, L. *Tetrahedron* **1990**, *46*, 6061−6066. (c) Okauchi, T.; Itonaga, M.; Minami, T.; Owa, T.; Kitoh, K.; Yoshino, H. *Org. Lett.* **2000**, *2*, 1485−1487. (d) Ottoni, O.; Neder, A. V. F.; Dias, A. K. B.; Cruz, R. P. A.; Aquino, L. B. *Org. Lett.* **2001**, *3*, 1005−1007. (e) Yeung, K.-S.; Farkas, M. E.; Qiu, Z.; Yang, Z. *Tetrahedron Lett.* **2002**, *43*, 5793−5795. (f) Guchhait, S. K.; Kashyap, M.; Kamble, H. *J. Org. Chem.* **2011**, *76*, 4753−4758. (g) Wu, W.; Su, W. *J. Am. Chem. Soc.* **2011**, *133*, 11924−11927. (h) Chen, J.; Liu, B.; Liu, D.; Liu, S.; Cheng, J. *Adv. Synth. Catal.* **2012**, *354*, 2438−2442. (i) Yu, L.; Li, P.; Wang, L. *Chem. Commun.* **2013**, *49*, 2368−2370. (j) Ma, Y.; You, J.; Song, F. *Chem. - Eur. J.* **2013**, *19*, 1189−1193. (k) Jiang, T.-S.; Wang, G.-W. *Org. Lett.* **2013**, *15*, 788−791. (l) Williams, T. J.; Greaney, M. F. *Org. Lett.* **2014**, *16*, 4024−4027. (m) Xing, Q.; Li, P.; Lv, H.; Lang, R.; Xia, C.; Li, F. *Chem. Commun.* **2014**, *50*, 12181−12184. (n) Tjutrins, J.; Arndtsen, B. A. *J. Am. Chem. Soc.* **2015**, *137*, 12050−12054. (o) Zhao, M.-N.; Ran, L.; Chen, M.; Ren, Z.-H.; Wang, Y.-Y.; Guan, Z.-H. *ACS Catal.* **2015**, *5*, 1210−1213. (p) Gu, L.; Jin, C.; Liu, J.; Zhang, H.; Yuan, M.; Li, G. *Green Chem.* **2016**, *18*, 1201−1205.

(10) For selected examples for the synthesis of indole-3-carboxylic esters, see: (a) Würtz, S.; Rakshit, S.; Neumann, J. J.; Dröge, T.; Glorius, F. *Angew. Chem., Int. Ed.* **2008**, *47*, 7230−7233. (b) Solé, D.; Serrano, O. *J. Org. Chem.* **2008**, *73*, 2476−2479. (c) Levesque, P.; Fournier, P.-A. *J. Org. Chem.* **2010**, *75*, 7033−7036. (d) Zhang, H.; Liu, D.; Chen, C.; Liu, C.; Lei, A. *Chem. - Eur. J.* **2011**, *17*, 9581−9585. (e) Lang, R.; Wu, J.; Shi, L.; Xia, C.; Li, F. *Chem. Commun.* **2011**, *47*, 12553−12555. (f) Neumann, J. J.; Rakshit, S.; Dröge, T.; Würtz, S.; Glorius, F. *Chem. - Eur. J.* **2011**, *17*, 7298−7303. (g) Lang, R.; Shi, L.; Li, D.; Xia, C.; Li, F. *Org. Lett.* **2012**, *14*, 4130−4133. (h) Yang, Q.-Q.; Marchini, M.; Xiao, W.-J.; Ceroni, P.; Bandini, M. *Chem. - Eur. J.* **2015**, *21*, 18052−18056. (i) Shen, D.; Han, J.; Chen, J.; Deng, H.; Shao, M.; Zhang, H.; Cao, W. *Org. Lett.* **2015**, *17*, 3283−3285. (j) Jiang, H.; Gao, S.; Xu, J.; Wu, X.; Lin, A.; Yao, H. *Adv. Synth. Catal.* **2016**, *358*, 188−194. (k) Yu, K.; Liang, Y.; Li, B.; Wang, B. *Adv. Synth. Catal.* **2016**, *358*, 661−666.

(11) For selected examples for the synthesis of C−S bonds at the C3 position of indoles, see: (a) Yadav, J. S.; Reddy, B. V. S.; Krishna, A. D.; Swamy, T. *Tetrahedron Lett.* **2003**, *44*, 6055−6058. (b) Nakamura, I.; Yamagishi, U.; Song, D.; Konta, S.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 2284−2287. (c) Chen, Y.; Cho, C.-H.; Shi, F.; Larock, R. C. *J. Org. Chem.* **2009**, *74*, 6802−6811. (d) Yang, F.-L.; Tian, S.-K. *Angew. Chem., Int. Ed.* **2013**, *52*, 4929−4932. (e) Kobayashi, K.; Kobayashi, A.; Ezaki, K. *Tetrahedron* **2013**, *69*, 7936−7942. (f) Sang, P.; Chen, Z.; Zou, J.; Zhang, Y. *Green Chem.* **2013**, *15*, 2096−2100. (g) Han, D.; Li, Z.; Fan, R. *Org. Lett.* **2014**, *16*, 6508−6511. (h) Miao, T.; Li, P.; Zhang, Y.; Wang, L. *Org. Lett.* **2015**, *17*, 832−835. (i) Qi, H.; Zhang, T.; Wan, K.; Luo, M. *J. Org. Chem.* **2016**, *81*, 4262−4268. (j) Chen, F.; Meng, Q.; Han, S.-Q.; Han, B. *Org. Lett.* **2016**, *18*, 3330−3333.

(12) (a) Heaney, H.; Ley, S. V. *Org. Synth.* **1974**, *54*, 58. (b) Espejo, V. R.; Rainier, J. D. *J. Am. Chem. Soc.* **2008**, *130*, 12894−12895.

(13) *The Chemistry of Indoles*; Sundberg, R. J., Ed.; Academic Press: New York, 1970.

(14) (a) Powers, J. C.; Meyer, W. P.; Parsons, T. G. *J. Am. Chem. Soc.* **1967**, *89*, 5812−5820. (b) Nunomoto, S.; Kawakami, Y.; Yamashita, Y.; Takeuchi, H.; Eguchi, S. *J. Chem. Soc., Perkin Trans. 1* **1990**, 111−114. (c) Zhu, X.; Ganesan, A. *J. Org. Chem.* **2002**, *67*, 2705−2708. (d) Bernardo, P. H.; Chai, C. L. L. *J. Org. Chem.* **2003**, *68*, 8906−8909.

(15) Lin, A.; Yang, J.; Hashim, M. *Org. Lett.* **2013**, *15*, 1950−1953.

(16) (a) Kimura, M.; Futamata, M.; Mukai, R.; Tamaru, Y. *J. Am. Chem. Soc.* **2005**, *127*, 4592−4593. (b) Trost, B. M.; Quancard, J. *J. Am. Chem. Soc.* **2006**, *128*, 6314−6315. (c) Zhu, Y.; Rawal, V. H. *J. Am. Chem. Soc.* **2012**, *134*, 111−114. (d) Kaiser, T. M.; Yang, J. *Eur. J. Org. Chem.* **2013**, *2013*, 3983−3987. (e) Ruchti, J.; Carreira, E. M. *J. Am. Chem. Soc.* **2014**, *136*, 16756−16759. (f) Müller, D.-C. J. M.; Stark, C. B. W. *Angew. Chem., Int. Ed.* **2016**, *55*, 4798−4802.

(17) (a) Ueda, M.; Hartwig, J. F. *Org. Lett.* **2010**, *12*, 92−94. (b) Lu, Q.; Zhang, J.; Zhao, G.; Qi, Y.; Wang, H.; Lei, A. *J. Am. Chem. Soc.* **2013**, *135*, 11481−11484. (c) Tang, X.; Huang, L.; Xu, Y.; Yang, J.; Wu, W.; Jiang, H. *Angew. Chem., Int. Ed.* **2014**, *53*, 4205−4208. (d) Xiao, F.; Chen, H.; Xie, H.; Chen, S.; Yang, L.; Deng, G.-J. *Org. Lett.* **2014**, *16*, 50−53.

(18) (a) Furukawa, N.; Ogawa, S.; Matsumura, K.; Fujihara, H. *J. Org. Chem.* **1991**, *56*, 6341−6348. (b) Hiroi, K.; Kato, F. *Tetrahedron* **2001**, *57*, 1543−1550. (c) Xue, F.; Wang, D.; Li, X.; Wan, B. *J. Org. Chem.* **2012**, *77*, 3071−3081.

(19) (a) Xiao, F.; Xie, H.; Liu, S.; Deng, G.-J. *Adv. Synth. Catal.* **2014**, *356*, 364−368. (b) Rao, H.; Wang, P.; Wang, J.; Li, Z.; Sun, X.; Cao, S. *RSC Adv.* **2014**, *4*, 49165−49169.

(20) (a) Holland, H. L. *Chem. Rev.* **1988**, *88*, 473−485. (b) Block, E. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1135−1178.

(21) (a) MacKay, J. A.; Bishop, R. L.; Rawal, V. H. *Org. Lett.* **2005**, *7*, 3421−3424. (b) Steinmetz, H.; Mohr, K. I.; Zander, W.; Jansen, R.; Gerth, K.; Müller, R. *J. Nat. Prod.* **2012**, *75*, 1803−1805. (c) Lathrop, S. P.; Pompeo, M.; Chang, W.-T. T.; Movassaghi, M. *J. Am. Chem. Soc.* **2016**, *138*, 7763−7769.

(22) Jansen, R.; Mohr, K. I.; Bernecker, S.; Stadler, M.; Müller, R. *J. Nat. Prod.* **2014**, *77*, 1054−1060.

(23) (a) Gao, D.; Back, T. G. *Synlett* **2013**, *24*, 389−393. (b) Gong, T.-J.; Cheng, W.-M.; Su, W.; Xiao, B.; Fu, Y. *Tetrahedron Lett.* **2014**, *55*, 1859−1862.

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