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Cite this: DOI: 10.1039/c0xx00000x

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COMMUNICATION

One-pot cascade synthesis of *N*-methoxyisoquinolinediones via Rh(III)-catalyzed carbenoid insertion C–H activation/cyclizationJingjing Shi,^a Jie Zhou,^{a,b} Yunnan Yan,^a Jinlong Jia,^a Xuelei Liu,^a Huacan Song,^b H. Eric Xu^{*a,c} and Wei Yi^{*a}⁵ Received (in XXX, XXX) Xth XXXXXXXXXX 20XX, Accepted Xth XXXXXXXXXX 20XX

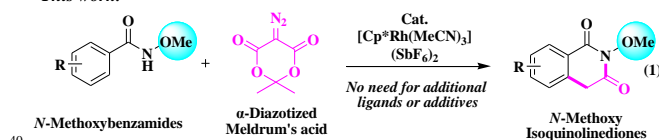
DOI: 10.1039/b000000x

Here a new, mild and versatile method for one-pot cascade synthesis of diversely *N*-methoxyisoquinolinediones via Rh(III)-catalyzed regioselective carbenoid insertion C–H activation/cyclization of *N*-methoxybenzamides by α -diazotized Meldrum's acid has been achieved. Extension of the developed Rh(III) catalysis for building new analogs of marketed drug-Edaravone has been also demonstrated.

Recognizing the great importance of *N*-heterocycles in organic synthesis, medicinal chemistry and material science,¹ chemists continue to devise novel methods for their synthesis.² Among those, transition-metal-catalyzed C–H functionalization has attracted considerable attention since it holds great potential in reshaping traditional organic synthesis.³ Indeed, it has emerged in recent years as one of the most powerful tools for efficient construction of molecular complex in a step-economical and waste-reducing fashion. However, to the best of our knowledge, application of such strategy to building the isoquinolinedione scaffold has not been reported to date. Driven by its biologically applied power,⁴ the development of novel C–H functionalization methods for general and rapid synthesis of the key scaffold would be highly desirable.

Over the past two decades, diazo compounds are widely used as powerful cross-coupling partners for direct C–H activation in transition-metal-catalyzed reaction, of which Rh complexes occupying a prevalent position.⁵ Despite these compelling progress, Rh(III)-catalyzed carbenoid insertion C–H activation for direct construction of *N*-heterocycles is still underexplored, and so far, a few protocols that only used the chain diazo compounds as carbenoid precursors have been reported.⁶ Obviously, more efforts are still need to search and develop new Rh(III)-catalyzed carbenoid insertion C–H activation reactions for efficient synthesis of privileged *N*-heterocycles.

This work:



Motivated by these and in continuation of our interest in the Rh(III)-catalyzed C–H activation,⁷ herein we reported for the first time the one-pot synthesis of *N*-methoxyisoquinolinediones via Rh(III)-catalyzed direct C–H functionalization of simple *N*-methoxybenzamides with cyclic α -diazotized Meldrum's acid (eqn (1)), an efficient cross-coupling partner for direct C–H

alkylation recently disclosed by Li⁸ and our groups.^{7d} Notably, the mild carbenoid insertion cascade C–H activation/cyclization could proceed smoothly under an atmosphere of air and thus obviated the need of additional ligands or additives to induce the catalytic turnover.

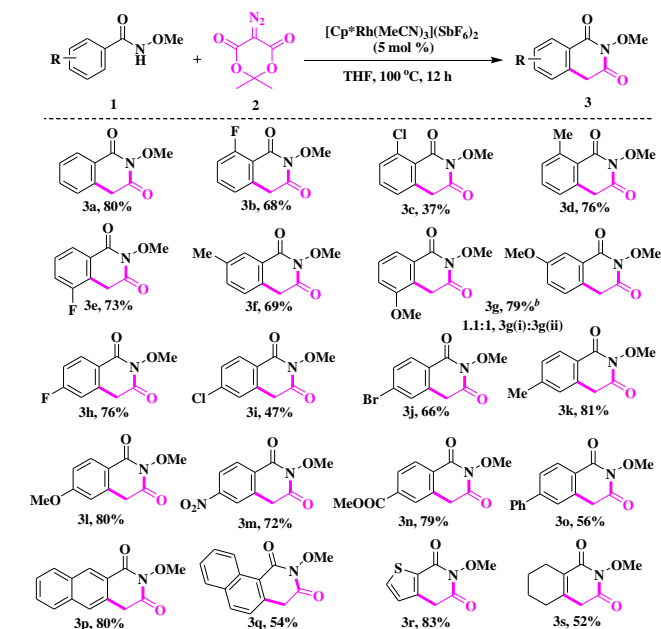
Table 1. Optimization of reaction conditions^a

Entry	Catalyst system (mol %)	Solvent	T(°C)	Yield ^b (%)
1	[Cp*Rh ^{III} (MeCN) ₃](SbF ₆) ₂ (5)	DCE	100	69
2	[Cp*Rh ^{III} (MeCN) ₃](SbF ₆) ₂ (5)	DMF	100	0
3	[Cp*Rh ^{III} (MeCN) ₃](SbF ₆) ₂ (5)	Toluene	100	30
4	[Cp*Rh ^{III} (MeCN) ₃](SbF ₆) ₂ (5)	MeCN	100	0
5	[Cp*Rh ^{III} (MeCN) ₃](SbF ₆) ₂ (5)	MeOH	100	0
5	[Cp*Rh ^{III} (MeCN) ₃](SbF ₆) ₂ (5)	Dioxane	100	75
6	[Cp*Rh ^{III} (MeCN) ₃](SbF ₆) ₂ (5)	THF	100	80
7	[Cp*RhCl ₂] ₂ (5)	THF	100	0
8	[Cp*Rh(OAc) ₂] ₂ (5)	THF	100	0
9	[Cp*Rh ^{III} (MeCN) ₃](SbF ₆) ₂ (2.5)	THF	100	65
10 ^c	[Cp*Rh ^{III} (MeCN) ₃](SbF ₆) ₂ (5)	THF	80	49
11 ^d	[Cp*Rh ^{III} (MeCN) ₃](SbF ₆) ₂ (5)	THF	100	78

^aReaction conditions: **1** (0.20 mmol, 1.0 equiv), **2** (0.22 mmol, 1.1 equiv), Rh catalyst (X mol%), solvent (1.0 mL), 12 h, under air. ^bIsolated yields. ^cFor 36 h.^dPerformed on a 5.0 mmol scale.

Recently, [Cp*Rh(MeCN)₃](SbF₆)₂ has proved to be as one of the most efficient catalysts for C–H activation reaction.⁹ However, based on our literature investigation, such Rh(III) species-catalyzed carbenoid insertion C–H activation for constructing the *N*-heterocycles remains unreported. Therefore, at the outset of this study, we chose [Cp*Rh(MeCN)₃](SbF₆)₂ as the catalyst and employed readily available *N*-methoxybenzamide **1a** and α -diazotized Meldrum's acid **2** as the model substrates. To our delight, the anticipated isoquinolinedione **3a** was obtained in 69% yield under the initial conditions (Table 1, entry 1), and the structure of **3a** was confirmed by single X-ray analysis. A survey of solvents revealed that THF was optimal (entries 1–6), affording the isoquinolinedione **3a** in 80% yield. Other Rh(III) catalysts such as [Cp*RhCl₂]₂ and [Cp*Rh(OAc)₂]₂ exhibited negligible

catalytic activities for the reaction (entries 7-8). Moreover, an attempt to decrease either the catalyst loading or the reaction temperature cut down the yield sharply (entries 9-10). Finally, we were pleased to find that the reaction could be performed on a 5.0 mmol scale under the optimized conditions without significant decrease in the product yield (entry 11).



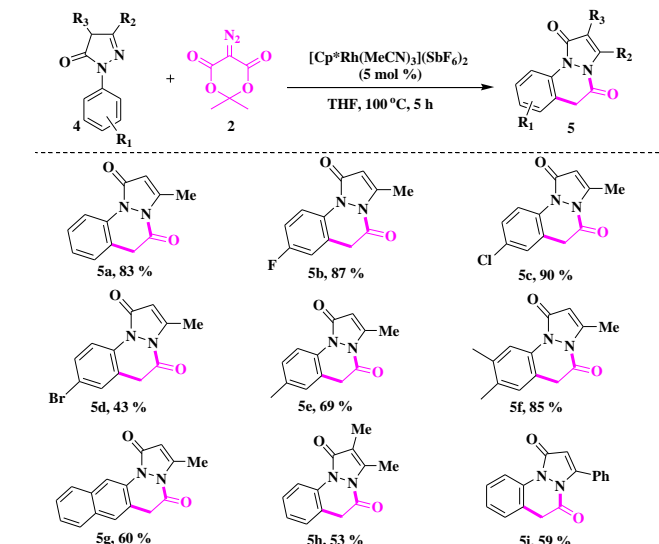
Scheme 2 Scope of *N*-methoxybenzamides. ^aReaction conditions: 1 (0.20 mmol) and 2 (0.22 mmol) in THF (1.0 mL) at 100 °C for 12 h under air. Isolated yields. ^bThe regioisomeric ratio was determined by ¹H NMR analysis.

With the efficient catalytic system in hand, we first explored the scope of *N*-methoxybenzamides (Scheme 2). In general, the reaction proceeded smoothly to give the desired products in high yields. Both electron-donating and -withdrawing groups either at the *ortho*- (3b-d), *meta*- (3e-f), or *para*- (3h-o) position were all well tolerated. Moreover, it was observed that the type of the substituent on the benzene ring had an obvious influence on the reaction outcome, and in the present cases, the chloro-substituted benzamides showed the relatively low reaction efficiency (for 3c: 37% and for 3i: 47%). Importantly, the reaction showed good compatibility with various functional groups. Tolerance to the chloro (3c and 3i), bromo (3j) and ester (3n) functional groups was especially noteworthy since they were very useful precursors for further transformation through standard cross-coupling reactions. It should be emphasized that, *N*-methoxybenzamides 1e and 1f bearing fluoro and methyl group at *meta*-position, respectively, afforded the corresponding products in reasonably good yields with exclusive regioselectivity, while the *meta*-methoxy derivative 1g gave a 1.1:1 mixture of regioisomers 3g(i) and 3g(ii), revealing that the type of substituents at *meta*-position had obvious effect on the regio-/site-selectivity.^{6c,10} Notably, the heteroaromatic thiophene, polyaromatic naphthalene and cyclohexene substrates could be accommodated in the catalytic system, giving their corresponding products in moderate to good yields (80% for 3p, 54% for 3q, 83% for 3r and 52% for 3s).

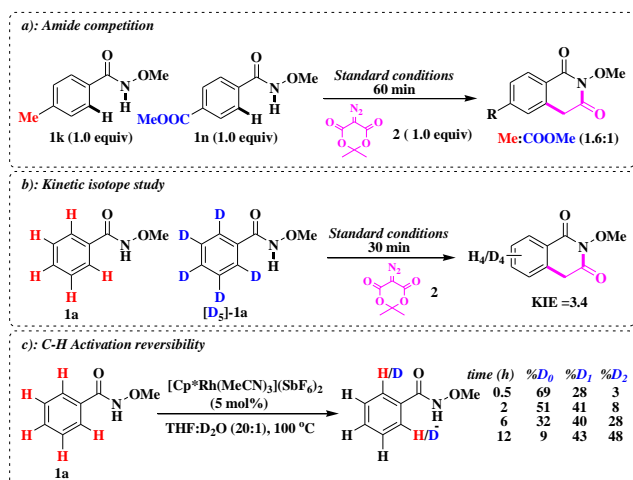
Encouraged by the above results, we were interested in extending the Rh(III)-catalyzed system to other valuable substrates such as marketed neuroprotective drug-Edaravone, for which so far only two examples for its C-H functionalization has been reported.¹¹ Therefore, we used Edaravone 4a as the model

substrate to test the availability of the established Rh(III) catalysis. As expected, the reaction of 4a and 2 proceeded smoothly to give the desired cross-coupling/cyclization product 5a in 83% yield.

Having the satisfactory result in hand, next we sought to probe the versatility of the reaction by employing various Edaravone analogs as the substrates (Scheme 3). To our delight, both diverse functional groups and varied substitution patterns were well tolerated, including electron-donating and -withdrawing groups, all providing their corresponding products 5a-i in good to excellent yields. The results not only further illustrated the remarkable robustness of our developed catalytic system but also offered an efficient and attractive strategy to generate new analogs of Edaravone for immediate drug screening.



Scheme 3 Exploring the versatility of reaction system by using Edaravones as substrates. ^aReaction conditions: 4 (0.20 mmol) and 2 (0.22 mmol) in THF (1.0 mL) at 100 °C for 5 h under air. Isolated yields.



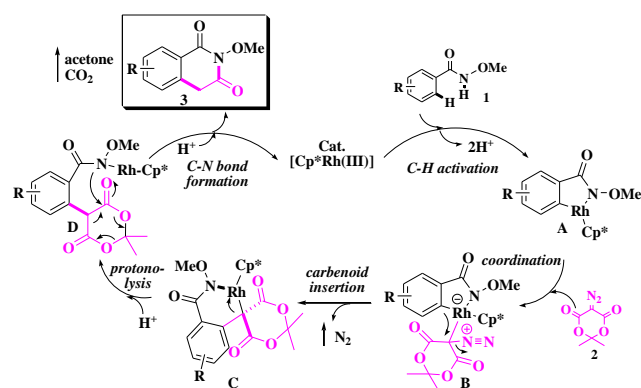
Scheme 4 Mechanistic experiments.

Considering the remarkably broad substrate scope displayed by the Rh(III) catalysis, we performed a series of experiments to explore the reaction mechanism (Scheme 4). First, the competition experiment between differently substituted *N*-methoxybenzamides was carried out to delineate the action mode of the reaction. As shown in Scheme 4a, The results indicated that electron-rich amides were preferentially converted (e.g. 3k/3n = 1.6:1), revealing that they might be better substrates than

electron-deficient amides, and also suggesting that the C-H activation might be *via* an internal electrophilic substitution (IES)-type mechanism.¹²

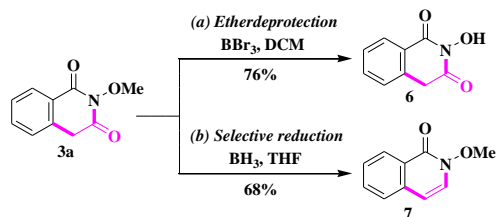
Next, the isotope-labeling experiment was conducted with a deuterium-labeled *N*-methoxybenzamide [D₅]-**1a**. As shown in Scheme 4b, treatment of a 1:1 mixture of **1a** and [D₅]-**1a** under the typical reaction conditions gave a relatively large KIE value ($k_H/k_D = 3.4$). It suggested that C-H bond cleavage was likely involved in the rate-limiting step.

Finally, the reversibility of the C-H activation step was defined by running the reaction in THF/D₂O in the absence of α -diazotized Meldrum's acid **2** (Scheme 4c). The deuterium incorporation was monitored by ESI-HRMS analysis and revealed significant deuterium of **1a** already after 0.5 h. Moreover, after 12 h only 9% undeuterated **1a** was left. The results revealed that the C-H bond activation step was largely reversible, which was consistent with previous reports by Glorius^{13a-b} and Ackermann.^{13c}



Scheme 5 Proposed mechanism.

On the basis of these results and literature precedent,^{6-9,14} a plausible reaction mechanism was proposed in Scheme 5. First, the coordination of *N*-methoxybenzamides **1** to a [Cp*Rh(III)] species was the key rate-determining step for the regioselective C-H bond cleavage to form a five-membered rhodacyclic intermediate **A**. Subsequently, coordination of the diazo compound **2** with **A** afforded the diazonium intermediate **B**. The region-selective transfer of carbenoid insertion gave six-membered rhodacycle intermediate **C** with the emission of N₂. Protonolysis of **C** delivered the intermediate **D**, which then underwent an addition/elimination/decarboxylation in the presence of hydrogen proton to give the desired *N*-methoxyisoquinolinediones **3** and the active Rh(III) catalyst with extrusion of CO₂ and acetone.



Scheme 6 Derivatization of **3a**.

Due to the importance of free-*N*-OH isoquinolinediones in modern medicinal chemistry,^{4a-b,15} we finally attempted to remove the methyl group of **3**. As illustrated in Scheme 6a, the etherdeprotection of **3a** was easily achieved by treatment with BBr₃ in DCM for 4 h to provide free-*N*-OH isoquinolinedione **6**.

In addition, isoquinolinedione **3** can be further transformed into other diverse derivatives. For example, the carbonyl moiety of **3a** could be selectively reduced to give the *N*-methoxyisoquinolinone **7** (Scheme 6b), a very valuable skeleton in natural products, drugs and biologically active compounds.¹⁶

In conclusion, we have developed the first example of a Rh(III)-catalyzed direct carbenoid insertion C-H functionalization for one-pot cascade synthesis of diversely *N*-methoxyisoquinolinediones by using simple *N*-methoxybenzamides and α -diazotized Meldrum's acid as the substrates. The remarkable features of this methodology included broad functional group/substrate tolerance, high product yields, the mild reaction conditions and no need of any external ligands or additives. The replacement of *N*-methoxybenzamides with marketed drug-Edaravone and its analogs also afforded satisfactory results. Through the mechanistic investigation, a plausible pathway was proposed. Synthetic application of *N*-methoxyisoquinolinediones to build the free-*N*-OH isoquinolinediones and *N*-methoxyisoquinolinones have been also successfully illustrated. We expect the present protocol to evoke more C-H activation reactions for convenient synthesis of other biologically important *N*-heterocycles.

We thank the Jay and Betty Van Andel Foundation, Amway (China) and the Chinese Postdoctoral Science Foundation (2012M511158, 2013T60477 and 2014M560363) for financial support on this study.

Notes and references

- ^a VARI/SIMM Center, Center for Structure and Function of Drug Targets, CAS-Key Laboratory of Receptor Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, P.R. China. Fax: +86-21-20231000-1715; Tel: 86-21-20231000-1715; e-mail: yiwei.simm@simmm.ac.cn or eric.xu@simmm.ac.cn
- ^b School of Chemistry and Chemical Engineering, Sun Yat-sen University, Guangzhou 510275, P.R. China
- ^c Laboratory of Structural Sciences, Program on Structural Biology and Drug Discovery, Van Andel Research Institute, Grand Rapids, Michigan 49503, USA
- [†] J. Shi and J. Zhou contributed equally to this work.
- [‡] Electronic Supplementary Information (ESI) available: Detailed experimental procedure and characterization of new compounds (NMR spectra and CIF of **3a** (CCDC 1030847)). See DOI: 10.1039/b000000x/
- For selected reports, see: (a) J. P. Michael, *Nat. Prod. Rep.*, 2008, **25**, 166; (b) B. Alcaide, P. Almendros and C. Aragoncillo, *Curr. Opin. Drug Discov. Devel.*, 2010, **13**, 685; (c) V. R. Solomon and H. Lee, *Curr. Med. Chem.*, 2011, **18**, 1488; (d) I. Khan, A. Ibrar, N. Abbas and A. Saeed, *Eur. J. Med. Chem.*, 2014, **76**, 193.
- For selected reviews, see: (a) T. Naito, *Chem. Pharm. Bull.*, 2008, **56**, 1367; (b) R. Giri, B. F. Shi, K. M. Engle, N. Maugel and J. Q. Yu, *Chem. Soc. Rev.*, 2009, **38**, 3242; (c) L. Ackermann, R. Vicente and A. R. Kapdi, *Angew. Chem. Int. Ed.*, 2009, **48**, 9792; (d) T. Satoh and M. Miura, *Chem. –Eur. J.* 2010, **16**, 11212; (e) J. F. Bower, J. Rujirawanicha, and T. Gallagher, *Org. Biomol. Chem.*, 2010, **8**, 1505; (f) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.*, 2010, **110**, 624; (g) N. Krause and C. Winter, *Chem. Rev.*, 2011, **111**, 1994; (h) T. Liu and H. Fu, *Synthesis*, 2012, **44**, 2805; (i) D. Garella, E. Borretto, A. D. Stilo, K. Martina, G. Cravotto and P. Cintas, *Med. Chem. Commun.*, 2013, **4**, 1323; (j) A. V. Gulevich, A. S. Dudnik, N. Chernyak and V. Gevorgyan, *Chem. Rev.*, 2013, **113**, 3084; (k) Y. Zhang, X. Jie, H. Zhao, G. Li and W. Su, *Org. Chem. Front.*, 2014, **1**, 843; (l) A. Dhakshinamoorthy and H. Garcia, *Chem. Soc. Rev.*, 2014, **43**, 5750; (m) T. Saget and N. Cramer, *Pure Appl. Chem.*, 2014, **86**, 265; (n) P. Majumdar, A. Pati, M. Patra, R. K. Behera and A. K. Behera, *Chem. Rev.*, 2014, **114**, 2942.
- For recent reviews, see: (a) F. W. Patureau, J. Wencel-Delord and F. Glorius, *Aldrichimica Acta*, 2012, **45**, 31; (b) K. M. Engle, T. S. Mei, M. Wasa and J. Q. Yu, *Acc. Chem. Res.*, 2012, **45**, 788; (c) G. Song,

- F. Wang and X. Li, *Chem. Soc. Rev.*, 2012, **41**, 3651; (d) D. A. Colby, A. S. Tsai, R. G. Bergman and J. A. Ellman, *Acc. Chem. Res.*, 2012, **45**, 814; (e) C. Zhu, R. Wang and J. R. Falck, *Chem. –Asian J.*, 2012, **7**, 1502; (f) N. Kuhl, M. N. Hopkinson, J. Wencel-Delord and F. Glorius, *Angew. Chem., Int. Ed.*, 2012, **51**, 10236; (g) S. R. Neufeldt and M. S. Sanford, *Acc. Chem. Res.*, 2012, **45**, 936; (h) J. Yamaguchi, A. D. Yamaguchi and K. Itami, *Angew. Chem., Int. Ed.*, 2012, **51**, 8960; (i) S. I. Kozhushkov and L. Ackermann, *Chem. Sci.*, 2013, **4**, 886; (j) J. Wencel-Delord and F. Glorius, *Nat. Chem.*, 2013, **5**, 369; (k) J. L. Jeffreya and R. Sarpong, *Chem. Sci.*, 2013, **4**, 4092; (l) G. Yan, X. Wu and M. Yang, *Org. Biomol. Chem.*, 2013, **11**, 5558; (m) G. Rouquet and N. Chatani, *Angew. Chem., Int. Ed.*, 2013, **52**, 11726; (n) S. Pan and T. Shibata, *ACS Catal.*, 2013, **3**, 704; (o) C. H. Jun and J. W. Park, *Top. Curr. Chem.*, 2014, **346**, 59; (p) V. S. Thirunavukkarasu, S. I. Kozhushkov and L. Ackermann, *Chem. Commun.*, 2014, **50**, 29; (q) L. Ackermann, *Acc. Chem. Res.*, 2014, **47**, 281; (r) N. Kuhl, N. Schröder and F. Glorius, *Adv. Synth. Catal.*, 2014, **356**, 1443.
- (a) M. Billamboz, F. Bailly, M. L. Barreca, L. De Luca, J. F. Mouscadet, C. Calmels, M. L. Andreola, M. Witvrouw, F. Christ, Z. Debyser and P. Cotellet, *J. Med. Chem.*, 2008, **51**, 7717; (b) M. Billamboz, F. Bailly, C. Lion, N. Touati, H. Vezin, C. Calmels, M. L. Andréola, F. Christ, Z. Debyser and P. Cotellet, *J. Med. Chem.*, 2011, **54**, 1812; (c) L. Li, Y. L. Zhao, H. Wang, Y. J. Li, X. Xu and Q. Liu, *Chem. Commun.*, 2014, **50**, 6458; (d) W. Zhao, P. Xie, M. Zhang, B. Niu, Z. Bian, C. Pittman and A. Zhou, *Org. Biomol. Chem.*, 2014, **12**, 7690.
- For selected reviews, see: (a) J. Barluenga and C. Valdés, *Angew. Chem., Int. Ed.*, 2011, **50**, 7486; (b) Z. Shao and H. Zhang, *Chem. Soc. Rev.*, 2012, **41**, 560; (c) Q. Xiao, Y. Zhang and J. Wang, *Acc. Chem. Res.*, 2013, **46**, 236; (d) Z. Liu and J. Wang, *J. Org. Chem.*, 2013, **78**, 10024; (e) Y. Xia, Y. Zhang and J. Wang, *ACS Catal.*, 2013, **3**, 2586.
- (a) W. W. Chan, S. F. Lo, Z. Zhou and W. Y. Yu, *J. Am. Chem. Soc.*, 2012, **134**, 13565; (b) Z. Shi, D. C. Koester, M. Bouladakis-Arapinis and F. Glorius, *J. Am. Chem. Soc.*, 2013, **135**, 12204; (c) T. K. Hyster, K. E. Ruhl and T. Rovis, *J. Am. Chem. Soc.*, 2013, **135**, 5364; (d) S. Cui, Y. Zhang, D. Wang and Q. Wu, *Chem. Sci.*, 2013, **4**, 3912; (e) H. W. Lam, K. Y. Man, W. W. Chan, Z. Zhou and W. Y. Yu, *Org. Biomol. Chem.*, 2014, **12**, 4112; (f) Y. Liang, K. Yu, B. Li, S. Xu, H. Song and B. Wang, *Chem. Commun.*, 2014, **50**, 6130; (g) B. Ye and N. Cramer, *Angew. Chem., Int. Ed.*, 2014, **53**, 7896.
- (a) J. Shi, B. Zhou, Y. Yang and Y. Li, *Org. Biomol. Chem.*, 2012, **10**, 8953; (b) Q. Li, Y. Yan, X. Wang, B. Gong, X. Tang, J. Shi, H. E. Xu and W. Yi, *RSC Adv.*, 2013, **3**, 23402; (c) B. Gong, J. Shi, X. Wang, Y. Yan, Q. Li, Y. Meng, H. E. Xu and W. Yi, *Adv. Synth. Catal.*, 2014, **356**, 137; (d) J. Shi, Y. Yan, Q. Li, H. E. Xu and W. Yi, *Chem. Commun.*, 2014, **50**, 6483; (e) J. Shi, G. Zhao, X. Wang, H. E. Xu and W. Yi, *Org. Biomol. Chem.*, 2014, **12**, 6831.
- X. Yu, S. Yu, J. Xiao, B. Wan and X. Li, *J. Org. Chem.*, 2013, **78**, 5444.
- For the representative examples, see: (a) N. Guimond and K. Fagnou, *J. Am. Chem. Soc.*, 2009, **131**, 12050; (b) D. R. Stuart, P. Alsabeh, M. Kuhn and K. Fagnou, *J. Am. Chem. Soc.*, 2010, **132**, 18326; (c) D. J. Schipper, M. Hutchinson and K. Fagnou, *J. Am. Chem. Soc.*, 2010, **132**, 6910; (d) M. P. Huestis, L. Chan, D. R. Stuart and K. Fagnou, *Angew. Chem., Int. Ed.*, 2011, **50**, 1338; (e) W. Zhen, F. Wang, M. Zhao, Z. Du and X. Li, *Angew. Chem. Int. Ed.*, 2012, **51**, 11819; (f) Y. Chen, F. Wang, W. Zhen, X. Li, *Adv. Synth. Catal.*, 2013, **355**, 353; (g) D. S. Kim, J. W. Park and C. H. Jun, *Adv. Synth. Catal.*, 2013, **355**, 2667; (h) T. Gong, B. Xiao, W. Cheng, W. Su, J. Xu, Z. Liu, L. Liu and Y. Fu, *J. Am. Chem. Soc.*, 2013, **135**, 10630; (i) Y. Lian, J. R. Hummel, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.*, 2013, **135**, 12548; (j) K. Nobushige, K. Hirano, T. Satoh and M. Miura, *Org. Lett.*, 2014, **16**, 1188.
- F. Xie, Z. Qi, S. Yu and X. Li, *J. Am. Chem. Soc.*, 2014, **136**, 4780.
- (a) K. Wu, Z. Fan, Y. Xue, Q. Yao and A. Zhang, *Org. Lett.*, 2014, **16**, 42; (b) Z. Fan, K. Wu, L. Xing, Q. Yao and A. Zhang, *Chem. Commun.*, 2014, **50**, 1682.
- (a) J. Oxgaard, W. J. Tenn, R. J. Nielsen, R. A. Periana and W. A. Goddard, *Organometallics*, 2007, **26**, 1565; (b) L. Ackermann, *Chem. Rev.*, 2011, **111**, 1315; (c) W. Ma, R. Mei, G. Tenti and L. Ackermann, *Chem. –Eur. J.*, 2014, **20**, 15248.
- (a) N. Schröder, J. Wencel-Delord and F. Glorius, *J. Am. Chem. Soc.*, 2012, **134**, 8298; (b) C. Grohmann, H. Wang and F. Glorius, *Org. Lett.*, 2012, **14**, 656; (c) W. Ma, K. Graczyk and L. Ackermann, *Org. Lett.*, 2012, **14**, 6318.
- For recently representative examples on Rh(III)-catalyzed C-H activation by employing the benzamides as the substrates, see: (a) H. Wang and F. Glorius, *Angew. Chem., Int. Ed.*, 2012, **51**, 7318; (b) H. Wang, C. Grohmann, C. Nimphius and F. Glorius, *J. Am. Chem. Soc.*, 2012, **134**, 19592; (c) X. Xu, Y. Liu and C. M. Park, *Angew. Chem., Int. Ed.*, 2012, **51**, 9372; (d) J. R. Huckins, E. A. Bercot, O. R. Thiel, T. L. Hwang and M. M. Bio, *J. Am. Chem. Soc.*, 2013, **135**, 14492; (e) N. J. Webb, S. P. Marsden and S. A. Raw, *Org. Lett.*, 2014, **16**, 4718.
- For the latest example, see: V. Suchaud, F. Bailly, C. Lion, C. Calmels, M. L. Andréola, F. Christ, Z. Debyser and P. Cotellet, *J. Med. Chem.*, 2014, **57**, 4640.
- (a) D. Weltin, V. Picard, K. Aupeix, M. Varin, D. Oth, J. Marchal, P. Dufour and P. Bischoff, *Int. J. Immunopharmac.*, 1995, **17**, 265; (b) T. Harayama, H. Akamatsu, K. Okamura, T. Miyagoe, T. Akiyama, H. Abe and Y. Takeuchi, *J. Chem. Soc. Perkin Trans. 1*, 2001, 523; (c) T. Harayama, T. Akiyama, Y. Nakano, K. Shibaike, H. Akamatsu, A. Hori, H. Abe and Y. Takeuchi, *Synthesis*, 2002, 237; (d) J. Karthikeyan and C. H. Cheng, *Angew. Chem., Int. Ed.*, 2011, **50**, 9880; (e) J. Karthikeyan, R. Haridharan and C. H. Cheng, *Angew. Chem., Int. Ed.*, 2012, **51**, 12343; (f) R. He, Z. T. Huang, Q. Y. Zheng, C. Wang, *Tetrahedron Lett.*, 2014, **55**, 5705.