Advanced Synthesis & Catalysis

## Accepted Article

**Title:** Cp*Rh(III)-Catalyzed Directed C-H Methylation and Arylation of Quinoline N-Oxides at the C-8 Position

**Authors:** Bao Wang, Chunpu Li, and Hong Liu



**To be cited as:** *Adv. Synth. Catal.* 10.1002/adsc.201700484

**Link to VoR:** http://dx.doi.org/10.1002/adsc.201700484

10.1002/adsc.201700484

UPDATE

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

# Cp*Rh(III)-Catalyzed Directed C-H Methylation and Arylation of Quinoline *N*-Oxides at the C-8 Position

Bao Wang,[a,b,c,‡] Chunpu Li,[b,c,‡] and Hong Liu [a,b,c,*]

a. School of Life Science and Technology, ShanghaiTech University, 100 Haike Road, Shanghai 201210, China.
b. State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zu Chong Zhi Road, Shanghai, 201203, China.
c. Key Laboratory of Receptor Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zu Chong Zhi Road, Shanghai, 201203, China.
E-mail: hliu@simm.ac.cn
‡ B. Wang and C. Li contributed equally to this work.

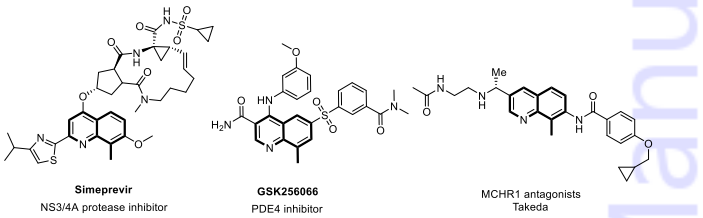
Received: ((will be filled in by the editorial staff))

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.** Herein, we report a Cp*Rh(III)-catalyzed directed C-H methylation of quinoline *N*-oxides at the C-8 position using commercially available organotrifluoroborates as reagents. This method features perfect regioselectivity, relatively mild reaction conditions, and diverse functional group tolerance with good to excellent yields. Additionally, direct C-8 arylated quinoline *N*-oxides products could also be obtained under the same conditions. Preliminary mechanistic experiments were conducted and a possible mechanism was proposed.

**Keywords:** Quinoline *N*-Oxides; C−H Methylation; Rhodium

Quinoline is an important structural motif in drug discovery[1-4] and materials science.[5] Notably, 8-methylquinoline derivatives are found in many drugs and biologically active molecules (Scheme 1).[6-8] Accordingly, the development of efficient methods to produce substituted quinoline is important. Over the past few decades, transition-metal-catalyzed C−H functionalization has emerged as a powerful strategy to synthesize complex molecules.[9-12] Recently, rhodium(III)-catalyzed C-H activation leading to C−C and C−X (X= O, and N) bond formation has attracted much attention due to the high efficiency.[13-17] Nevertheless, how to control the regioselectivity if the substrates have more than one reacting C−H bond remains a challenge. Therefore, chelation-assisted transformation has become a common and powerful method for the regioselective functionalization of C–H bonds.[18, 19]



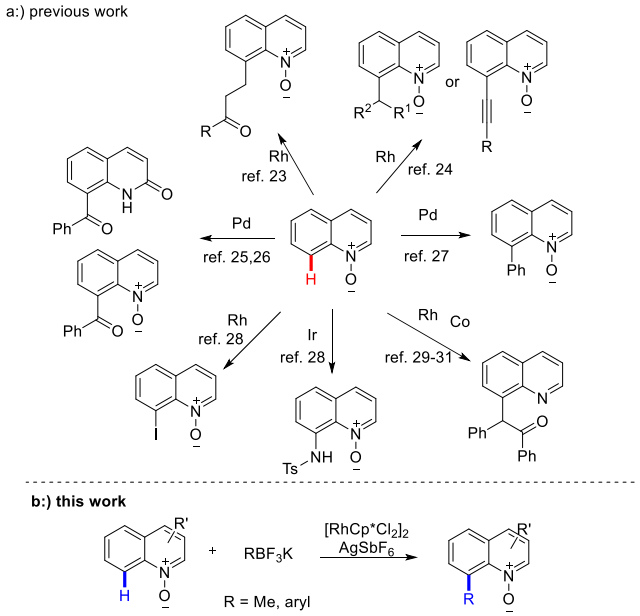

**Scheme 1.** Selected examples of biologically active compounds containing 8-methylquinoline core.

Recently, much effort has been made in the area of C−H functionalization of quinoline at different positions.[20, 21] *N*-Oxide as a directing group has attracted significant attention, which has been used to achieve the desired regioselective control. A significant number of methods exist for transition-metal-catalyzed functionalization at the C2 position of quinoline *N*-oxides, such as olefination,[22] sulfonylation,[23] alkylation,[24] acetoxylation,[25] phosphonation, arylation,[26, 27] and amination.[28, 29] By contrast, only a few examples have been reported for the selective C-8 functionalization of quinoline *N*-oxides.[30-39] In 2014, Chang and co-workers developed two catalytic procedures to 8-iodinated and 8-aminated quinolines using rhodium and iridium catalytic systems.[35] Rh- and Co-catalyzed C−C coupling with alkynes at the C8 position of quinoline *N*-oxides was disclosed by Li's,[36] Chang's,[37] and Sundararaju's groups.[38] In addition, Larionov developed the palladium-catalyzed C8 arylation and selective homocoupling of quinoline *N*-oxides.[34, 39] Recently, organoboron reagents, especially alkyl boron reagents, have been used extensively in C−H functionalization.[40-44] However, related alkylation at the C8 position of quinoline *N*-oxides with

10.1002/adsc.201700484

organoboron reagents remains unexplored.[45-49] Inspired by the previous work by Li[50] and our groups,[51] we disclose a Rh(III)-catalyzed C8 functionalization of quinoline *N*-oxides with organoboron reagents (Scheme 2).

Initially, our studies focused on the rhodium-catalyzed cross coupling between 4-methylquinoline 1-oxide **1a** and readily available potassium methyltrifluoroborate **2a** (Table 1). In the presence of 5 mol% $[RhCp^*Cl_2]_2$, 20 mol% $AgSbF_6$, and 1.5 equivalents of $Ag_2O$ under argon at 65 °C, an 18% yield of product **3a** was detected by $^1H$ NMR analysis (entry 1). After a series of oxidants were screened, AgOAc was found to be the most effective, giving **3a** at 36% yield (entry 3); $Ag_2CO_3$ and AgF

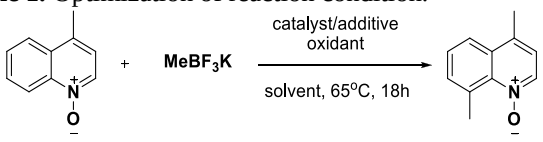



**Scheme 2.** C8-Selective Functionalization of quinoline *N*-oxides.

showed comparable efficiency (entries 2 and 7), while other oxidants gave no product (entries 4-6). On the other hand, no product was formed with $[IrCp^*Cl_2]_2$ or $[RuCl_2(p\text{-Cymene})]_2$ (entries 8 and 9). The efficiency of this catalytic C-H methylation was dependent on the solvents employed. Dimethoxyethane (DME) was the most effective solvent among those examined (entries 10-14). Encouraged by these results, a survey of the amount of **2a** was conducted, and with the use of 2 equivalents of **2a**, the reaction proceeded more smoothly to afford 89% yield of **3a** upon isolation (entry 15). By contrast, the reaction gave poor conversion when AgSbF6 was absent (entry 16). Therefore, the standard conditions for the Rh-catalyzed C-H functionalization reaction are: 5 mol% $[RhCp^*Cl_2]_2$, 20 mol% $AgSbF_6$, 2 equiv of AgOAc, and 2 equiv of $MeBF_3K$ in DME at 65 °C for 18 h under argon.

Having identified the optimal reaction conditions, we first turned our attention to examining the scope and limitation of quinoline *N*-oxide derivatives, as illustrated in Table 2. It was found that this reaction could tolerate various substrates with both electron-donating and electron-withdrawing substituents (such as Me, phenyl, Cl, Br, and CN) and other functional groups in the quinoline system, and provided the corresponding methylated products at good to excellent yields (**3a-q**). Generally, quinoline *N*-oxides with electron-donating substituents gave higher yields compared with electron-withdrawing substituents (compare compounds **3a**–**d** with **3h**, **3j** and **3l**). In particular, the 4-phenyl substituted substrate 3f showed the best reactivity under the standard reaction conditions. The efficiency of quinoline *N*-oxide methylation was affected significantly by steric hindrance. For instance, compound **3d** with 7-methyl substituents gave only a moderate yield relative to the

**Table 1.** Optimization of reaction condition.[a,b]




**1a** **2a** **3a**

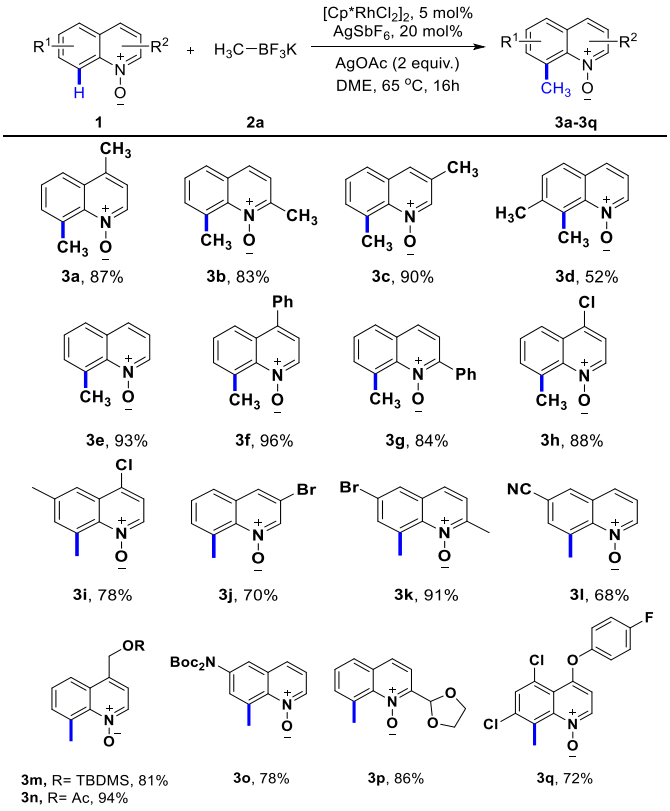
| entry | Catalyst (mol %) | Additive (mol %) | Oxidant (equiv) | Solvent | **3a** Yield (%)[b] |
|---|---|---|---|---|---|
| 1 | $[RhCp^*Cl_2]_2$ (5) | $AgSbF_6$ (20) | $Ag_2O$ (1.5) | DCE | 18 |
| 2 | $[RhCp^*Cl_2]_2$ (5) | $AgSbF_6$ (20) | $Ag_2CO_3$ (1.5) | DCE | 35 |
| 3 | $[RhCp^*Cl_2]_2$ (5) | $AgSbF_6$ (20) | AgOAc (1.5) | DCE | 36 |
| 4 | $[RhCp^*Cl_2]_2$ (5) | $AgSbF_6$ (20) | $AgBF_4$ (1.5) | DCE | ND |
| 5 | $[RhCp^*Cl_2]_2$ (5) | $AgSbF_6$ (20) | AgTFA (1.5) | DCE | ND |
| 6 | $[RhCp^*Cl_2]_2$ (5) | $AgSbF_6$ (20) | AgOTf (1.5) | DCE | ND |
| 7 | $[RhCp^*Cl_2]_2$ (5) | $AgSbF_6$ (20) | AgF (1.5) | DCE | 25 |
| 8 | $[IrCp^*Cl_2]_2$ (5) | $AgSbF_6$ (20) | AgOAc (1.5) | DCE | ND |
| 9 | $[RuCl_2(p\text{-Cymene})]_2$ (5) | $AgSbF_6$ (20) | AgOAc (1.5) | DCE | ND |
| 10 | $[RhCp^*Cl_2]_2$ (5) | $AgSbF_6$ (20) | AgOAc (1.5) | Toluene | 65 |
| 11 | $[RhCp^*Cl_2]_2$ (5) | $AgSbF_6$ (20) | AgOAc (1.5) | MeCN | 55 |
| 12 | $[RhCp^*Cl_2]_2$ (5) | $AgSbF_6$ (20) | AgOAc (1.5) | DMF | 58 |
| 13 | $[RhCp^*Cl_2]_2$ (5) | $AgSbF_6$ (20) | AgOAc (1.5) | DME | 78 |
| 14 | $[RhCp^*Cl_2]_2$ (5) | $AgSbF_6$ (20) | AgOAc (1.5) | THF | 74 |
| **15** | **$[RhCp^*Cl_2]_2$ (5)** | **$AgSbF_6$ (20)** | **AgOAc (2)** | **DME** | **95(89)** |
| 16 | $[RhCp^*Cl_2]_2$ (5) | -- | AgOAc (2) | DME | 16 |

[a] Reaction conditions: **1a** (0.4 mmol), **2a** (1.2 mmol), catalyst (5 mol %), additive (20 mol %) and oxidant in solvent (2.0 mL) under argon at 65 °C for 18 h.

[b] NMR yields using $CH_2Br_2$ as an internal standard, isolated yields in parentheses.

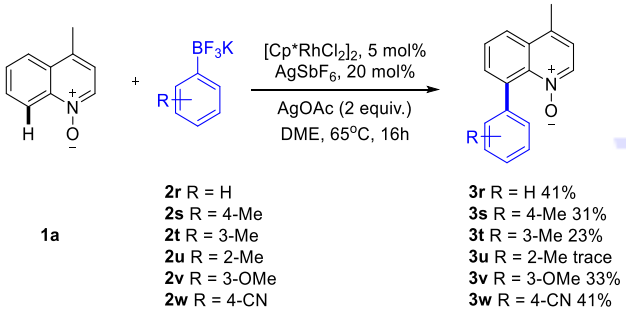
2-, 3- and 4-methyl-substituted quinoline *N*-oxides (**3d** *vs* **3a**−**3c**). It should be mentioned that the substituents of quinoline *N*-oxide at different positions of its aromatic ring did not alter the reaction efficiency; the methylated substrates (**3a**−**c**) provided the desired products in fair yields. Halogenated quinoline *N*-oxides could work without difficulty to provide the desired products such as, 4-chloro-8-methylquinoline *N*-oxide, 4-chloro-6,8-dimethylquinoline *N*-oxide, 3-bromo-8-methylquinoline *N*-oxide, and 6-bromo-2,8-dimethylquinoline *N*-oxide at 88% (**3h**), 78% (**3i**), 70% (**3j**), and 91% (**3k**) yields, respectively. This finding indicated that the products of this reaction were compatible in transition-metal-catalyzed coupling reactions, thus significantly expanding the synthetic utility of this reaction for further transformation. Notably, Various functional groups commonly used in synthetic chemistry, such as cyan (**3l**), silyloxy (**3m**), esters (**3n**), carbamate (**3o**), and acetal (**3p**), were all compatible with the standard reaction conditions to generate the desired products in moderate to good yields, which guaranteed the synthetic application of the current methylation protocol. In addition, the 8-methyl derivative of selective agrochemical fungicide quinoxyfen could be obtained by this directed C-H methylation (**3q**).

**Table 2.** Scope of Quinoline *N*-oxide Derivatives.[a]



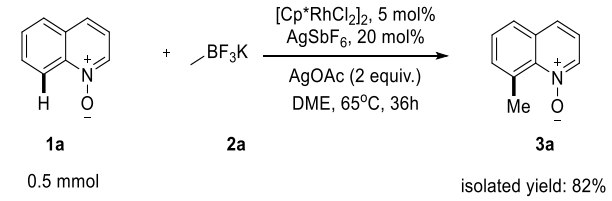

[a] all the reactions were carried out with 0.4 mmol of **1**, 1.2 mmol of **2a**, 0.02 mmol of $[Cp^*RhCl_2]_2$, 0.08 mmol of $AgSbF_6$, 0.8 mmol of AgOAc, 2 mL of DME as solvent under argon atmosphere at 65 °C for 16 h. All listed yields are isolated ones.

Next, in order to expand the utility of this reaction, we investigated a variety of potassium alkyltrifluoroborate derivatives (such as potassium butyltrifluoroborate, potassium cyclopropyltrifluoroborate, potassium allyltrifluoroborate, and potassium benzyltrifluoroborate) as the nucleophilic reagent to obtain the corresponding alkylated products (see Scheme S1 in the supporting information for details). Unfortunately, none of the tested potassium alkyltrifluoroborates provided the desired alkylated products under the optimal reaction conditions and the reactant **1a** can be recovered in 90% amount approximately. GC-MS results show that no self-coupling products or uncontrolled beta-hydride eliminations products of **2** were formed (see the supporting information for details). However, some of the 8-arylated quinoline *N*-oxides were produced using the corresponding potassium aryltrifluoroborates, but only in acceptable yields (23%-41%) (scheme 3). This quinoline *N*-oxide C-8 arylation transformation tolerated either electron-donating or with-drawing substituents in the *para*- or *meta*- positions of the aryltrifluoroborates. In addition, steric hindrance played an important role in the yield of this transformation. For example, methyl substituent at the less sterically hindered *para*-position of the trifluoroborate gave a higher yield than the *meta*-methyl substituted trifluoroborate, while the *ortho*-methylated trifluoroborate was detrimental (**3s-3u**), which indicated the influence of the steric hindrance.



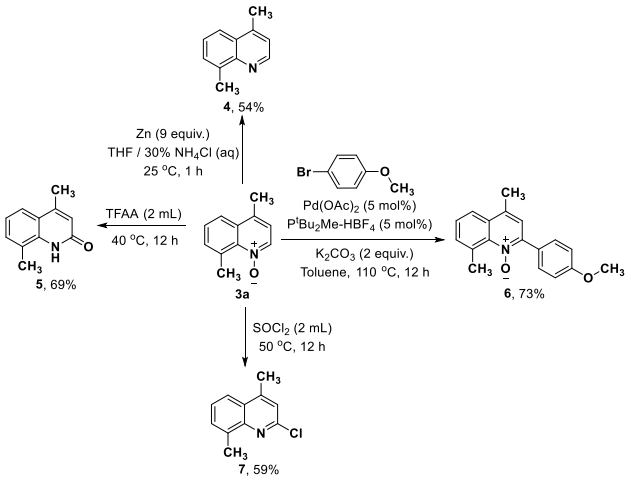

**Scheme 3.** Preliminary study of C-8 arylation transformation.

To demonstrate the synthetic utility of the current methylation protocol, a reaction of **1a** and **2a** was performed on a 5 mmol scale of quinoline *N*-oxide (Scheme 4). Gratifyingly, the methylation efficiency was maintained at a high level in this large scale reaction to give the desired product **3a** at 82% yield when the reaction time was prolonged to 36 hours.



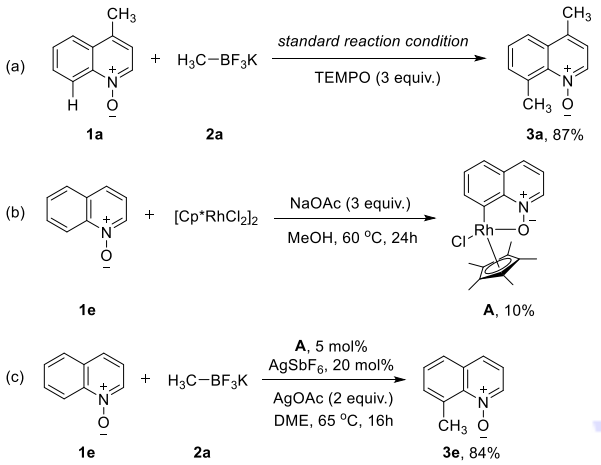

**Scheme 4.** Gram-scale reaction.

As a versatile structural motif, the diversification of quinoline *N*-oxide has been investigated actively. We have performed several transformations of the methylated product **3a**. As depicted in Scheme 5, selective deoxygenation of **3a** was mediated by zinc reagent, leading to the reductive quinoline compound **4** at 54% yield. A 2-Quinolone skeleton was also readily achieved by a rearrangement reaction using trifluoroacetic anhydride (TFAA), gaving a yield of 69%. Furthermore, the N-O moiety was used to incorporate a *p*-methoxyphenyl group at the C2 position at 73% yield by means of a palladium-catalyzed direct arylation reaction. Compound **7** was accomplished at 59% yield via a regioselective conversion of the corresponding quinoline *N*-oxide with thionyl chloride.



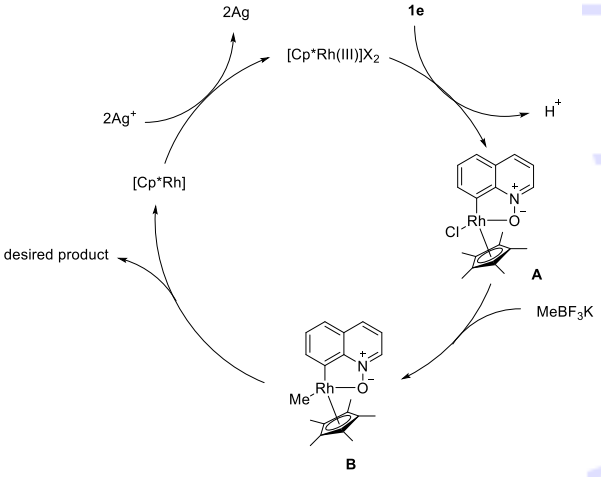

**Scheme 5.** Derivatization of C8-methylated products.

To obtain more insight into the mechanism, a series of control experiments were performed (Scheme 6). First, radical scavenger experiments were conducted in the presence of a typical radical scavenger 2,2,6,6-tetramethylpiperidyl-1-oxyl (TEMPO) under standard reaction conditions (Scheme 6a). No significant effect on the performance of the reaction was observed, which suggested the irrelevancy of the organic radical process in this reaction. Next, we synthesized a five-membered rhodacycle **A** by treating **1e** with $[Cp^*RhCl_2]_2$ and NaOAc (Scheme 6b).[52] Complex **A** was submitted to the reaction to replace the rhodium catalyst and successfully catalyzed the reaction of **1e** with **2a** to afford the desired product **3e** at 84% yield (Scheme 6c). These experiments suggested that the five-membered rhodacycle **A** could be the possible active intermediate species in the catalytic cycle of this reaction.




**Scheme 6.** Preliminary mechanistic studies.

A plausible mechanism is proposed on the basis of preliminary mechanistic experiments and previous reports.[28,29] As shown in Scheme 7, the five-membered rhodacycle **A** intermediate was formed via coordination of the rhodium catalyst with the O atom from the *N*-oxide moiety, and undergoes electrophilic C-H bond cleavage at the C8 position. Next, the complex **A** could convert into intermediate **B** through the transmetalation with the organoboron reagent. Finally, the C-C reductive elimination of intermediate **B** gives rise to the desired product **3a** and the Rh(I) species. The active cationic Cp*Rh(III) species could regenerated by Ag(I)-mediated reoxidization of the Rh(I) species for the next cycle.




**Scheme 7.** Proposed mechanism.

In summary, we have developed a simple, and highly efficient Rh(III)-catalyzed direct site-selective C8-H-methylation and arylation of quinoline *N*-oxides methylation and arylation using potassium trifluoroborates under mild conditions. This reaction features high regioselectivity at the C8 position of quinolines with broad substrate scopes. This concise protocol and further chemical transformations of the

products might have important applications in the synthesis of biologically active compounds. Future exploration of the Rh(III)-catalyzed C8-H activation of quinoline *N*-oxides are underway in our laboratory.

## Experimental Section

**Typical Procedure**

To a 25 mL of Schlenk tube were added quinoline *N*-oxide **1** (0.4 mmol), potassium trifluoroborate **2** (1.2 mmol), $[RhCp^*Cl_2]_2$ (5.0 mol %), $AgSbF_6$ (20.0 mol %), and AgOAc (2.0 equiv) under air. The mixture was then evacuated and backfilled with Ar (3 times). 1,2-dimethoxyethane (DME, 2.0 mL) were added subsequently. The Schlenck tube was screw capped and stirred at 65 $^oC$ for 16 h. After that, the crude product was filtered through a kieselguhr pad and washed with EA/MeOH (10:1, 30 mL). Then, the solvents were removed under vacuo, and the residue was purified by a silica gel column chromatography (EA/MeOH = 10:1) to give the desired products **3**.

## Acknowledgements

*We gratefully acknowledge financial support from the National Natural Science Foundation of China (81620108027, 21632008, 91229204, 81220108025 and 81602975), the Major Project of Chinese National Programs for Fundamental Research and Development (2015CB910304), and National S&T Major Projects (2014ZX09507002-001).*

## References

[1] J. P. Michael, *Nat. Prod. Rep.*, 2008, **25**, 166-187.
[2] V. R. Solomon, H. Lee, *Curr. Med. Chem.*, 2011, **18**, 1488-1508.
[3] A. B. Burgin, O. T. Magnusson, J. Singh, P. Witte, B. L. Staker, J. M. Bjornsson, M. Thorsteinsdottir, S. Hrafnsdottir, T. Hagen, A. S. Kiselyov, L. J. Stewart and M. E. Gurney, *Nat. Biotechnol.*, 2010, **28**, 63-70.
[4] W. A. Denny, B. F. Cain, G. J. Atwell, C. Hansch, A. Panthananickal and A. Leo, *J. Med. Chem.*, 1982, **25**, 276-315.
[5] G. Yang, Y. Si and Z. Su, *Org. Biomol. Chem.*, 2012, **10**, 8418-8425.
[6] Å. Rosenquist, B. Samuelsson, P.-O. Johansson, M. D. Cummings,O. Lenz, P. Raboisson, K. Simmen, S. Vendeville, H. de Kock, M. Nilsson, A. Horvath, R. Kalmeijer, G. de la Rosa and M. Beumont-Mauviel, *J. Med. Chem.*, 2014, **57**, 1673-1693.
[7] M. D. Woodrow, S. P. Ballantine, M. D. Barker, B. J. Clarke, J. Dawson, T. W. Dean, C. J. Delves, B. Evans, S. L. Gough, S. B. Guntrip, S. Holman, D. S. Holmes, M. Kranz, M. K. Lindvaal, F. S. Lucas, M. Neu, L. E. Ranshaw, Y. E. Solanke, D. O. Somers, P. Ward and J. O. Wiseman, *Bioorg. Med. Chem. Lett.*, 2009, **19**, 5261-5265.
[8] M. Kamata, T. Yamashita, T. Imaeda, T. Tanaka, S. Masada, M. Kamaura, S. Kasai, R. Hara, S. Sasaki, S. Takekawa, A. Asami, T. Kaisho, N. Suzuki, S. Ashina, H. Ogino, Y. Nakano, Y. Nagisa, K. Kato, K. Kato and Y. Ishihara, *J. Med. Chem.*, 2012, **55**, 2353-2366.
[9] O. Daugulis, H. Q. Do and D. Shabashov, *Acc. Chem. Res.*, 2009, **42**, 1074-1086.
[10] K. M. Engle, T. S. Mei, M. Wasa and J. Q. Yu, *Acc. Chem. Res.*, 2012, **45**, 788-802.
[11] R. G. Bergman, *Nature*, 2007, **446**, 391-393.
[12] D. A. Colby, R. G. Bergman and J. A. Ellman, *Chem. Rev.*, 2010, **110**, 624-655.
[13] J. Wencel-Delord, T. Droge, F. Liu and F. Glorius, *Chem. Soc. Rev.*, 2011, **40**, 4740-4761.
[14] T. Satoh, M. Miura, *Synthesis*, 2010, **20**, 3395-3409.
[15] T. Satoh, M. Miura, *Chem. Eur. J.*, 2010, **16**, 11212-11222.
[16] D. R. Stuart, M. Bertrand-Laperle, K. M. N. Burgess and K. Fagnou, *J. Am. Chem. Soc.*, 2008, **130**, 16474-16475.
[17] N. Guimond, K. Fagnou, *J. Am. Chem. Soc.*, 2009, **131**, 12050-12051.
[18] H. Kim and S. Chang, *ACS Catal.*, 2016, **6**, 2341-2351.
[19] P. B. Arockiam, C. Bruneau and P. H. Dixneuf, *Chem. Rev.*, 2012, **112**, 5879-5918.
[20] D. E. Stephens, O. V. Larionov, *Tetrahedron*, 2015, **71**, 8683-8716.
[21] T. Iwai, M. Sawamura, *ACS Catal.*, 2015, **5**, 5031-5040.
[22] J. Wu, X. Cui, L. Chen, G. Jiang and Y. Wu, *J. Am. Chem. Soc.*, 2009, **131**, 13888-13889.
[23] B. Du, P. Qian, Y. Wang, H. Mei, J. Han and Y. Pan, *Org. Lett.*, 2016, **18**, 4144-4147.
[24] J. Ryu, S. H. Cho and S. Chang, *Angew. Chem. Int. Ed.*, 2012, **51**, 3677-3681.
[25] X. Chen, C. Zhu, X. Cui and Y. Wu, *Chem. Commun.*, 2013, **49**, 6900-6902.
[26] L. C. Campeau, D. R. Stuart, J. P. Leclerc, M. Bertrand-Laperle, E. Villemure, H. Y. Sun, S. Lasserre, N. Guimond, M. Lecavallier and K. Fagnou, *J. Am. Chem. Soc.*, 2009, **131**, 3291-3306.
[27] S. H. Cho, S. J. Hwang and S. Chang, *J. Am. Chem. Soc.*, 2008, **130**, 9254-9256.
[28] W. Xie, J. H. Yoon and S. Chang, *J. Am. Chem. Soc.*, 2016, **138**, 12605-12614.
[29] C. Zhu, M. Yi, D. Wei, X. Chen, Y. Wu and X. Cui, *Org. Lett.*, 2014, **16**, 1840-1843.
[30] D. Kalsi, R. A. Laskar, N. Barsu, J. R. Premkumar and B. Sundararaju, *Org. Lett.*,

2016, **18**, 4198-4201.
[31] J. Jeong, P. Patel, H. Hwang and S. Chang, *Org. Lett.*, 2014, **16**, 4598-4601.
[32] X. Chen, X. Cui and Y. Wu, *Org. Lett.*, 2016, **18**, 2411-2414.
[33] X. Chen, X. Cui and Y. Wu, *Org. Lett.*, 2016, **18**, 3722-3725.
[34] D. E. Stephens, J. Lakey-Beitia, A. C. Atesin, T. A. Atesin, G. Chavez, H. D. Arman and O. V. Larionov, *ACS Catal.*, 2015, **5**, 167-175.
[35] H. Hwang, J. Kim, J. Jeong and S. Chang, *J. Am. Chem. Soc.*, 2014, **136**, 10770-10776.
[36] X. Zhang, Z. Qi and X. Li, *Angew. Chem. Int. Ed.*, 2014, **53**, 10794-10798.
[37] U. Sharma, Y. Park and S. Chang, *J. Org. Chem.*, 2014, **79**, 9899-9906.
[38] N. Barsu, M. Sen, J. R. Premkumar and B. Sundararaju, *Chem. Commun.*, 2016, **52**, 1338-1341.
[39] D. E. Stephens, J. Lakey-Beitia, G. Chavez, C. Ilie, H. D. Arman and O. V. Larionov, *Chem. Commun.*, 2015, **51**, 9507-9510.
[40] D.-H. Wang, M. Wasa, R. Giri and J.-Q. Yu, *J. Am. Chem. Soc.*, 2008, **130**, 7190-7191.
[41] D. Sarkar and V. Gevorgyan, *Chem. -Eur J.*, 2016, **22**, 11201-11204.
[42] X. Chen, C. E. Goodhue and J.-Q. Yu, *J. Am. Chem. Soc.*, 2006, **128**, 12634-12635.
[43] B.-F. Shi, N. Maugel, Y.-H. Zhang and J.-Q. Yu, *Angew. Chem. Int. Ed.*, 2008, **47**, 4882-4886.
[44] Y. Liu, C. Long, L. Zhao and M.-X. Wang, *Org. Lett.*, 2016, **18**, 5078-5081.
[45] J. K. Matsui, G. A. Molander, *Org. Lett.* 2017, **19**, 950-953.
[46] W. Ren, J. Li, D. Zou, Y. Wu and Y. Wu, *Tetrahedron*. 2012, **68**, 1351-1358.
[47] G.-X. Li, C. A. Morales-Rivera, Y. Wang, F. Gao, G. He, P. Liu and G. Chen, *Chem. Sci.*, 2016, **7**, 6407-6412.
[48] T. Nishida, A. Fukazawa, E. Yamaguchi, H. Oshima, S. Yamaguchi, M. Kanai and Y. Kuninobu, *Chem. -Eur J.*, 2014, **9**, 1026-1030.
[49] H. Brodnik, F. Pozgan and B. Stefane, *Org. Biomol. Chem.*, **2016**, *14*, 1969-1981.
[50] H. Wang, S. Yu, Z. Qi and X. Li, *Org. Lett.*, 2015, **17**, 2812-2815.
[51] P. Peng, J. Wang, H. Jiang and H. Liu, *Org. Lett.*, 2016, **18**, 5376-5379.
[52] R. Sharma, R. Kumar, I. Kumar and U. Sharma, *Eur. J. Org. Chem.*, 2015, 7519-7528.

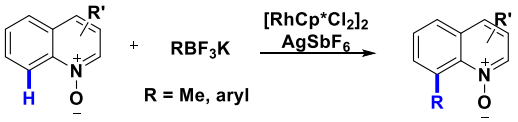
10.1002/adsc.201700484

## UPDATE

# Cp*Rh(III)-Catalyzed Directed C-H Methylation and Arylation of Quinoline *N*-Oxides at the C-8 Position

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

Bao Wang,[‡] Chunpu Li,[‡] and Hong Liu [*]




22 examples, up to 96% yield

- Mild condition & Moderate to excellent yields
- Good regioselectivity
- Good functional group compatability