C–H Activation

DOI: 10.1002/anie.201403782

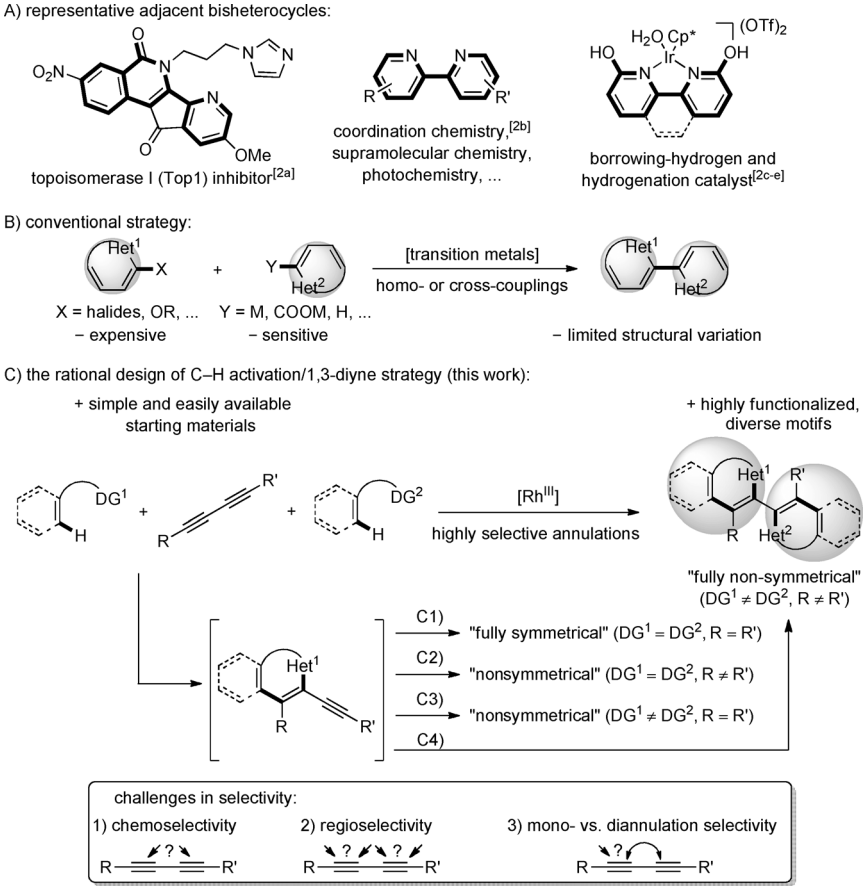
The C–H Activation/1,3-Diyne Strategy: Highly Selective Direct Synthesis of Diverse Bisheterocycles by Rh^{III} Catalysis**

*Da-Gang Yu, Francisco de Azambuja, Tobias Gensch, Constantin G. Daniliuc, and Frank Glorius**

Dedicated to Professor John F. Hartwig on the occasion of his 50th birthday

Abstract: *The reactivity and selectivity of 1,3-diynes in transition-metal-catalyzed C–H activation is exploited to quickly assemble diverse polysubstituted bisheterocycles, which are highly important but difficult to access. By using the C–H activation/1,3-diyne strategy, we overcame the challenges of selectivity (chemo-, regio-, and mono-/diannulation) and constructed seven kinds of adjacent bisheterocycles through the formation of four strategic bonds with high efficiency and high selectivity.*

Heterocycle synthesis is a very important topic in natural products, materials, and pharmaceutical chemistry.[1] Besides single heterocycles, adjacent bisheterocycles, for example, 7-azaindenoisoquinolines (e.g. Top1 inhibitor), 2,2′-bipyridines, and the complexes of bisheterocycles, play similar or even more important roles in numerous areas of chemistry (Scheme 1 A).[2] Taking advantage of transition-metal catalysis, homo- or cross-coupling reactions between two preformed heterocycles became some of the most common ways to construct such structures (Scheme 1 B).[3] Initially, the reaction partners were limited to expensive haloheterocyles and sensitive heterocyclic metal reagents. Recently, the direct C–H functionalization of heterocycles has made their synthesis more straightforward, obviating the need for prefunctionalization of heterocycles.[4] Despite these advantages, these methods still have several drawbacks, including the limited availability of heterocyclic motifs, poor selectivity for nonsymmetrical bisheterocycles, and low reactivity of the substrates with steric and electronic limitations (i.e. *ortho* substitutions or specific functional groups), and thus new methods are called for.[5] Herein, we report a C–H activation/1,3-diyne strategy for the highly selective direct synthesis of diverse bisheterocycles by Rh^{III} catalysis (Scheme 1 C).[6] With this method, symmetrical and nonsymmetrical bisheterocycles with the same or different core structures were efficiently constructed in high yields and



Scheme 1. Synthesis of adjacent bisheterocycles. DG = directing group.

[*] Dr. D.-G. Yu, F. de Azambuja, T. Gensch, Dr. C. G. Daniliuc, Prof. Dr. F. Glorius
Westfälische Wilhelms-Universität Münster
Organisch-Chemisches Institut
Corrensstrasse 40, 48149 Münster (Germany)
E-mail: glorius@uni-muenster.de
Homepage: http://www.uni-muenster.de/Chemie.oc/glorius/

[**] We thank Prof. Zhuangzhi Shi, Prof. Honggen Wang, Dr. Dongbing Zhao, Dr. Mélissa Boultadakis-Arapinis, Dr. Karl D. Collins, and Nils Schröder for helpful discussions. We are very grateful to the Alexander von Humboldt Foundation (D.G.Y.), São Paulo Research Foundation (grant 2013/14209-9, F.d.A.), the European Research Council (ERC) under the European Community's Seventh Framework Program (FP7 2007–2013)/ERC grant agreement no. 25936, and the DFG (Leibniz award; F.G.) for generous financial support.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201403782.

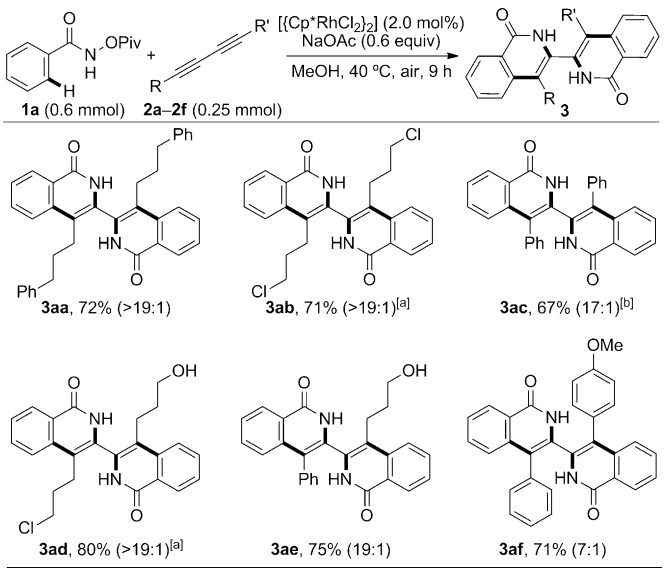
with high selectivity. Moreover, the individual coupling steps are controllable so that optional monoannulation is also possible.

1,3-Diynes have been thoroughly investigated since the discovery of the Glaser–Hay Reaction in 1869. They are readily available by a number of methods[7] and widely used in the synthesis of arenes and heteroarenes.[8] Nevertheless, there are only a few examples of the synthesis of bisheterocycles from 1,3-diynes.[9] For example, the research groups of Lee[9a,b] and Satoh and Miura[9c] independently realized the intra- and intermolecular annulations of 1,3-diynes to generate bisheterocycles through electrophilic substitution or decarboxylation. However, the synthesis of bisheterocycles from 1,3-diynes through transition-metal-catalyzed C–H activation has not yet been achieved. Inspired by our previous work in heterocycle synthesis with Rh^{III} catalysis,[10] we envisioned a modular and flexible C–H activation/1,3-diyne general strategy for the quick assembly of polysubstituted bisheterocycles through rational design of reaction conditions and partners, including 1,3-diynes and different kinds of easily available substrates that are suitable for C–H activation.

From the beginning of this investigation, we observed similarities, but also significant differences between 1,3-diynes and monoalkynes. From the initial results, we outlined four challenges:

1) Chemoselectivity between two alkyne motifs: In the monoannulation stage of nonsymmetrical 1,3-diynes, it is very challenging to realize the selective reaction with a specific alkyne motif, especially for those with two similar substituents.
2) Regioselectivity in each migratory insertion: Besides the chemoselectivity, the migratory insertion step for each C–C triple bond must be regioselective. With these controls, highly selective annulations are expected to assemble bisheterocycles in good yields.
3) Selectivity between mono- and diannulations: While it might be less difficult to synthesize bisheterocycles with the same core structure through diannulations with 1,3-diynes (Scheme 1, C1 and C2), it is very challenging to form nonsymmetrical bisheterocycles with different core structures (C3 and C4). To achieve such a goal, selective monoannulation must be realized to generate alkynylated heterocycles as intermediates, which then undergo another annulation to form bisheterocycles.
4) Inhibition through coordination of the bisheterocycles with the catalyst: Many kinds of bisheterocycles are known to coordinate well with transition metals, which may inhibit catalysis.

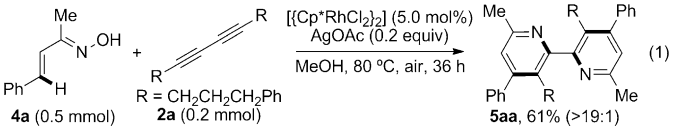
With these challenges in mind, we chose the synthesis of bisisoquinolone as the starting point because of the high importance and ease of derivatizing isoquinolones, including transformations to other important heterocycles (such as isoquinolines and 3,4-dihydroisoquinolones).[11] We discovered a smooth and efficient formation of bisisoquinolone **3aa** from *N*-(pivaloyloxy)benzamide (**1a**) and dialkyl diyne **2a** with excellent selectivity (Scheme 2).[12] Remarkably, the reactions were carried out in air at 40 °C, without precautions against moisture. Not only dialkyl diynes **2a** and **2b**, but also



Scheme 2. Formation of bisisoquinolones. For reaction conditions, see the Supporting Information. The structures and yields of the isolated major isomers are shown. The ratio of the major isomer to other isomers, based on ^{1}H NMR spectroscopy, is given in parentheses. [a] 4.0 mol% [{Cp*RhCl$_2$}$_2$] (Cp* = C$_5$Me$_5$). [b] 1.0 mol% [{Cp*RhCl$_2$}$_2$].

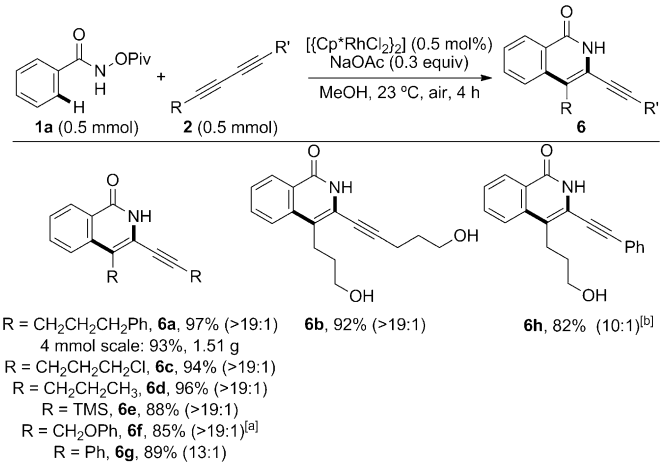
diaryl diyne **2c** showed good reactivity and selectivity with a lower catalyst loading. More sophisticated products (Scheme 1, C2) were addressed by changing to nonsymmetrical diynes, which are readily obtained by the method developed by Lei and co-workers.[7b] Again, good yields were achieved for all combinations of the diyne substituents, namely, dialkyl- (**2d**), diaryl- (**2f**), and alkyl aryl diynes (**2e**; Scheme 2).

Moreover, it is highly desirable to apply this strategy to the concise synthesis of polysubstituted 2,2′-bipyridines.[5] We exemplified this with the reaction of **4a** to generate **5aa** with excellent selectivity and an average yield of 78% for each annulation [Eq. (1)].[13]



(1)

Following these results, we then investigated the preparation of nonsymmetrical bisheterocycles bearing two different core structures (Scheme 1, C3 and C4). To our delight, we overcame the discussed challenges and realized selective monoannulation under milder reaction conditions with a 1:1 ratio of **1a** to **2** and a lower catalyst loading (Scheme 3). The high efficiency was also demonstrated by the gram-scale synthesis of **6a**. Since alkynylated heterocycles are also valuable compounds,[14] we verified the feasibility of this transformation with other diynes **2**. Although trace amounts



Scheme 3. Formation of alkynylated heterocycles. For reaction conditions, see the Supporting Information. The structures and yields of the isolated major isomers are shown. The ratio of the major isomer to other isomers based on ^{1}H NMR spectroscopy is given in parentheses. [a] 1.0 mol% [{Cp*RhCl$_2$}$_2$], 16 h. [b] 2.0 mol% [{Cp*RhCl$_2$}$_2$], 0.2 mmol scale.

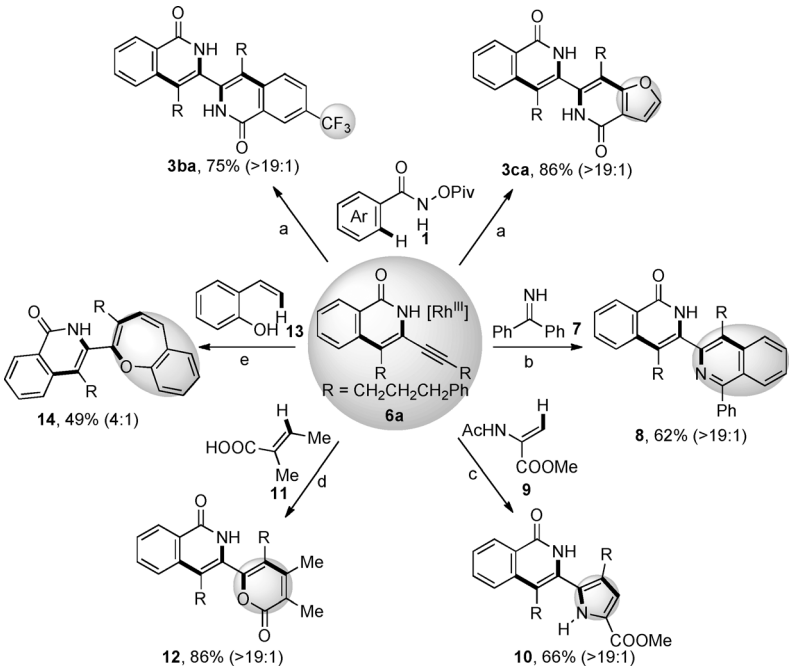
of bisisoquinolones **3** were observed in some cases, most dialkyldiynes **2** resulted in the generation of the corresponding alkynylated heterocycles **6** in high yields and with excellent regioselectivity. Moreover, the diphenyldiyne also reacted nicely to produce **6g**, albeit with a slightly lower regioselectivity. Notably, the nonsymmetrical diyne also afforded the desired product **6h** in a good yield with high chemo- and regioselectivity,[15] thereby providing a great opportunity for the generation of nonsymmetrical bisheterocycles (Scheme 1, C4). Importantly, both structures of **6b** and **6h** were confirmed by single-crystal X-ray analysis.[16]

Using the readily prepared product **6a**, we then demonstrated multiple annulation with many kinds of substrates (Scheme 4).[17–21] As expected, benzamides with a functional group (**1b**) or heteroarene (**1c**) reacted smoothly with **6a** to generate nonsymmetrical bisisoquinolones **3** in good yields and excellent selectivity. By using this stepwise approach, we also demonstrated the formation of other kinds of heterocycles, including isoquinolines,[17] pyrroles,[18] α-pyrones,[19] and benzoxepines,[20] as the second core structure (Scheme 4). For example, isoquinolone-isoquinoline **8** was generated in high efficiency when diphenylketimine **7** was used. Besides the C–H activation of arenes, several kinds of substrates were successfully applied to generate the corresponding five-, six-, and seven-membered heterocycles from enamide **9**, acrylic acid **11**, and *o*-vinylphenol **13** by alkenyl C–H activation.

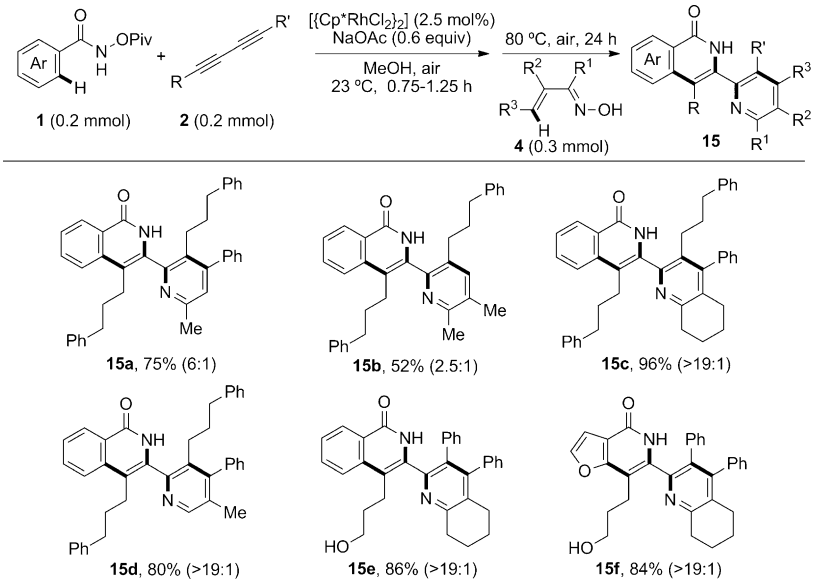
Even more interestingly, the one-pot generation of nonsymmetrical bisheterocycles with different core structures was also successfully realized (Scheme 1, C3). After completion of the first annulation at room temperature, oximes **4** were added in one portion and the reaction mixture was heated at 80 °C to give the corresponding isoquinolone-pyridines **15** in moderate to excellent yields and selectivity (Scheme 5).[2a,12b] Besides ketone oximes, aldehyde oxime **4d** provided **15d** in a high yield.

Prompted by these results and especially the selective monoannulation to generate **6h** (Scheme 3), we moved on to the more challenging one-pot "fully nonsymmetrical" diannulation (Scheme 1, C4). It is important to note that up to 16 possible isomers might be generated in this transformation. Excitingly, we successfully addressed the selectivity problem and directly generated the polysubstituted products **15e** and **15f** in good yields and with excellent selectivity (Scheme 5).

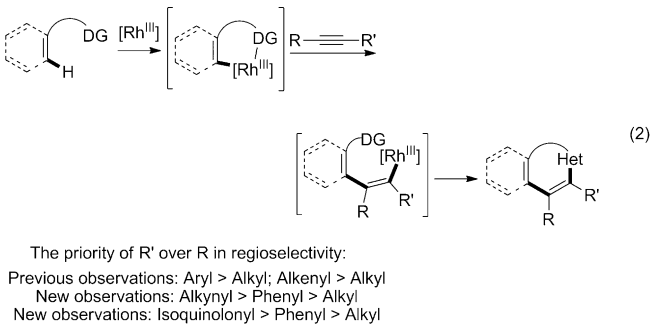
Apart from the synthetic achievements, the inherent selectivity of 1,3-diynes in the migratory insertion also attracted our attention (see also the Supporting Information). Although the selectivity of aryl alkyl alkynes and alkenyl alkyl alkynes has been well investigated,[12–14,17–21] the selectivity between the substituents of alkynes, such as alkynyl, isoquinolonyl, phenyl, and alkyl groups, has not been studied in C–H activation.[8] Based on our observations, the regioselectivity of the migratory insertion in this study is highly affected by the hybridization of the carbon atom and the coordinative ability of the substituents, with the order of preference being alkynyl and isoquinolonyl, phenyl, and



Scheme 4. Synthesis of nonsymmetrical bisheterocycles through a second annulation. a) [{Cp*RhCl$_2$}$_2$] (2.5 mol%), NaOAc (0.6 equiv), MeOH, 40 °C, 8 h, air; b) [{Cp*RhCl$_2$}$_2$] (2.5 mol%), Cu(OAc)$_2$·H$_2$O (2.0 equiv), DMF, 80 °C, 24 h, argon; c) [Cp*Rh(MeCN)$_3$](SbF$_6$)$_2$ (5.0 mol%), Cu(OAc)$_2$·H$_2$O (0.2 equiv), cyclohexanone, 60 °C, 24 h, O$_2$; d) [{Cp*RhCl$_2$}$_2$] (2.5 mol%), Ag$_2$CO$_3$ (1.0 equiv), DMF, 120 °C, 24 h, argon; e) [{Cp*RhCl$_2$}$_2$] (2.5 mol%), Cu(OAc)$_2$·H$_2$O (0.5 equiv), CH$_3$CN, 85 °C, 24 h, air.



Scheme 5. One-pot formation of bisheterocycles. For reaction conditions, see the Supporting Information. The structures and yields of the isolated major isomers are shown. The ratio of the major isomer to other isomers based on ^{1}H NMR spectroscopy is given in parentheses.



The priority of R' over R in regioselectivity:
Previous observations: Aryl > Alkyl; Alkenyl > Alkyl
New observations: Alkynyl > Phenyl > Alkyl
New observations: Isoquinolonyl > Phenyl > Alkyl

finally alkyl groups to remain in the position adjacent to the heteroatom of the heterocycles [Eq. (2)].

In conclusion, we have demonstrated a versatile and modular C–H activation/1,3-diyne general strategy for the quick assembly of diverse bisheterocycles in high yields and high selectivity through formation of four strategic[4p] bonds. The rational design of reaction conditions and substrates allowed us to overcome the great challenges of selectivity (chemo-, regio-, and mono- versus diannulation). Thus, we presented the formation of seven kinds of bisheterocycles in four patterns:

1) fully symmetrical ones (Scheme 1, C1),
2) nonsymmetrical ones with the same core structures but different substituents (C2),
3) nonsymmetrical ones with two different core structures but with the same substituents arising from the symmetrical diynes (C3), and
4) fully nonsymmetrical ones with different cores and substituents (C4).

Moreover, a range of functional groups, such as halides, alcohols, and heteroarenes were tolerated, thus allowing further derivatization of the products. Besides the great potential applications of the C–H activation/1,3-diyne strategy, the excellent selectivity in the migratory insertions of 1,3-diynes observed in these reactions could also inspire future research.

Received: March 27, 2014
Published online: July 1, 2014

Keywords: alkynes · heterocycles · C–H activation · Rh^{III} catalysis · selectivity

[1] J. A. Joule, K. Mills, *Heterocyclic Chemistry, 5th ed.*, Wiley-Blackwell, Chichester, **2010**.
[2] a) E. Kiselev, D. Sooryakumar, K. Agama, M. Cushman, Y. Pommier, *J. Med. Chem.* **2014**, *57*, 1289; b) I. A. I. Mkhalid, J. H. Barnard, T. B. Marder, J. M. Murphy, J. F. Hartwig, *Chem. Rev.* **2010**, *110*, 890; c) R. Kawahara, K.-i. Fujita, R. Yamaguchi, *J. Am. Chem. Soc.* **2012**, *134*, 3643; d) W.-H. Wang, J. T. Muckerman, E. Fujita, Y. Himeda, *ACS Catal.* **2013**, *3*, 856; e) K.-i. Fujita, Y. Tanaka, M. Kobayashi, R. Yamaguchi, *J. Am. Chem. Soc.* **2014**, *136*, 4829.
[3] a) L.-C. Campeau, K. Fagnou, *Chem. Soc. Rev.* **2007**, *36*, 1058; b) I. V. Seregin, V. Gevorgyan, *Chem. Soc. Rev.* **2007**, *36*, 1173; c) D. Zhao, J. You, C. Hu, *Chem. Eur. J.* **2011**, *17*, 5466.
[4] For recent reviews of C–H activation, see a) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624; b) J. Roger, A. L. Gottumukkala, H. Doucet, *ChemCatChem* **2010**, *2*, 20; c) L. Ackermann, *Chem. Rev.* **2011**, *111*, 1315; d) T. Newhouse, P. S. Baran, *Angew. Chem.* **2011**, *123*, 3422; *Angew. Chem. Int. Ed.* **2011**, *50*, 3362; e) H. M. L. Davies, J. Du Bois, J.-Q. Yu, *Chem. Soc. Rev.* **2011**, *40*, 1855; f) L. McMurray, F. O'Hara, M. J. Gaunt, *Chem. Soc. Rev.* **2011**, *40*, 1885; g) O. Baudoin, *Chem. Soc. Rev.* **2011**, *40*, 4902; h) S. H. Cho, J. Y. Kim, J. Kwak, S. Chang, *Chem. Soc. Rev.* **2011**, *40*, 5068; i) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215; j) J. Yamaguchi, A. D. Yamaguchi, K. Itami, *Angew. Chem.* **2012**, *124*, 9092; *Angew. Chem. Int. Ed.* **2012**, *51*, 8960; k) P. B. Arockiam, C. Bruneau, P. H. Dixneuf, *Chem. Rev.* **2012**, *112*, 5879; l) B.-J. Li, Z.-J. Shi, *Chem. Soc. Rev.* **2012**, *41*, 5588; m) K. M. Engle, T.-S. Mei, M. Wasa, J.-Q. Yu, *Acc. Chem. Res.* **2012**, *45*, 788; n) S. R. Neufeldt, M. S. Sanford, *Acc. Chem. Res.* **2012**, *45*, 936; o) E. P. Kündig, Y. Jia, D. Katayev, M. Nakanishi, *Pure Appl. Chem.* **2012**, *84*, 1741; p) J. Wencel-Delord, F. Glorius, *Nat. Chem.* **2013**, *5*, 369; q) R. Rossi, F. Bellina, M. Lessi, C. Manzini, *Adv. Synth. Catal.* **2014**, *356*, 17; for selected reports, see r) P. Xi, F. Yang, S. Qin, D. Zhao, J. Lan, G. Gao, C. Hu, J. You, *J. Am. Chem. Soc.* **2010**, *132*, 1822; s) Z. Liang, J. Zhao, Y. Zhang, *J. Org. Chem.* **2010**, *75*, 170; t) Y. Li, W.-H. Wang, S.-D. Yang, B.-J. Li, C. Feng, Z.-J. Shi, *Chem. Commun.* **2010**, *46*, 4553; u) D. Mandal, A. D. Yamaguchi, J. Yamaguchi, K. Itami, *J. Am. Chem. Soc.* **2011**, *133*, 19660; v) W. Han, P. Mayer, A. R. Ofial, *Angew. Chem.* **2011**, *123*, 2226; *Angew. Chem. Int. Ed.* **2011**, *50*, 2178; w) M. Nishino, K. Hirano, T. Satoh, M. Miura, *Angew. Chem.* **2012**, *124*, 7099; *Angew. Chem. Int. Ed.* **2012**, *51*, 6993; x) N. Kuhl, M. N. Hopkinson, F. Glorius, *Angew. Chem.* **2012**, *124*, 8354; *Angew. Chem. Int. Ed.* **2012**, *51*, 8230; y) X. Qin, H. Liu, D. Qin, Q. Wu, J. You, D. Zhao,

Q. Guo, X. Huang, J. Lan, *Chem. Sci.* **2013**, *4*, 1964; z) Y. Shang, X. Jie, H. Zhao, P. Hu, W. Su, *Org. Lett.* **2014**, *16*, 416.

[5] For a leading report on bisheterocycle functionalization, see J. Kwak, Y. Ohk, Y. Jung, S. Chang, *J. Am. Chem. Soc.* **2012**, *134*, 17778.

[6] a) T. Satoh, M. Miura, *Chem. Eur. J.* **2010**, *16*, 11212; b) D. A. Colby, A. S. Tsai, R. G. Bergman, J. A. Ellman, *Acc. Chem. Res.* **2012**, *45*, 814; c) G. Song, F. Wang, X. Li, *Chem. Soc. Rev.* **2012**, *41*, 3651; d) S. Chiba, *Chem. Lett.* **2012**, *41*, 1554; e) F. W. Patureau, J. Wencel-Delord, F. Glorius, *Aldrichimica Acta* **2012**, *45*, 31; f) Y.-F. Han, G.-X. Jin, *Chem. Soc. Rev.* **2014**, *43*, 2799; g) X.-S. Zhang, K. Chen, Z.-J. Shi, *Chem. Sci.* **2014**, *5*, 2146; h) N. Kuhl, N. Schröder, F. Glorius, *Adv. Synth. Catal.* **2014**, *356*, 1443.

[7] a) R. Chinchilla, C. Nájera, *Chem. Rev.* **2014**, *114*, 1783; b) W. Yin, C. He, M. Chen, H. Zhang, A. Lei, *Org. Lett.* **2009**, *11*, 709; c) R. Hua, Q. Zheng, Y. Wan, *Appl. Organomet. Chem.* **2010**, *24*, 314; d) Z. Chen, H. Jiang, A. Wang, S. Yang, *J. Org. Chem.* **2010**, *75*, 6700; e) A. Dermenci, R. E. Whittaker, G. Dong, *Org. Lett.* **2013**, *15*, 2242.

[8] a) C. Yuan, C.-T. Chang, A. Axelrod, D. Siegel, *J. Am. Chem. Soc.* **2010**, *132*, 5924; b) H. Jiang, W. Zeng, Y. Li, W. Wu, L. Huang, W. Fu, *J. Org. Chem.* **2012**, *77*, 5179; c) D. Niu, P. H. Willoughby, B. P. Woods, B. Baire, T. R. Hoye, *Nature* **2013**, *501*, 531; d) W. Shi, A. Lei, *Tetrahedron Lett.* **2014**, *55*, 2763.

[9] a) J. Mo, D. Eom, E. Lee, P. H. Lee, *Org. Lett.* **2012**, *14*, 3684; b) J. Mo, W. Choi, J. Min, C.-E. Kim, D. Eom, S. H. Kim, P. H. Lee, *J. Org. Chem.* **2013**, *78*, 11382; c) M. Itoh, M. Shimizu, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2013**, *78*, 11427; see also Ref. [8a].

[10] a) H. Wang, C. Grohmann, C. Nimphius, F. Glorius, *J. Am. Chem. Soc.* **2012**, *134*, 19592; b) Z. Shi, C. Grohmann, F. Glorius, *Angew. Chem.* **2013**, *125*, 5503; *Angew. Chem. Int. Ed.* **2013**, *52*, 5393; c) D. Zhao, Z. Shi, F. Glorius, *Angew. Chem.* **2013**, *125*, 12652; *Angew. Chem. Int. Ed.* **2013**, *52*, 12426; d) D.-G. Yu, F. de Azambuja, F. Glorius, *Angew. Chem.* **2014**, *126*, 2792; *Angew. Chem. Int. Ed.* **2014**, *53*, 2754.

[11] a) V. A. Glushkov, Y. V. Shklyaev, *Chem. Heterocycl. Compd.* **2001**, *37*, 663; b) C. Kelley, Y. Zhang, A. Parhi, M. Kaul, D. S. Pilch, E. J. LaVoie, *Bioorg. Med. Chem.* **2012**, *20*, 7012.

[12] a) S. Mochida, N. Umeda, K. Hirano, T. Satoh, M. Miura, *Chem. Lett.* **2010**, *39*, 744; b) N. Guimond, C. Gouliaras, K. Fagnou, *J. Am. Chem. Soc.* **2010**, *132*, 6908; c) T. K. Hyster, T. Rovis, *J. Am. Chem. Soc.* **2010**, *132*, 10565; d) N. Guimond, S. I. Gorelsky, K. Fagnou, *J. Am. Chem. Soc.* **2011**, *133*, 6449; e) G. Song, X. Gong, X. Li, *J. Org. Chem.* **2011**, *76*, 7583; f) X. Xu, Y. Liu, C.-M. Park, *Angew. Chem.* **2012**, *124*, 9506; *Angew. Chem. Int. Ed.* **2012**, *51*, 9372; g) N. Quinones, A. Seoane, R. Garcia-Fandino, J. L. Mascarenas, M. Gulias, *Chem. Sci.* **2013**, *4*, 2874.

[13] a) P. C. Too, T. Noji, Y. J. Lim, X. Li, S. Chiba, *Synlett* **2011**, 2789; b) T. K. Hyster, T. Rovis, *Chem. Commun.* **2011**, *47*, 11846; c) F. Wang, G. Song, X. Li, *Angew. Chem.* **2012**, *124*, 12514; *Angew. Chem. Int. Ed.* **2012**, *51*, 12348; d) D.-S. Kim, J.-W. Park, C.-H. Jun, *Chem. Commun.* **2012**, *48*, 11334; e) H. Lee, Y.-K. Sim, J.-W. Park, C.-H. Jun, *Chem. Eur. J.* **2014**, *20*, 323.

[14] a) I. J. S. Fairlamb, *Chem. Soc. Rev.* **2007**, *36*, 1036; b) N. Matsuyama, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2009**, *11*, 4156; c) X. Jie, Y. Shang, P. Hu, W. Su, *Angew. Chem.* **2013**, *125*, 3718; *Angew. Chem. Int. Ed.* **2013**, *52*, 3630; d) C. Feng, T.-P. Loh, *Angew. Chem.* **2014**, *126*, 2760; *Angew. Chem. Int. Ed.* **2014**, *53*, 2722; e) F. Xie, Z. Qi, S. Yu, X. Li, *J. Am. Chem. Soc.* **2014**, *136*, 4780.

[15] Although another isomer was also observed, we were not able to confirm if it arose from a different regio- or chemoselectivity.

[16] CCDC 993840 (**6b**) and CCDC 993841 (**6h**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[17] a) T. Fukutani, N. Umeda, K. Hirano, T. Satoh, M. Miura, *Chem. Commun.* **2009**, 5141; b) N. Guimond, K. Fagnou, *J. Am. Chem. Soc.* **2009**, *131*, 12050; c) P. C. Too, Y.-F. Wang, S. Chiba, *Org. Lett.* **2010**, *12*, 5688; d) Y.-F. Wang, K. K. Toh, J.-Y. Lee, S. Chiba, *Angew. Chem.* **2011**, *123*, 6049; *Angew. Chem. Int. Ed.* **2011**, *50*, 5927; e) P. C. Too, S. H. Chua, S. H. Wong, S. Chiba, *J. Org. Chem.* **2011**, *76*, 6159; f) X. Wei, M. Zhao, Z. Du, X. Li, *Org. Lett.* **2011**, *13*, 4636; g) X. Zhang, D. Chen, M. Zhao, J. Zhao, A. Jia, X. Li, *Adv. Synth. Catal.* **2011**, *353*, 719; h) L. Zheng, J. Ju, Y. Bin, R. Hua, *J. Org. Chem.* **2012**, *77*, 5794; i) S.-C. Chuang, P. Gandeepan, C.-H. Cheng, *Org. Lett.* **2013**, *15*, 5750; j) X.-C. Huang, X.-H. Yang, R.-J. Song, J.-H. Li, *J. Org. Chem.* **2014**, *79*, 1025; k) B. Liu, F. Hu, B.-F. Shi, Adv. Synth. Catal. 2014, DOI: 10.1002/adsc.201400292.

[18] a) D. R. Stuart, P. Alsabeh, M. Kuhn, K. Fagnou, *J. Am. Chem. Soc.* **2010**, *132*, 18326; b) M. P. Huestis, L. Chan, D. R. Stuart, K. Fagnou, *Angew. Chem.* **2011**, *123*, 1374; *Angew. Chem. Int. Ed.* **2011**, *50*, 1338; c) J. Du, B. Zhou, Y. Yang, Y. Li, *Chem. Asian J.* **2013**, *8*, 1386.

[19] a) S. Mochida, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2009**, *74*, 6295; b) X. G. Li, K. Liu, G. Zou, P. N. Liu, *Adv. Synth. Catal.* **2014**, *356*, 1496.

[20] A. Seoane, N. Casanova, N. Quiñones, J. L. Mascareñas, M. Gulías, *J. Am. Chem. Soc.* **2014**, *136*, 834.

[21] For other Rh^{III}-catalyzed heterocycle formation from alkynes, see a) K. Ueura, T. Satoh, M. Miura, *Org. Lett.* **2007**, *9*, 1407; b) D. R. Stuart, M. Bertrand-Laperle, K. M. N. Burgess, K. Fagnou, *J. Am. Chem. Soc.* **2008**, *130*, 16474; c) X. Tan, B. Liu, X. Li, B. Li, S. Xu, H. Song, B. Wang, *J. Am. Chem. Soc.* **2012**, *134*, 16163; d) M. V. Pham, B. Ye, N. Cramer, *Angew. Chem.* **2012**, *124*, 10762; *Angew. Chem. Int. Ed.* **2012**, *51*, 10610; e) J. Jayakumar, K. Parthasarathy, C.-H. Cheng, *Angew. Chem.* **2012**, *124*, 201; *Angew. Chem. Int. Ed.* **2012**, *51*, 197; f) D. Zhao, Q. Wu, X. Huang, F. Song, T. Lv, J. You, *Chem. Eur. J.* **2013**, *19*, 6239; g) C. Wang, H. Sun, Y. Fang, Y. Huang, *Angew. Chem.* **2013**, *125*, 5907; *Angew. Chem. Int. Ed.* **2013**, *52*, 5795; h) G. Zhang, L. Yang, Y. Wang, Y. Xie, H. Huang, *J. Am. Chem. Soc.* **2013**, *135*, 8850; i) G. Liu, Y. Shen, Z. Zhou, X. Lu, *Angew. Chem.* **2013**, *125*, 6149; *Angew. Chem. Int. Ed.* **2013**, *52*, 6033; j) W. Dong, L. Wang, K. Parthasarathy, F. Pan, C. Bolm, *Angew. Chem.* **2013**, *125*, 11787; *Angew. Chem. Int. Ed.* **2013**, *52*, 11573; k) B. Liu, C. Song, C. Sun, S. Zhou, J. Zhu, *J. Am. Chem. Soc.* **2013**, *135*, 16625; l) S. Park, B. Seo, S. Shin, J.-Y. Son, P. H. Lee, *Chem. Commun.* **2013**, *49*, 8671; m) J.-R. Huang, Q.-R. Zhang, C.-H. Qu, X.-H. Sun, L. Dong, Y.-C. Chen, *Org. Lett.* **2013**, *15*, 1878; n) L. Xing, Z. Fan, C. Hou, G. Yong, A. Zhang, *Adv. Synth. Catal.* **2014**, *356*, 972; for other partners, see o) T. K. Hyster, L. Knörr, T. R. Ward, T. Rovis, *Science* **2012**, *338*, 500; p) B. Ye, N. Cramer, *Science* **2012**, *338*, 504; q) R. Zeng, C. Fu, S. Ma, *J. Am. Chem. Soc.* **2012**, *134*, 9597; r) X. Shi, C.-J. Li, *Adv. Synth. Catal.* **2012**, *354*, 2933; s) Y. Lian, T. Huber, K. D. Hesp, R. G. Bergman, J. A. Ellman, *Angew. Chem.* **2013**, *125*, 657; *Angew. Chem. Int. Ed.* **2013**, *52*, 629; t) Y. Lian, J. R. Hummel, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2013**, *135*, 12548; u) S. Cui, Y. Zhang, D. Wang, Q. Wu, *Chem. Sci.* **2013**, *4*, 3912; v) W. Hou, B. Zhou, Y. Yang, H. Feng, Y. Li, *Org. Lett.* **2013**, *15*, 1814; w) Q. Jiang, D. Duan-Mu, W. Zhong, H. Chen, H. Yan, *Chem. Eur. J.* **2013**, *19*, 1903; x) T. A. Davis, T. K. Hyster, T. Rovis, *Angew. Chem.* **2013**, *125*, 14431; *Angew. Chem. Int. Ed.* **2013**, *52*, 14181; y) B. Ye, P. A. Donets, N. Cramer, *Angew. Chem.* **2014**, *126*, 517; *Angew. Chem. Int. Ed.* **2014**, *53*, 507; z) J. Zhou, B. Li, Z.-C. Qian, B.-F. Shi, *Adv. Synth. Catal.* **2014**, *356*, 1038.

