

Accepted Article

Title: Ligand-Promoted Rhodium(III)-Catalyzed ortho-C-H Amination with Free Amines

Authors: Huai-Wei Wang, Yi Lu, Bing Zhang, Jian He, Hua-Jin Xu, Yan-Shang Kang, Wei-Yin Sun, and Jin-Quan Yu

This manuscript has been accepted after peer review and appears as an Accepted Article online prior to editing, proofing, and formal publication of the final Version of Record (VoR). This work is currently citable by using the Digital Object Identifier (DOI) given below. The VoR will be published online in Early View as soon as possible and may be different to this Accepted Article as a result of editing. Readers should obtain the VoR from the journal website shown below when it is published to ensure accuracy of information. The authors are responsible for the content of this Accepted Article.

To be cited as: Angew. Chem. Int. Ed. 10.1002/anie.201703300 Angew. Chem. 10.1002/ange.201703300

Link to VoR: http://dx.doi.org/10.1002/anie.201703300 http://dx.doi.org/10.1002/ange.201703300

WILEY-VCH

Ligand-Promoted Rhodium(III)-Catalyzed *ortho*-C–H Amination with Free Amines

Huai-Wei Wang, Yi Lu,^{*} Bing Zhang, Jian He, Hua-Jin Xu, Yan-Shang Kang, Wei-Yin Sun,^{*} Jin-Quan Yu^{*}

Abstract: Ligand development for Rh(III)-catalyzed C–H activation reactions are largely limited to Cp based scaffolds. 2-Methylquinoline is identified as a feasible ligand which can coordinate to the metal center of Cp*RhCl to accelerate the cleavage of C–H bond of N-pentafluorophenylbenzamides, providing a new structural lead for ligand design. The compatibility of this reaction with secondary free amines and anilines also overcomes the limitations of Pd(II)-catalyzed C–H amination reactions.

Aryl amines are privileged structural fragments in modern drug discovery.^[1] Recently, transition-metal-catalyzed C–H activation/amination of arenes via an organometallic metal insertion approach has emerged as a significant area of research towards developing new methods for the synthesis of aryl amines.^[2] A redox catalytic cycle proceeding via metal insertion and subsequent oxidation with chalcogenide type N–O or N-halogen amino donors (such as *N*-benzoate alkylamines, *N*-chloroamines, *N*-



Scheme 1. Transition-Metal-Catalyzed C-H Amination Reactions

[*] Mr. H.-W. Wang, Prof. Dr. Y.Lu, Mr. B. Zhang, Mr. H.-J. Xu, Mr. Y.-S. Kang, Prof. Dr. W.-Y. Sun

Coordination Chemistry Institute, State Key Laboratory of Coordination Chemistry, School of Chemistry and Chemical Engineering, Nanjing National Laboratory of Microstructures, Collaborative Innovation Center of Advanced Microstructures, Nanjing University, Nanjing 210023, China. E-mail: <u>luyi@nju.edu.cn</u>; <u>sunwy@nju.edu.cn</u> Dr. J. He, Prof. Dr. J.-Q. Yu

Department of Chemistry, The Scripps Research Institute (TSRI) 10550 North Torrey Pines Road, La Jolla, CA 92037 (USA) E-mail: vu200@scripps.edu

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201xxxxxx. hydroxycarbamates, O-acylhydroxylamines, nitrosobenzenes, azides, and 1,4,2-dioxazol-5-one) has been extensively explored with Pd(II),^[3,4] Ir(III),^[5] Rh(III),^[6] Ru(II),^[7] Cu(II),^[8] Co(II)^[9] and Fe(II)^[10] catalysts (Scheme **1a**). While these reactions establish the feasibility of the C–H insertion and C–N reductive elimination steps with a number of synthetically useful directing groups, the use of a chalcogenide type amino electrophiles is not ideal due to the costs and limited scope of amino groups that can be introduced. Thus, the development of the direct intermolecular coupling of arenes with free amines as nucleophiles is a significant task.

Although the Pd(II)-catalyzed C-H coupling with organometallic carbon nucleophiles via Pd(II)/Pd(0) catalysis has been demonstrated.^[11] analogous coupling using strongly coordinative free amines remains an unmet challenge. On the other hand, C-H amination with secondary and primary amines has been made possible with Cu(II), Ni(II) and Co(III) catalysts (Scheme 1b).^[12] Although the use of bidentate directing groups containing quinoline or oxazoline moieties substantially improved the scope of amine coupling partners, anilines, especially are poor coupling partners in general, with N-alkyl anilines being completely inactive. Significant progress has also been made with Ir(III) catalyst to enable ortho-C-H amination of benzamides using simple anilines and alkylamines as coupling partners. However, the involvement of a nitrene insertion pathway excluded secondary amines (Scheme 1b).^[13] Moreover, Rh(III)-catalyzed intermolecular C-H amination is uniformly limited to pre-activated amine coupling partners.^[6] Such limitations point to the need of development of new ligands for Rh(III) catalysts. Herein, we report the identification of a new quinoline ligand to promote Rh(III)-catalyzed ortho-C-H amination with free amines. Notably, both secondary amines and primary anilines are compatible with this newly developed catalytic system.

The combination of mono-dentate weakly coordinating amide substrates and ligands has enabled a great number of Pd(II)catalyzed C-H activation reactions. The synthetic utility and practicality of our N-pentafluorophenylbenzamide directing group has been demonstrated by an elegant synthetic route developed by a Novartis process team.^[14] Inspired by the aforementioned progress on C-H amination, we began to investigate the possibility of achieving Rh(III)-catalyzed C-H amination with morpholine using a simple mono-dentate amide directing group, anticipating potential ligand development. We commenced our investigation with Narylamide substrate 1a and morpholine 2a using [RhCp*Cl₂]₂ as the catalyst (Table S1). We found that the addition of Ag₂CO₃ and NaOAc in MeCN afforded the aminated product 3a in 8% yield (Table S1, entry 1). We further optimized reaction parameters by carrying out the screening of oxidants, solvents, and bases to obtain the optimum yield and found that the presence of PhCO2Na increased the yield to 34% (Table S1, entry 7).

Based on the impact of ligand development in Pd(II)-catalyzed C–H amination reactions,^[3c,3d] it is reasonable to assume that the use of proper ligands could accelerate $C(sp^2)$ –H cleavage and promote subsequent the C–N formation step by potentially tuning the steric

and electronic properties of the active catalyst. Notably, ligand scaffolds for Rh(III) catalysts are largely limited to Cp-based ligand scaffolds. To identify new ligand scaffolds for Rh(III) catalysts, a series of simple pyridine-based ligands were tested for their efficiency of promoting amination (Table 1). Encouragingly, pyridine (L1) gave the desired product in 54% yield. Further ligand screening showed that an electron-withdrawing substituent (L2) had a slightly negative impact on the reaction, while the electrondonating ones (L3-L7) significantly improved the yield of the desired product (46-79%). We further investigated quinoline-based ligands (L8-L19) and found that 2-methylquinoline (L9) possessed an optimal balance of steric and electronic properties to provide 3a in the highest yield (82%). Reducing catalyst loading to 2.5 and 5 mol% decreased the yields to 45 and 67% respectively. To elucidate the role of the ligand, we examined the influence of L9 on the rate profile (Figure S2), which revealed that the ligand significantly accelerates the rate of this C-H amination reaction. The mono-Nprotected amino acid (MPAA) and phosphine ligands had been studied for this reaction as well, and we found that MPAA could also accelerate this C(sp²)-H amination reaction to some extent (Table S2).

Table 1. Screening of Ligands.[a,b]



[a] Conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), [RhCp*Cl₂]₂ (5 mol %), Ag₂CO₃ (0.2 mmol), **ligand** (20 mol %), PhCO₂Na (0.2 mmol) and dry toluene (2 mL) under N₂, 16 h, 90 °C. [b] The yield was determined by ¹H NMR analysis of the crude product using CH₂Br₂ as the internal standard.

With the optimized conditions in hand, we examined the scope of N-pentafluoroarylbenzamides (**1b–1t**) with morpholine **2a** (Table 2). To our delight, the substrates bearing various substituents were compatible with the reaction system, affording the desired products

in moderate to good yields (56-88%). In general, the reactivity of electron-rich substrates (1a-1h) was more efficient compared to that of electron-deficient substrates (1k-1r). Nonsubstituted benzamide substrate 1i afforded the desired product in good yield (77%). Notably, only monoaminated products were formed in all cases. Moreover, for *meta*-substituted benzamides (1b, 1d, and 1l), selective C-H functionalization occurred exclusively at the less hindered position, showing good regioselectivity in this reaction system. Gratifyingly, 2-naphthamide 1j was also applicable under the standard conditions, affording the desired product 3j in reasonable yield. Noteworthy, this transformation also well tolerated halogenated substituents, especially the iodo group, which was apt to participate in cross-coupling reactions. In addition, we were pleased to find that heterocyclic amides, including furan 1s and thiophene 1t, are competent substrates and could also be aminated in moderate yields (3s and 3t, 56% and 68%, respectively). We also prepared 3g on a gram scale in order to demonstrate the preparative utility of this transformation. After treatment of the aminated products with BF₃•Et₂O in methanol, the auxiliary can be readily removed and converted to methyl esters in good yields (Supporting Information).

Table 2. Scope of Benzamide Substrates.[a,b]



$$\label{eq:lagrangian} \begin{split} \text{[a] Conditions: $1a$-1t (0.1 mmol), $2a$ (0.2 mmol), $[RhCp*Cl_2]_2$ (5 mol %), Ag_2CO_3 (0.2 mmol), $L9$ (20 mol %), $PhCO_2Na$ (0.2 mmol) and dry toluene (2 mL) under N_2, $16 h, $90 °C. [b] Isolated yield. [c] The reaction was performed on a 3 mmol scale. \end{split}$$

To further explore the scope of the amination reaction, various secondary amines had been tested. As shown in Table 3, the reaction of substrate 1a with a series of six-membered cyclic secondary amines, such as piperidine, 4-methylpiperidine, ethylisonipecotate, 4-cyanopiperidine, 1,4-dioxa-8-azaspiro[4.5]decane and Bocprotected 4-aminopiperidine under the optimized conditions afforded the corresponding aminated products in 62-80% yields (4b-4g). Moreover, the coupling of 1a with some simple secondary amines, such as N-methylpropan-1-amine and N-ethylethanamine also gave the aminated products 4h and 4i in 72% and 52% yields, respectively. Notably, with respect to 1a, 4-tert-butyl benzamide 1g afforded a higher yield (4i vs 4j). Meanwhile, the reaction of substrate 1g with N-methylbenzylamine afforded the desired product 4k in moderate yield. The reaction conditions are also applicable for amination with N-substituted aniline. To the best of our knowledge, no examples of arenes with N-substituted aniline as the coupling partners were demonstrated before. Gratifyingly, we found that the coupling of 1g with N-substituted anilines, such as N-methylaniline and N-ethylaniline could afford the corresponding products 41 and 4m in excellent yields (89% and 80%, respectively).

Table 3. Scope of Secondary Amines.[a,b]



[a] Conditions: **1a** or **1g** (0.1 mmol), **2** (0.2 mmol), $[RhCp*Cl_2]_2$ (5 mol %), Ag₂CO₃ (0.2 mmol), **L9** (20 mol %), PhCO₂Na (0.2 mmol) and dry toluene (2 mL) under N₂, 16 h, 90 °C. [b] Isolated yield. [c] 4 equiv of alkylamines were used.

The successful use of *N*-alkyl anilines prompted us to examine the compatibility of this reaction with free anilines. Transitionmetal-catalyzed amination of arenes with primary amines has been developed using several systems.^[12k,12l,13] However, few examples of electron-rich anilines were demonstrated. Daugulis^[12k] and Jana^[12l] recently disclosed copper-mediated, bidentate auxiliarydirected amination with electron-donating anilines. We were pleased to observe that the present amination conditions were compatible with a wide range of anilines in the reaction of **1a** (Table 4). Anilines bearing electron-withdrawing substituents, such as nitro, nitrile, trifluromethyl, and halogen groups, afforded the desired products **5a–5f** in moderate yields (44–63%). Interestingly, 1-naphthylamine also reacted to furnish the corresponding aminated product **5g** in a moderate yield (56%). Gratifyingly, reactivity of aniline or its derivatives bearing electron-donating functional groups was observed to be good under present conditions. Simple aniline also reacted with **1a**, providing the desired product **5h** in moderate yield (54%). Anilines possessing a methyl substituent afforded the aminated products **5i–5k** in good yields (60–65%). 3,5-Dimethylaniline gave **5l** in the highest yield of 70%. Importantly, anilines possessing electron-donating substituents, such as methoxy and *tert*-butyl groups, also furnished the desired products **5m–5o** in good yields (62–67%).

We next carried out extensive mechanistic investigations to gain further understanding of this ligand-promoted C–H amination reaction. To test the possibility of in situ conversion of the amines to some electrophilic/reactive amines, we monitored the quantity of the free aniline (4-methoxyaniline) and the corresponding amination product **5m** by NMR throughout the reaction course. Only unreacted anilines were observed. Although we observed that large proportion of free aniline was oxidized to diazene species (see the Supporting Information) in the absence of the substrate, control experiment showed that such diazene species are not reactive for this amination reaction. Competition experiments using free anilines (4-(trifluoromethyl)aniline and *p*-toluidine) also revealed that the electron-rich aniline with the stronger nucleophilic property was more reactive in this reaction (see the Supporting Information).

To probe whether C-H activation is rate-determining step in this catalytic cycle, we performed a series of experiments to determine the kinetic isotope effect (KIE). The observed intermolecular KIE of 1.87 and parallel KIE of 1.70 revealed that the ortho-C-H bond cleavage may be the rate-determining step (see the Supporting Information). The key C-H insertion intermediate is also characterized (cyclorhodacyclic complex 7', see the Supporting Information), and transformed into the desired product 5m in isolated yield of 46% under the standard reaction conditions (see the Supporting Information), supporting the involvement of this intermediate. Based on the reaction conditions, a plausible reaction mechanism for this transformation is proposed in Scheme 2. The reaction process is initiated by the coordination of amide 1i to Rh(III) bound to the quinoline ligand (L), which is followed by C-H activation to give the corresponding five-membered rhodacycle intermediate 7. Subsequent ligand exchange at Rh(III) center leads to intermediate 8, which undergoes C-N reductive elimination to give the ortho-aminated product 3i and Rh(I) species. The ligand exchange process has also been observed with phosphine ligands.^[15] The oxidation of Rh(I) by Ag₂CO₃ completes the catalytic cycle.

In summary, we have developed a ligand-promoted Rh(III)catalyzed amination reaction of aryl C–H bonds with free secondary alkyl amines as well as a variety of anilines using a readily removable *N*-pentafluorophenylamide auxiliary. This transformation exhibits a broad substrate scope and tolerates various functional groups. The significant enhancing effect with quinolines also provides a new lead for ligand design in Rh(III)-catalyzed C–H activation reactions.



[a] Conditions: **1a** (0.1 mmol), **3** (0.2 mmol), [RhCp*Cl₂]₂ (5 mol %), Ag₂CO₃ (0.2 mmol), **L9** (20 mol %), PhCO₂Na (0.2 mmol) and dry toluene (2 mL) under N₂, 16 h, 90 °C. [b] Isolated yield. [c] 4 equiv of primary amines were used.



Scheme 2. Proposed Reaction Mechanism.

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

Acknowledgement

We gratefully acknowledge the National Natural Science Foundation of China (grant no. 21671097, 21331002 and 21201100), the National Science Foundation (CHE-1465292) and the Fundamental Research Funds for the Central Universities (020514380071) for financial support.

Keywords: ligand-promoted • amination • free amines • quinoline ligand

- [1] a) R. Hili, A. K. Yudin, Nat. Chem. Biol. 2006, 2, 284; b) A. Ricci, Amino Group Chemistry: From Synthesis to the Life Sciences; Wiley-VCH: Weinheim, 2008; c) J. Yamaguchi, A. D. Yamaguchi, K. Itami, Angew. Chem. Int. Ed. 2012, 51, 8960; Angew. Chem. 2012, 124, 9092.
- [2] For selected reviews of C-H amination, see: a) M.-L. Louillat, F. W. Patureau, *Chem. Soc. Rev.* 2014, 43, 901; b) V. S. Thirunavukkarasu, S. I. Kozhushkov, L. Ackermann, *Chem. Commun.* 2014, 50, 29; c) N. Yoshikai, *ChemCatChem* 2015, 7, 732; d) N. Moselage, J. Li, L. Ackermann, ACS Catal. 2016, 6, 498; e) Y. R. Zhou, J. J. Yuan, Q. Yang, Q. Xiao, Y. Y. Peng, *ChemCatChem* 2015, 8, 2178.
- a) E. J. Yoo, S.; Ma, T.-S. Mei, K. S. L. Chan, J.-Q. Yu, J. Am. Chem. Soc. 2011, 133, 7652; b) M. Anand, R. B. Sunoj, H. F. Schaefer, III. J. Am. Chem. Soc. 2014, 136, 5535; c) D. J. Zhu, G. Q. Yang, J. He, L. Chu, G. Chen, W. Gong, M. D. Eastgate, J.-Q. Yu, Angew. Chem. Int. Ed. 2015, 54, 2497; Angew. Chem. 2015, 127, 2527; d) J. He, T. Shigenari, J.-Q. Yu, Angew. Chem. Int. Ed. 2015, 54, 6545; Angew. Chem. 2015, 127, 6645; e) Q. Gou, G. Liu, Z.-N. Liu, J. Qin, Chem. Eur. J. 2015, 21, 15491; f) M. Anand, R. B. Sunoj, H. F. Schaefer, III. ACS Catal. 2016, 6, 696.
- [4] For Pd-catalyzed C-N bond formation via a plausible nitrene insertion mechanism, see: a) K.-H. Ng, A. S. C. Chan, W.-Y. Yu, J. Am. Chem. Soc. 2010, 132, 12862; b) K.-H. Ng, F.-N. Ng, W.-Y. Yu, Chem. Commun. 2012, 48, 11680.
- [5] a) D. Lee, Y. Kim, S. Chang, J. Org. Chem. 2013, 78, 11102; b) J. Ryu, J. Kwak, K. Shin, D. Lee, S. Chang, J. Am. Chem. Soc. 2013, 135, 12861; c) T. M. Figg, S. Park, J. Park, S. Chang, D. G. Musaev, Organometallics 2014, 33, 4076; d) H. Hwang, J. Kim, J. Jeong, S. Chang, J. Am. Chem. Soc. 2014, 136, 10770; e) J. Kim, S. Chang, Angew. Chem. Int. Ed. 2014, 53, 2203; Angew. Chem. 2014, 126, 2235; f) H. Chen, M. P. Huestis, ChemCatChem 2015, 77, 743. g) P. Becker, R. Pirwerdjan, C. Bolm, Angew. Chem. Int. Ed. 2015, 54, 15493; Angew. Chem. 2015, 127, 15713; h) B. F. Zhu, X. L. Cui, C. Pi, D. Chen, Y. J. Wu, Adv. Synth. Catal. 2016, 358, 326; i) G. N. Hermann, P. Becker, C. Bolm, Angew. Chem. Int. Ed. 2016, 55, 3781; Angew. Chem. 2016, 128, 3845; j) J.-B. Liu, X.-H. Sheng, C.-Z. Sun, F. Huang, D.-Z. Chen, ACS Catal. 2016, 6, 2452.
- a) C. Grohmann, H. G. Wang, F. Glorius, Org. Lett. 2012, 14, 656; b) K.-[6] H. Ng, Z. Y. Zhou, W.-Y. Yu, Org. Lett. 2012, 14, 272; c) J. Y. Kim, S. H. Park, J. Ryu, S. H. Cho, S. H. Kim, S. Chang, J. Am. Chem. Soc. 2012, 134, 9110; d) J. Ryu, K. Shin, S. H. Park, J. Y. Kim, S. Chang, Angew. Chem. Int. Ed. 2012, 51, 9904; Angew. Chem. 2012, 124. 10042; e) K. Shin, Y. Baek, S. Chang, Angew. Chem. Int. Ed. 2013, 52, 8031; Angew. Chem. 2013, 125. 8189; f) D.-G. Yu, M. Suri, F. Glorius, J. Am. Chem. Soc. 2013, 135, 8802; g) Y. Lian, J. R. Hummel, R. G. Bergman, J. A. Ellman, J. Am. Chem. Soc. 2013, 135, 12548; h) S. J. Yu, B. S. Wan, X. W. Li, Org. Lett. 2013, 15, 3706; i) R.-J. Tang, C.-P. Luo, L. Yang, C.-J. Li, Adv. Synth. Catal. 2013, 355, 869; j) B. Zhou, J. J. Du, Y. X. Yang, H. J. Feng, Y. C. Li, Org. Lett. 2013, 15, 6302; k) C. H. Tang, Y. Z. Yuan, Y. X. Cui, N. Jiao, Eur. J. Org. Chem. 2013, 7480; 1) H. J. Kim, M. J. Ajitha, Y. Cull, N. Jiao, Eur. J. Org. Chem. 2010, 1700, 1710, 17 16, 42; o) B. Zhou, J. J. Du, Y. X. Yang, H. J. Feng, Y. C. Li, Org. Lett. 2014, 16, 592; p) W. Yang, J. Q. Sun, X. X. Xu, Q. Zhang, Q. Liu, Chem. Commun. 2014, 50, 4420; q) Y. Park, K. T. Park, J. G. Kim, S. Chang, J. Am. Chem. Soc. 2015, 137, 4534.
- [7] a) M. Bhanuchandra, M. R. Yadav, R. K. Rit, M. R. Kuram, A. K. Sahoo, *Chem. Commun.* 2013, 49, 5225; b) Q.-Z. Zheng, Y.-F. Liang, C. Qin, N. Jiao, *Chem. Commun.* 2013, 49, 5654; c) M. Shang, S.-H. Zeng, S.-Z. Sun, H.-X. Dai, J.-Q. Yu, *Org. Lett.* 2013, 15, 5286; d) V. S. Thirunavukkarasu, K. Raghuvanshi, L. Ackermann, *Org. Lett.* 2013, 15, 3286; e) L-L. Zhang, L.-H. Li, Y.-Q. Wang, Y.-F. Yang, X.-Y. Liu, Y.-M. Liang, *Organometallics* 2014, 33, 1905; f) K. Shin, J. Ryu, S. Chang, *Org. Lett.*

2014, *16*, 2022; g) M. R. Yadav, M. Shankar, E. Ramesh, K. Ghosh, A. K. Sahoo, *Org. Lett.* **2015**, *17*, 1886.

- [8] a) J. L. Peng, Z. Q. Xie, M. Chen, J. Wang, Q. Zhu, Org. Lett. 2014, 16, 4702; b) J. L. Peng, M. Chen, Z. Q. Xie, S. Luo, Q. Zhu, Org. Chem. Front. 2014, 1, 777.
- [9] a) B. Sun, T. Yoshino, S. Matsunaga, M. Kanai, Adv. Synth. Catal. 2014, 356, 1491; b) B. Sun, T. Yoshino, S. Matsunaga, M. Kanai, Chem. Commun. 2015, 51, 4659; c) P. Patel, S. Chang, ACS Catal. 2015, 5, 853; d) J. Park, S. Chang, Angew. Chem. Int. Ed. 2015, 54, 14103; Angew. Chem. 2015, 127, 14309; e) Y. J. Liang, Y.-F. Liang, C. H. Tang, Y. Z. Yuan, N. Jiao, Chem. Eur. J. 2015, 21, 16395; f) R. H. Mei, J. Loup, L. Ackermann, ACS Catal. 2016, 6, 793; g) F. Wang, H. Wang, Q. Wang, S. J. Yu, X. W. Li, Org. Lett. 2016, 18, 1306.
- [10] T. Matsubara, S. Asako, L. Ilies, E. Nakamura, J. Am. Chem. Soc. 2014, 136, 646.
- [11] a) X. Chen, J.-J. Li, X.-S. Hao, C. E. Goodhue, J.-Q. Yu, J. Am. Chem. Soc. 2006, 128, 78; b) X. Chen, C. E. Goodhue, J.-Q. Yu, J. Am. Chem. Soc. 2006, 128, 12634.
- [12] a) X. Chen, X.-S. Hao, C. E. Goodhue, J.-Q. Yu, J. Am. Chem. Soc. 2006, 128, 6790; b) T. Uemura, S. Imoto, N. Chatani, Chem. Lett. 2006, 35, 842; c) A. John, K. M. Nicholas, J. Org. Chem. 2011, 76, 4158. d) L. D. Tran, J. Roane, O. Daugulis, Angew. Chem. Int. Ed. 2013, 52, 6043; Angew. Chem.

2013, 125, 6159; e) A. M. Martínez, N. Rodríguez, R. G. Arrayas, J. C. Carretero, Chem. Commun. 2014, 50, 2801; f) Q. Li, S.-Y. Zhang, G. He, Z. Ai, W. Nack, G. Chen, Org. Lett. 2014, 16, 1764; g) M. Shang, S.-Z. Sun, H.-X. Dai, J.-Q. Yu, J. Am. Chem. Soc. 2014, 136, 3354; h) L. Wang, D. L. Priebbenow, W. R. Dong, C. Bolm, Org. Lett. 2014, 16, 2661; i) Q. Q. Yan, Z. K. Chen, W. L. Yu, H. Yin, Z. X. Liu, Y. H. Zhang, Org. Lett. 2015, 17, 2482; j) P. Sadhu, T. Punniyamurthy, Chem. Commun. 2016, 52, 2803; k) J. Roane, O. Daugulis, J. Am. Chem. Soc. 2016, 138, 4601; l) K. B. Singh, A. Polley, R. Jana, J. Org. Chem. 2016, 81, 4295; m) L. B. Zhang, S. K. Zhang, D. H. Wei, X. J. Zhu, X. Q. Hao, J. H. Su, J. L. Niu, M. P. Song, Org. Lett. 2016, 18, 1318.

- [13] a) H. Kim, K. Shin, S. Chang, J. Am. Chem. Soc. 2014, 136, 5904; b) H. Kim, S. Chang, ACS Catal. 2015, 5, 6665.
- [14] M. H. Daniels, J. R. Armand, K. L. Tan, Org. Lett. 2016, 18, 3310.
- [15] a) X. Yu, Y. Dian, W. Guo, T. Wang, Q. Xie, S. Wu, C. Jiang, Z. Fan, J. Wang, G. Liu, *Organometallics* **2017**, *36*, 1027; b) S. Y. Hong, J. Jeong, S. Chang, *Angew. Chem. Int. Ed.* **2017**, *56*, 2408; *Angew. Chem.* **2017**, *129*, 2448.

C–H Amination

Huai-Wei Wang, Yi Lu,^{*} Bing Zhang, Jian He, Hua-Jin Xu, Yan-Shang Kang, Wei-Yin Sun,^{*} Jin-Quan Yu^{*}

Page – Page

Ligand-Promoted Rhodium(III)-Catalyzed *ortho*-C–H Amination with Free Amines



2-Methylquinoline is identified as an efficient ligand for promoting rhodium(III)catalyzed directed C–H amination of *N*-pentafluorophenylbenzamides, providing a new structural lead for ligand design in Rh(III)-catalyzed C–H activation reactions. Both secondary amines and primary anilines are compatible, thus significantly expanding the scope of C–H amination reaction with free amines.