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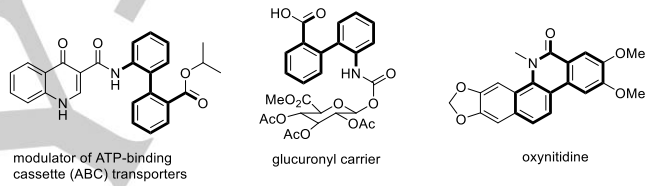
Oxidative C−H/C−H Cross-Coupling Reactions between *N*-Acylanilines and Benzamides Enabled by a Cp*-Free $RhCl_3$/TFA Catalytic System

Yang Shi, Luoqiang Zhang, Jingbo Lan*, Min Zhang, Fulin Zhou, Wenlong Wei, and Jingsong You*

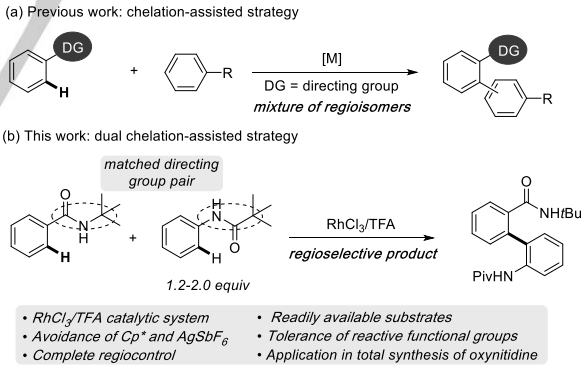
Abstract: Using the dual chelation-assisted strategy, a completely regiocontrolled oxidative C−H/C−H cross-coupling reaction between an *N*-acylaniline and a benzamide has been accomplished for the first time, which enables a step-economical and highly efficient pathway to 2-amino-2'-carboxybiaryl scaffolds from readily available substrates. A Cp*-free $RhCl_3$/TFA catalytic system has been developed to replace the generally used $[Cp^*RhCl_2]_2/AgSbF_6$ (Cp* = pentamethyl cyclopentadienyl) in oxidative C−H/C−H cross-coupling reactions between two (hetero)arenes. The $RhCl_3$/TFA system avoids the use of expensive Cp* ligand and $AgSbF_6$. As an illustrative example, the protocol developed herein greatly streamlines access to naturally occurring benzo[*c*]phenanthridine alkaloid oxynitidine in an excellent overall yield.

2,2'-Difunctional biaryls are important structure motifs in natural products, pharmaceuticals, organic functional materials and ligands for transition metal catalysts.[1] Among various 2,2'-difunctional biaryls, 2-amino-2'-carboxybiaryl scaffolds show versatile biological activities and medicinal properties (Scheme 1).[2] Traditional routes to 2-amino-2'-carboxybiaryls are mainly dependent on the Suzuki coupling reaction after prior *ortho*-halogenation or *ortho*-borylation of benzoic acid and aniline.[2b,3,4] However, *ortho*-prefunctionalization of both substrates typically requires multi-step synthesis and purification procedures. Moreover, an *ortho*-directing group or blocking group at *para*-position is commonly necessary to achieve *ortho*-selectivity,[5] which renders the difficulty in the preparation of substrates. Given that benzoic acids and anilines are both readily available raw materials,[6] from the perspective of starting material availability and step economy, transition metal-catalyzed oxidative cross-coupling between two different *ortho*-C−H bonds of *N*-acylaniline and benzamide is doubtless one of the most attractive approaches to access 2-amino-2'-carboxybiaryls.

Recently, transition metal-catalyzed oxidative C−H/C−H cross-coupling reactions between two arenes have made significant advance.[7] However, controlling the regioselectivity of C−H activation for each coupling partner remains challenging. Besides the chelation-assisted strategy, the regioselectivity of arenes mainly relies on steric and electronic effects.[8] The substrate without distinct electronic effect or steric hindrance inevitably leads to an intractable mixture of regioisomers (Scheme 2a).[9] Thus, the dual chelation-assisted strategy would be an ideal tool to simultaneously accomplish the regioseclective control for both substrates. Despite practical usefulness, such a dual chelation-assisted strategy is rarely reported and appeared until 2015.[10] Manipulating this strategy to access unsymmetrical 2,2'-difunctional biaryls is still a challenging task due to consistent obstacles associated with the chemoselectivity of cross-ccoupling over homo-coupling. In those pioneering works, significant substrate excess is required (usually 3 to 8 equivalents) to increase the amount of the cross-coupled product,[10a,b,d] which restrains the practicality of strategy. Herein, we wish to present the first example of completely regiocontrolled oxidative C−H/C−H cross-coupling reactions between *N*-acylanilines and benzamides *via* a Cp*-free $RhCl_3$/TFA catalytic system to forge 2-amino-2'-carboxybiaryl scaffolds even with a low molar ratio of coupling partners (Scheme 2b).



Scheme 1. Selected examples of 2-amino-2'-carboxybiaryls.



Scheme 2. Evolution of the chelation-assisted oxidative C−H/C−H cross-coupling reactions between two arenes.

Given that $[Cp^*RhCl_2]_2/AgSbF_6$ is most frequently used in rhodium-catalyzed chelation-assisted C−H activation to access bi(hetero)aryls.[11] An initial investigation of the coupling reaction was conducted in the $[Cp^*RhCl_2]_2/AgSbF_6$ catalytic system using *N*-(*tert*-butyl)benzamide (**1a**) and *N*-phenylpivalamide (**2a**) as the model substrates (Table S1). To our delight, the desired biaryl **3a** was obtained in 10% yield (Table S1, entry 1). Using 1.0 equiv of TFA as an additive, the yield increased to 26% (Table S1, entry 2). In addition to the yield, the chemoselectivity of cross-coupling over homo-coupling could be efficiently improved with an increasing amount of TFA. Considering that CF_3COO^- ($OTFA^-$) as

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the anion enables to enhance the electrophilicity of the Rh(III) center,[12] the intermediates were next investigated *via* NMR and HRMS (Figure 1 and Section IX, SI). ESI-HRMS analysis of a mixture of $[Cp^*RhCl_2]_2$, $AgSbF_6$, Ag_2CO_3 and TFA in toluene implies the formation of $[Cp^*Rh(OTFA)]^+$ (**I**) (calcd: 351.0079, found 351.0074) [Eq. (S8)], indicative of the presence of $OTFA^-$ coordinated to the Rh center. ^1H NMR analysis indicates that the methyl hydrogen of $[Cp^*RhCl_2]_2$ shifts from 1.26 to 5.52 ppm. The remarkable downfield chemical shift demonstrates a more electron-deficient rhodium core, suggesting a greater electrophilicity. To our surprise, in the presence of both coupling substrates, $[RhAr^1Ar^2]^+$ (**II**) (Ar^1 = PhCONH*t*Bu; Ar^2 = *p*-CH_3PhNHPiv) (calcd: 469.1362, found 469.1359) was detected rather than $[Cp^*RhAr^1Ar^2]$ (**III**) in ESI-HRMS [Eq. (S9)], implying that Cp* could not be essential in this reaction. Thus, we replaced the $[Cp^*RhCl_2]_2/AgSbF_6$ system with lower-cost $RhCl_3$/TFA. As expected, the yield of the cross-coupled product **3a** remained basically unchanged (Table S1, entry 6).

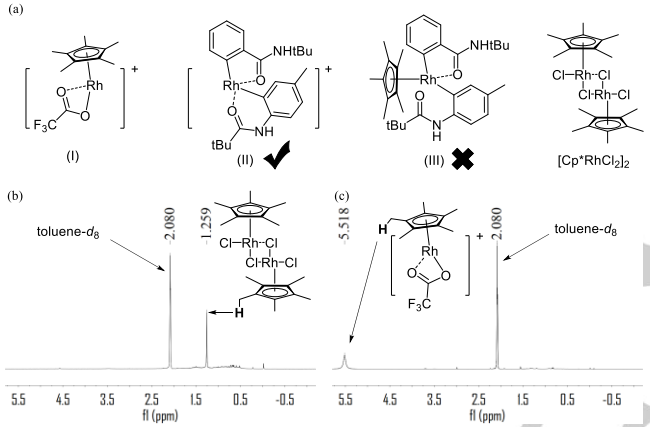
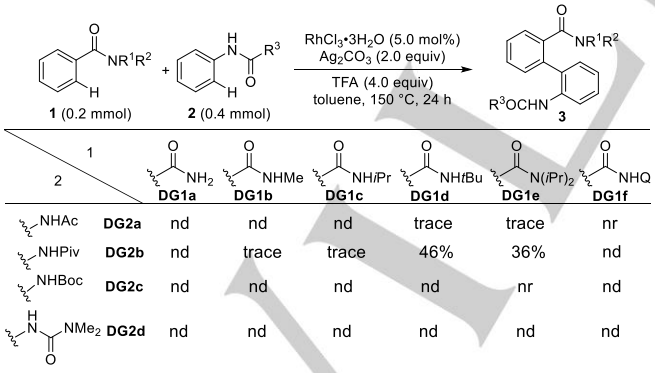
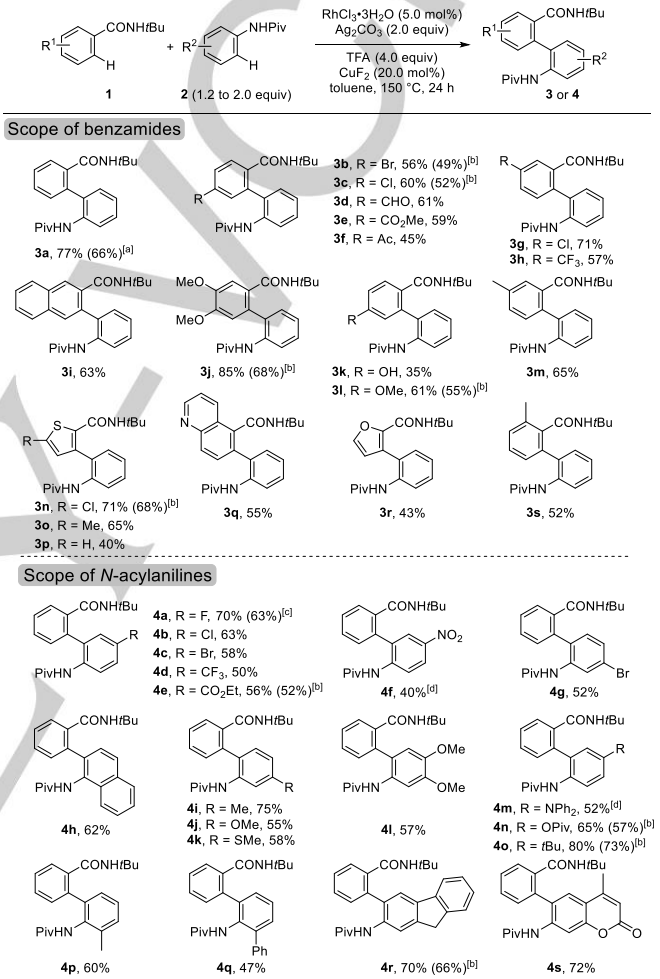


Figure 1. (a) Rh(III) intermediates. ^1H NMR analysis of (b) $[Cp^*RhCl_2]_2$ and (c) $[Cp^*RhCl_2]_2$, $AgSbF_6$, Ag_2CO_3 and TFA-d_1 in toluene-d_8.



Scheme 3. Directing group screening. nd = not detected; nr = no reaction; Q = quinolin-8-yl.

The directing group is known to have a distinct impact on the substrate reactivity associated with electronic nature and steric hindrance. Thus, the oxidative C−H/C−H cross-coupling reactions between benzoic acids and anilines could be conducted by judicious choice of the directing group pair to match the reactivities of both substrates. Subsequently, various directing groups were screened in the $RhCl_3$/TFA system. As a result, the more sterically hindered pivalamido (**DG2b**) and *N*-(*tert*-butyl) carbamoyl (**DG1d**) groups were designated as a matched directing group pair for anilines and benzoic acids, respectively (Scheme 3). After screening of various oxidants, additives and solvents (Tables S3-S6), the optimized result was obtained in toluene at 150 ℃ for 24 h using 5 mol% of $RhCl_3•3H_2O$ as a catalyst, Ag_2CO_3 as an oxidant, TFA and CuF_2 as additives (Table S6, entry 1).



Scheme 4. Scopes of benzamides and *N*-acylanilines. Reaction conditions: **1** (0.2 mmol) and **2** (2.0 equiv) in toluene at 150 °C under N_2 for 24 h. [a] **1a** (5.0 mmol) and **2a** (1.5 equiv). [b] **1** (0.2 mmol) and **2** (1.2 equiv). [c] **1** (0.2 mmol) and **2** (1.5 equiv). [d] AgOTFA (4.0 equiv) instead of Ag_2CO_3 and TFA.

With the optimized reaction conditions in hand, we embarked on exploring substrate scope of benzamides. The benzamides with various electron-withdrawing groups such as halogen, aldehyde, acetyl and ester could smoothly couple with **2a** to deliver the corresponding biaryls (Scheme 4, **3b**-**3h**). Electron-donating groups including alkyl, methoxyl, and even hydroxyl could also be tolerated (Scheme 4, **3j**-**3m** and **3s**). Gratefully, a series of heteroaromatic amides including thiophene, furan and quinoline could also couple with **2a**. The reaction of **1a** (5.0 mmol) with **2a** (7.5 mmol) was carried out on a gram-scale, delivering **3a** in 66% yield (1.16 g), suggesting a potential for mass preparation. It is worthy of note that 1.2 equiv of *N*-acylanilines could give the

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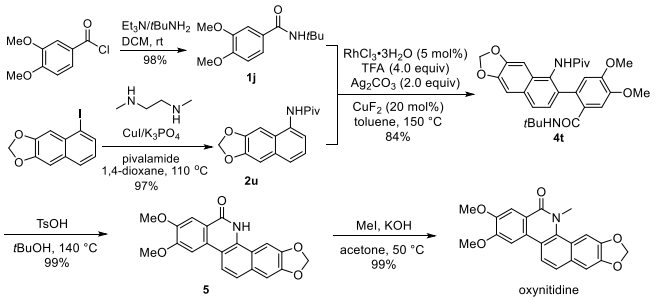
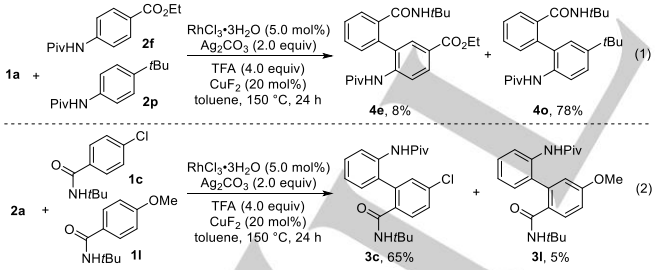
corresponding products in slightly decreased yields (**3b**, **3c**, **3j**, **3l** and **3n**).

The scope of *N*-phenylpivalamide derivatives was also investigated (Scheme 4). The substituents at *ortho*-, *meta*- or *para*-position of anilines showed a negligible effect on the coupling yields. A wide range of substituents from electron-withdrawing groups (Scheme 4, **4a**-**4e, 4g**) to electron-donating groups (Scheme 4, **4i-4j**, **4l-4q**) were compatible with this $RhCl_3$/TFA catalytic system. The nitro and diphenylamino groups could be tolerated using AgOTFA instead of Ag_2CO_3 and TFA (Scheme 4, **4f** and **4m**). The readily oxidizable methene in **4r** could survive from this oxidative catalytic system. Moreover, the natural product coumarin-120 was also modified by this protocol without obstacle (Scheme 4, **4s**).

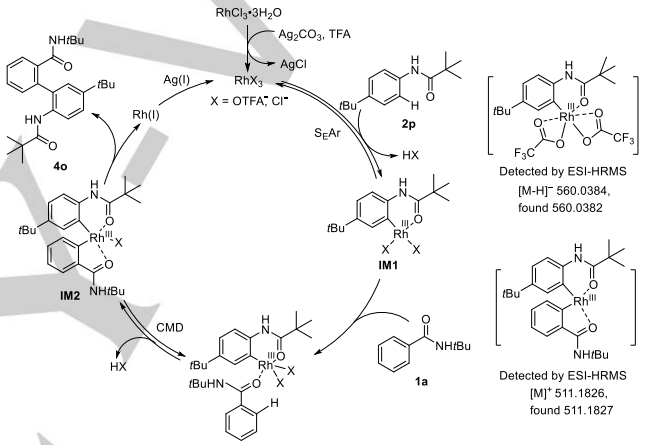


Scheme 5. Total synthesis of oxynitidine.

It is worth noting that many naturally occurring benzo[*c*]phenanthridine alkaloids are of significant biological and drug activities.[2d,13] For example, oxynitidine can effectively inhibit DNA replication in hepatitis B virus.[14] The precedent synthetic routes typically require multistep procedures and complex starting materials and suffered from relatively low yields.[14] To our delight, the current protocol provided a more step-economical and highly efficient pathway to oxynitidine from readily available materials in an excellent overall yield of about 80% (Scheme 5).



To get some insights into the reaction mechanism, a series of experiments were conducted. When *N*-phenylpivalamide (**2a**) was treated with 20.0 equiv of D_2O and 4.0 equiv of TFA-d_1 under the standrad condition for 2 h, the H/D exchange ratio of **2a** was 35% [Eq. (S3)]. This result illustrates that the C−H activation of **2a** is reversible. In contrast, no deuterated [D_n]-**1a** was observed while *N*-(*tert*-butyl)benzamide (**1a**) reacted with 20.0 equiv of D_2O and 4.0 equiv of TFA-d_1 [Eq. (S4)]. However, treatment of **1a** and **2a** in one pot with 20.0 equiv of D_2O and and 4.0 equiv of TFA-d_1 resulted in 10% H/D exchange ratio of **1a** [Eq. (S5)], indicating that the C−H cleavage of **1a** became reversible in the presence of **2a**. Furthermore, the H/D exchange of the amido group of **1a** was not detected in the above experiments, suggesting that **1a** could coordinate to the rhodium center through the carbonyl oxygen atom rather than the nitrogen atom in the formation of cyclometallic complex. Next, kinetic isotope effect (KIE) experiments were performed for both coupling partners. The competition reactions between **1a** or [D_5]-**1a** with **2a** were carried out, and the KIE value was found to be 2.21 [Eq. (S6)], indicating the probable involvement of the C–H bond cleavage of **1a** in the rate-determining step. A KIE value of 1.10 was observed for parallel competition reactions between **2a** or [D_5]-**2a** with **1a** [Eq. (S7)], suggesting that the C–H activation of **2a** might not be involved in the rate-determining step. Finally, the intermolecular competition experiments of electronically differentiated **2f** and **2p** with **1a** as well as **1c** and **1l** with **2a** indicate an electrophilic aromatic substitution (S_EAr) process for the C−H activation of *N*-acylanilines and a concerted metalation-deprotonation (CMD) pathway for the C−H activation of benzamides [Eqs. (1) and (2)].



Scheme 6. Plausible mechanistic pathway.

Based on the above mechanistic studies,[11] a plausible pathway is proposed (scheme 6). Firstly, $RhCl_3$ is transformed to a cationic Rh(III) species in the presence of Ag_2CO_3 and TFA, further increasing the electrophilicity of rhodium core. The more electron-rich aniline substrate **2p** is activated preferentially to form intermediate **IM1** through a S_EAr process,[15] confirmed by ESI-HRMS analysis [Eq. (S10)]. Then, **1a** coordinates with **IM1** and undergoes the second C−H activation *via* a CMD pathway to generate **IM2**, detected by ESI-HRMS [Eq. (S11)]. Next, the reductive elimination of diarylrhodium complex delivers the cross-coupled product **4o**. The generated Rh(I) is re-oxidized to Rh(III) species by Ag(I) to accomplish the catalytic cycle.

In conclusion, we have developed a $RhCl_3$/TFA catalytic system instead of $[Cp^*RhCl_2]_2$/$AgSbF_6$ and have accomplished for the first time the completely regiocontrolled oxidative C−H/C−H cross-coupling reactions between benzamides and *N*-acylanilines through the dual chelation-assisted strategy. This protocol enables a step-economical and highly efficient pathway to 2-amino-2'-carboxybiaryl scaffolds from readily available substrates. The $RhCl_3$/TFA catalytic system exhibits high catalytic activity and excellent tolerance of reactive functional groups. This strategy has been successfully applied in the total synthesis of natural product, which greatly shortens the synthetic route to oxynitidine. This work represents a new perspective for the study of the

oxidative C–H/C–H cross-coupling reaction between two functionality-containing arenes to access unsymmetrical 2,2'-difunctional biaryls.

Acknowledgements

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Keywords: oxidative C−H/C−H cross-coupling • 2-amino-2'-carboxybiaryls • dual chelation-assisted strategy • high regioselectivity • synthesis of oxynitidine

[1] a) G. Bringmann, A. J. P. Mortimer, P. A. Keller, M. J. Gresser, J. Garner, M. Breuning, *Angew. Chem. Int. Ed*. **2005**, *44*, 5384; *Angew. Chem.* **2005**, *117*, 5518; b) J. Yamaguchi, A. D. Yamaguchi, K. Itami, *Angew. Chem. Int. Ed*. **2012**, *51*, 8960; *Angew*. *Chem*. **2012**, *124*, 9092.

[2] a) R. G. G. Leenders, H. W. Scheeren, *Tetrahedron Lett.* **2000**, *41*, 9173; b) S. S. Hadida Ruah, A. R. Hazlewood, P. D. J. Grootenhuis, F. F. van Goor, A. K. Singh, J. Zhou, J. Mccartney, WO 2006/002421A2; c) E. Wahlberg, T. Karlberg, E. Kouznetsova, N. Markova, A. Macchiarulo, A.-G. Thorsell, E. Pol, Å. Frostell, T. Ekblad, D. Öncü, B. Kull, G. M. Robertson, R. Pellicciari, H. Schüler, J. Weigelt, *Nat. Biotechnol*. **2012**, *30*, 283; d) C.-T. Chang, S.-L. Doong, I.-L. Tsai, I.-S. Chen, *Phytochemistry* **1997**, *45*, 1419.

[3] For the Suzuki coupling reactions, see: a) M. A. Siddiqui, V. Snieckus, *Tetrahedron Lett*. **1988**, *29*, 5463; b) E. Perissutti, F. Frecentese, A. Lavecchia, F. Fiorino, B. Severino, F. de Angelis, V. Santagada, G. Caliendo, *Tetrahedron* **2007**, *63*, 12779; c) E. A. Makhneva, A. V. Lipeeva, E. E. Shults, M. M. Shakirov, G. A. Tolstikov, *Russ. J. Org. Chem*. **2012**, *48*, 1094; d) S. Ito, S. Hiroto, H. Shinokubo, *Org. Lett*. **2013**, *15*, 3110.

[4] For the Ullmann-type coupling reactions, see: S. Patil, S. Kamath, T. Sanchez, N. Neamati, R. F. Schinazi, J. K. Buolamwini, *Bioorg. Med. Chem*. **2007**, *15*, 1212.

[5] a) S. H. Lee, B.-B. Jang, Z. H. Kafafi, *J. Am. Chem. Soc*. **2005**, *127*, 9071; b) R. B. Bedford, M. F. Haddow, C. J. Mitchell, R. L. Webster, *Angew. Chem. Int. Ed*. **2011**, *50*, 5524; *Angew. Chem*. **2011**, *123*, 5638; c) N. Schröder, J. Wencel-Delord, F. Glorius, *J. Am. Chem. Soc*. **2012**, *134*, 8298.

[6] a) J. L. Radomski, *Annu. Rev. Pharmacol. Toxicol*. **1979**, *19*, 129; b) L. J. Gooβen, N. Rodríguez, K. Gooβen, *Angew. Chem. Int. Ed*. **2008**, *47*, 3100; *Angew. Chem*. **2008**, *120*, 3144.

[7] For selected reviews on C−H/C−H cross-couplings of two (hetero)arenes, see: a) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu, *Angew. Chem. Int. Ed*. **2009**, *48*, 5094; *Angew. Chem*. **2009**, *121*, 5196; b) J. A. Ashenhurst, *Chem. Soc. Rev*. **2010**, *39*, 540; c) C. S. Yeung, V. M. Dong, *Chem. Rev*. **2011**, *111*, 1215; d) S. H. Cho, J. Y. Kim, J. Kwak, S. Chang, *Chem. Soc. Rev*. **2011**, *40*, 5068; e) N. Kuhl, M. N. Hopkinson, J. Wencel-Delord, F. Glorius, *Angew. Chem. Int. Ed*. **2012**, *51*, 10236; *Angew. Chem*. **2012**, *124*, 10382; f) K. Hirano, M. Miura, *Chem. Commun*. **2012**, *48*, 10704; g) C. Liu, J. Yuan, M. Gao, S. Tang, W. Li, R. Shi, A. Lei, *Chem. Rev*. **2015**, *115*, 12138; h) Y. Yang, J. Lan, J. You, *Chem. Rev*. **2017**, *117*, 8787.

[8] a) C. S. Yeung, X. Zhao, N. Borduas, V. M. Dong, *Chem. Sci*. **2010**, *1*, 331; b) F. Yang, F. Song, W. Li, J. Lan, J. You, *RSC Adv*. **2013**, *3*, 9649; c) Z. Yang, F.-C. Qiu, J. Gao, Z.-W. Li, B.-T. Guan, *Org. Lett*. **2015**, *17*, 4316.

[9] a) B.-J. Li, S.-L. Tian, Z. Fang, Z.-J. Shi, *Angew. Chem. Int. Ed*. **2008**, *47*, 1115; *Angew. Chem*. **2008**, *120*, 1131; b) J. Wencel-Delord, C. Nimphius, H. Wang, F. Glorius, *Angew. Chem. Int. Ed*. **2012**, *51*, 13001; *Angew. Chem*. **2012**, *124*, 13175.

[10] a) X.-S. Zhang, Y.-F. Zhang, Z.-W. Li, F.-X. Luo, Z.-J. Shi, *Angew. Chem. Int. Ed*. **2015**, *54*, 5478; *Angew. Chem*. **2015**, *127*, 5568; b) C. Zhang, Y. Rao, *Org. Lett*. **2015**, *17*, 4456; c) C. Du, P.-X. Li, X. Zhu, J.-F. Suo, J.-L. Niu, M.-P. Song, *Angew. Chem. Int. Ed*. **2016**, *55*, 13571; *Angew. Chem*. **2016**, *128*, 13769; d) C. Zhang, T. Li, L. Wang, Y. Rao, *Org. Chem. Front*. **2017**, *4*, 386; e) C. Zhang, Y. Song, Z. Sang, L. Zhan, Y. Rao, *J. Org. Chem*. **2018**, *83*, 2582.

[11] For selected examples for chelation-assisted Rh(III)-catalyzed C−H activation, see: a) G. Song, X. Li, *Acc. Chem. Res*. **2015**, *48*, 1007; b) J. Wencel-Delord, C. Nimphius, F. W. Patureau, F. Glorius, *Angew. Chem. Int. Ed*. **2012**, *51*, 2247; *Angew. Chem*. **2012**, *124*, 2290; c) J. Dong, Z. Long, F. Song, N. Wu, Q. Guo, J. Lan, J. You, *Angew. Chem. Int. Ed*. **2013**, *52*, 580; *Angew. Chem*. **2013**, *125*, 608; d) B. Li, J. Lan, D. Wu, J. You, *Angew. Chem. Int. Ed*. **2015**, *54*, 14008; *Angew. Chem*. **2015**, *127*, 14214; e) Y. Zhang, H. Zhao, M. Zhang, W. Su, *Angew. Chem. Int. Ed*. **2015**, *54*, 3817; *Angew. Chem*. **2015**, *127*, 3888; f) H. Gong, H. Zeng, F. Zhou, C.-J. Li, *Angew. Chem. Int. Ed*. **2015**, *54*, 5718; *Angew. Chem*. **2015**, *127*, 5810.

[12] J. Zakzeski, A. Behn, M. Head-Gordon, A. T. Bell, *J. Am. Chem. Soc*. **2009**, *131*, 11098.

[13] a) K. W. Bentley, *Nat. Prod. Rep.* **1992**, *9*, 365; b) S. E. Nasrabady, A. Kuzhandaivel, M. Mladinic, A. Nistri, *Cell Mol Neurobiol*. **2011**, *31*, 503.

[14] a) M. Hanaoka, H. Yamagishi, M. Marutani, C. Mukai, *Chem. Pharm. Bull*. **1987**, *35*, 2348; b) R. D. Clark, Jahangir, *J. Org. Chem*. **1988**, *53*, 2378; c) D. Pérez, E. Guitián, L. Castedo, *J. Org. Chem*. **1992**, 57, 5911; d) T. N. Le, S. G. Gang, W.-J. Cho, *Tetrahedron Lett*. **2004**, *45*, 2763; e) T. N. Le, S. G. Gang, W.-J. Cho, *J. Org. Chem*. **2004**, *69*, 2768; f) T. N. Le, W.-J. Cho, *Chem. Pharm. Bull*. **2006**, *54*, 476; g) T. N. Le, H. T. M. Van, S.-H. Lee, H. J. Choi, K. Y. Lee, B. Y. Kang, W.-J. Cho, *Arch. Pharm. Res*. **2008**, *31*, 6; h) R. P. Korivi, C.-H. Cheng, *Chem. Eur. J*. **2010**, *16*, 282; i) P. Lv, K. Huang, L. Xie, X. Xu, *Org. Biomol. Chem*. **2011**, *9*, 3133; j) E. D. D. Calder, F. I. McGonagle, A. H. Harkiss, G. A. McGonagle, A. Sutherland, *J. Org. Chem*. **2014**, *79*, 7633.

[15] Although the possibility that the initial metallization process occurs at **2p** is more favourable, at this stage the catalytic cycle starting from the C–H activation of **1a** cannot be ruled out.

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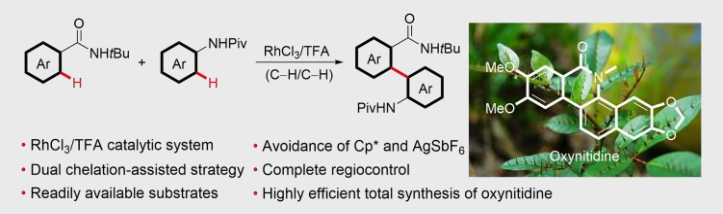

Dual chelation-assisted strategy: A completely regiocontrolled oxidative C−H/C−H cross-coupling reaction between benzamide and *N*-acylaniline has been accomplished for the first time through a Cp*-free $RhCl_3$/TFA catalytic system instead of expensive Cp* ligand and $AgSbF_6$. The strategy greatly streamlines access to naturally occurring benzo[*c*]phenanthridine alkaloid oxynitidine in an excellent overall yield.

Yang Shi, Luoqiang Zhang, Jingbo Lan, Min Zhang, Fulin Zhou, Wenlong Wei, and Jingsong You**

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Oxidative C−H/C−H Cross-Coupling Reactions between *N*-Acylanilines and Benzamides Enabled by a Cp*-Free $RhCl_3$/TFA Catalytic System