C. R. Chimie 15 (2012) 1081–1085

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Account/Revue

On the selectivity in some Rh(III) catalyzed C–H activation cross-couplings

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ARTICLE INFO

Article history:
Received 21 March 2012
Accepted after revision 7 August 2012
Available online 18 September 2012

Keywords:
C–H activation
Rh(III)-catalysis
Oxidative olefination
Structural determination

ABSTRACT

In the last few years, Rh(III)-catalyzed C–H functionalizations have made tremendous progress and, consequently, have recently received increasing attention. These C–H activation reactions, generally involving a chelate assisting directing group, have been utilized to form valuable heterocycles and to run useful coupling reactions. In this paper, three different transformations are presented and discussed. In order to unequivocally determine the stereochemistry of some of these transformations, crystal structural analysis data are provided.

RÉSUMÉ

Ces dernières années, les fonctionnalisations de liaisons C–H catalysées au Rh(III) ont fait des progrès considérables, et par conséquent, ont suscité l'attention de bon nombre de chercheurs. Ces réactions d'activation de liaisons C–H impliquent souvent un groupement directeur coordonnant, et ont été largement employées pour la préparation d'hétérocycles et d'autres réactions importantes de couplage. Dans ce compte rendu, nous souhaitons revenir sur, et discuter, la régiosélectivité de trois différentes réactions, structures cristallographiques à l'appui.

1. Introduction

The construction of C–C bonds through C–H activation techniques is on the rise, as it typically obviates the need for costly and tedious pre-activation steps [1]. These transformations are highly atom economical as they usually produce little or no waste (in the case of redox neutral C–H activation cross-couplings). These reactions are usually easy to implement, operator friendly, and scalable to some extent [2]. Even when large amounts of oxidant are required, techniques have been elaborated to use air, or O_2 as terminal oxidant, making these promising leads for the future of organic chemistry [1,3]. Nevertheless, these reactions still suffer from selectivity issues, an obvious problem as most substrates have many different C–H positions between which the catalyst must discriminate. In this account, we wish to revisit the selectivity issues, which we have encountered in several of our works on Rh catalyzed C–H activation oxidative cross-couplings. We chose to highlight in particular three topics: the pyrrole synthesis and its reactivity switch between vinylic C–H and allylic C–H activation (section 2.1), the double oxidative annulated lactam synthesis and its peculiar trisubstituted *exo*cyclic double bond formation (section 2.2), and finally the linear diene synthesis, and its many possible diastereomers (section 2.3).

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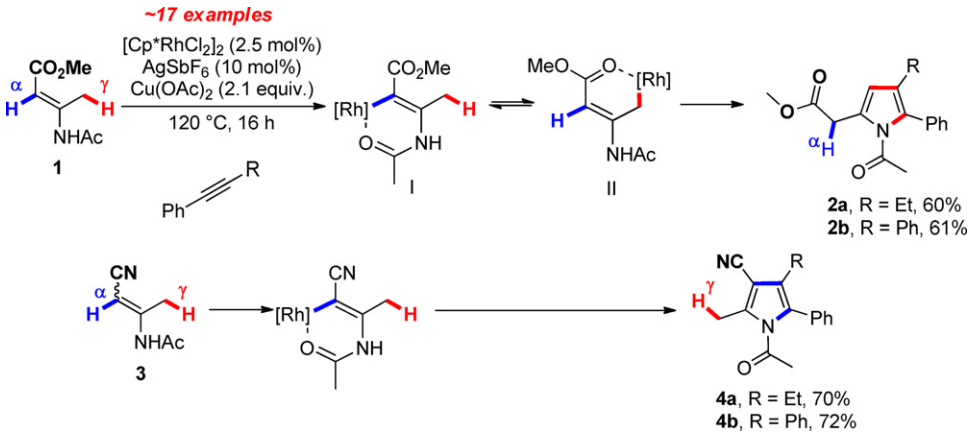
1631-0748/$ – see front matter
http://dx.doi.org/10.1016/j.crci.2012.08.003



Scheme 1. Pyrrole synthesis.

2. Results and discussions

2.1. C–H activation for pyrrole synthesis

While studying the C–H activation of a series of protected β-amino acid precursors with RhCp* catalysts, we discovered that the nature of the carboxylic acid protecting groups was essential for directing which C–H position would be functionalized (see molecules **1** and **3**, Scheme 1) [4]. Indeed, with an ester protected substrate (molecule **1**), only the allylic C–H functionalization is observed, whereas with a nitrile protecting group (molecule **3**), only the vinylic one is functionalized (Scheme 1). This is explained by a metallacycle rearrangement. Through deuterium control experiments, it was established that the vinylic C–H activation occurs first (intermediate I) and rearranges to the allylic metallacycle, provided that an ester group can stabilize it by chelation (intermediate II). The subsequent alkyne insertion, rearrangement and reductive elimination lead to a series of substituted pyrroles with exclusive selectivity. The identity of these compounds was first tackled through a series of advanced NMR techniques, and then later in the X-ray structure of compounds **2b**, **4a**

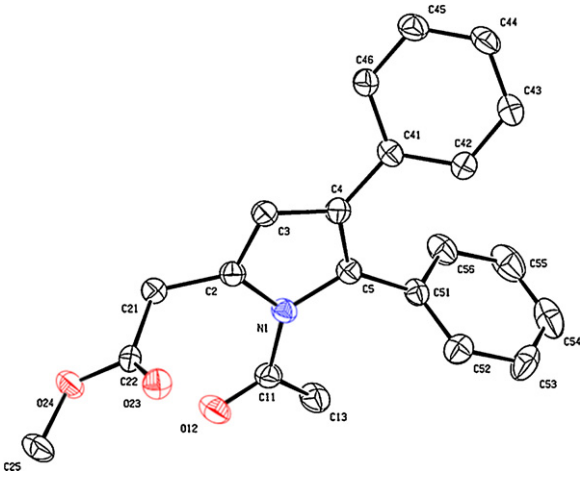


Fig. 1. X-ray structure (Ortep view 30% probability level) of pyrrole **2b**. Hydrogen atoms have been omitted for clarity.

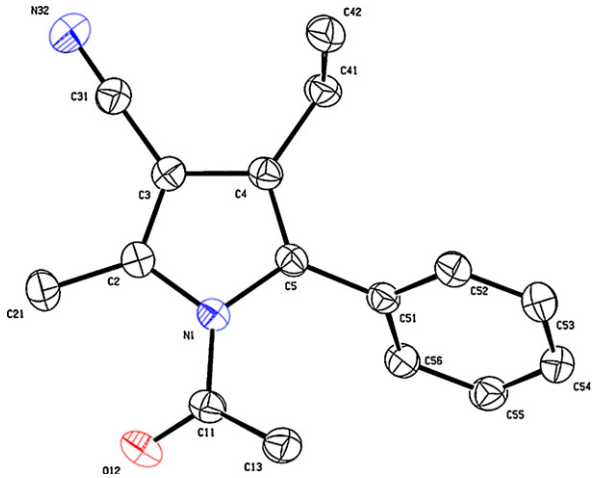


Fig. 2. X-ray structure (Ortep view 30% probability level) of pyrrole **4a**.

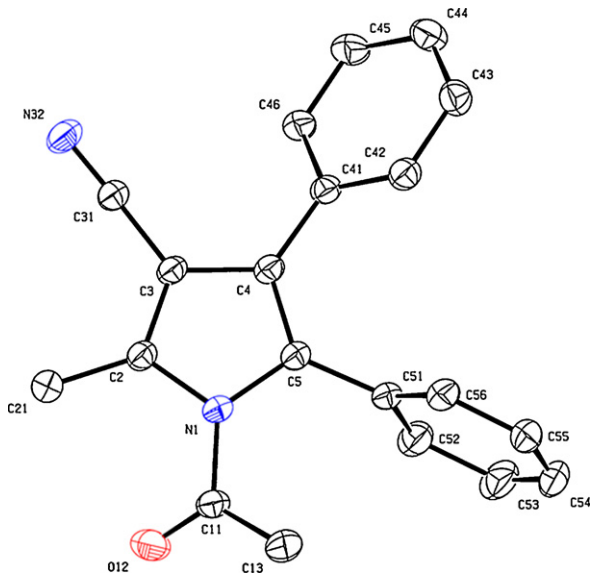


Fig. 3. X-ray structure (Ortep view 30% probability level) of pyrrole **4b**.

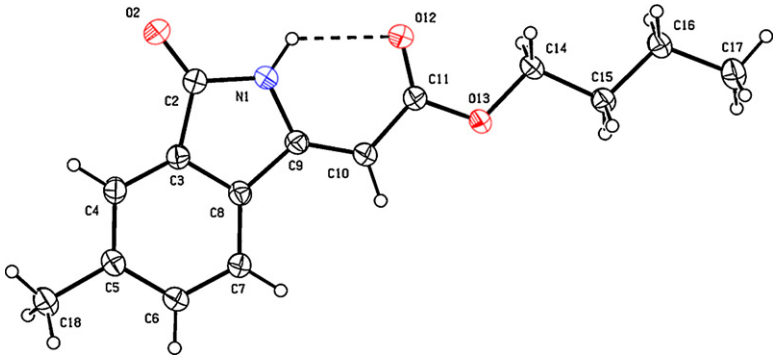
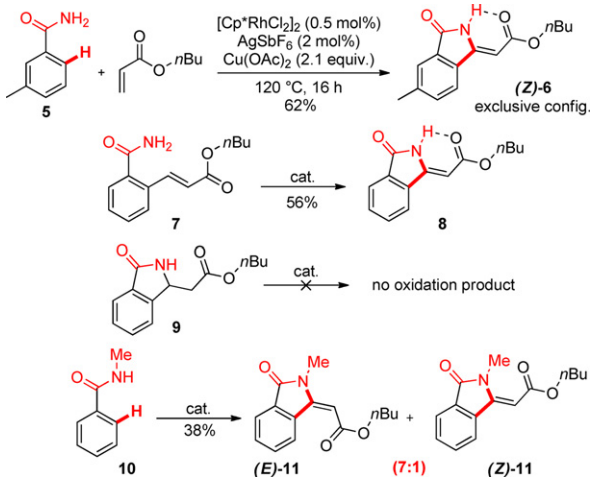


Fig. 4. X-ray structure (Ortep view 30% probability level) of lactam **6**. Selected atomic distances (Å): N1-H1 = 0.90(2), O12-H1 = 2.13(2), C9-C10 = 1.346(2), C10-C11 = 1.453(2). Selected dihedral angle: C9-N1-012-C11 = -1.4(2)°.



Scheme 2. Annulated lactam synthesis.

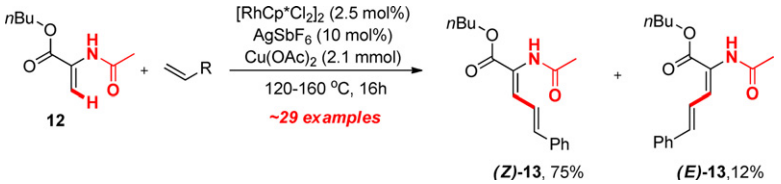
and **4b** (Figs. 1–3, respectively). Structure **4a** especially, is interesting because it is the only tetra-substituted pyrrole of the series, bearing four different substituents. Intriguingly, only the depicted isomer is detectable in the reaction mixture, which is arguably outstanding for a dehydrogenative one step cross-coupling of two very simple components. The reader should also note that in the case of unsymmetrical internal alkynes as coupling partners, the aryl moiety is always on the side of the N atom (position *2* in the case of **4a**), whereas the alkyl chain takes up position *3*.

2.2. Double C–H activation for annulated lactam synthesis

In the course of studying the oxidative olefination of primary benzamides with Michael acceptors such as *n*-butylacrylate, we came across a peculiar cyclization reaction (Scheme 2) [5–7]. Through control experiments, we established that: 1) the first step of the reaction is a classical oxidative olefination (indeed, when **7** is engaged under the catalytic conditions, the intramolecular cyclization product **8** is formed); 2) the second step does *not* go through a Michael type addition, as the cyclic conjugate addition adduct **9** did not lead to the product when submitted to the reaction conditions. Thus, the product may have formed through a second, vinylic C–H activation event, followed by reductive elimination with the benzamide part. Nevertheless, an electrophilic mechanism cannot be excluded. The configuration of the *exo* double bond can be assigned through astute NMR experiments. We were also fortunate enough to obtain crystals suitable for X-ray crystal structural analysis (Fig. 4). This confirmed that the double bond is exclusively *Z*-configured in lactam product **6**, a diasteroselectivity that is linked to the intramolecular H-bond between N–H and ester moieties. Indeed, usage of a substituted benzamide **10** leads to a mixture of *E* and *Z*-configured products **11**.

2.3. C–H activation for linear diene synthesis

While we discovered that a number of acrylate derivatives were suitable substrates for C–H activation and oxidative olefination, we faced a new type of selectivity problem with competing β-hydride elimination pathways [8,9]. Especially in substrates in which two functional groups are competing for the rhodacycle intermediate, such as α amino-acid precursors like methyl acetamidoacrylate derivatives (**12**, Scheme 3). The products are typically composed of a mixture of major *Z* and minor *E* configured linear dienes, usually separable through Silica gel column chromatography. Interestingly,



Scheme 3. Unnatural amino-acid precursor synthesis.

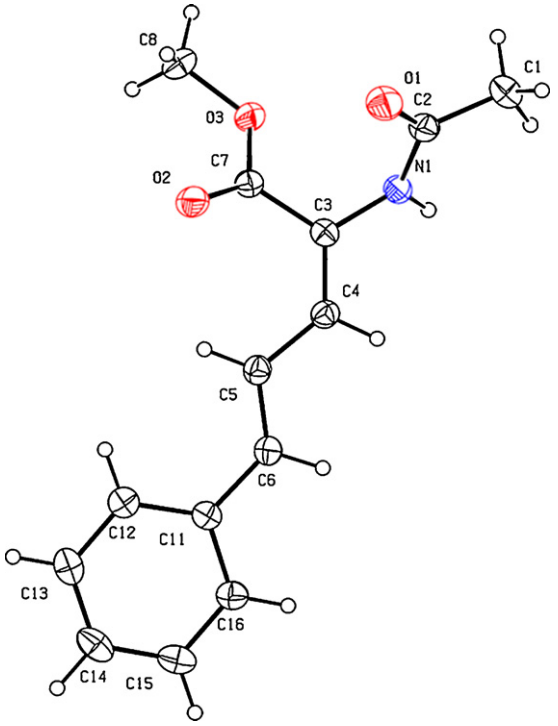


Fig. 5. X-ray structure (Ortep view 30% probability level) of α amino-acid precursor ***E*-13**. Selected atomic distances (Å): C3-C4 = 1.338(3), C4-C5 = 1.436(3), C5-C6 = 1.341(4), C6-C11 = 1.459(3), H5-O2 = 2.51(3). Selected dihedral angles: O2-C7-C3-C4 = 36.5(4)°, C4-C3-N1-C2 = −131.5(3)°, C6-C5-C4-C3 = 174.8(3)°, C16-C11-C6-C5 = 175.4(3)°.

no branched isomer was ever detected in this sort of reaction using these conditions, significantly simplifying the issue of selectivity. Because these molecules are highly functionalized, it is generally trivial to determine the absolute configurations of every single isomer through standard NOE experiments, even within mixtures. In the particular case of molecule ***E*-13**, an X-ray structure confirmed the stereochemistry, also assigned by the help of other methods (Fig. 5). A slight H-bonding effect between the ester group and one of the vinylic C–H is visible (H5-O2 = 2.51 Å), which may partly be linked to the systematic formation of this minor isomer, through a H-bonding directed β-hydride elimination (Table 1). We have attempted to tune the electronic properties of the substituents, but this only had a minor effect on the regioselective outcome, and the resulting yields are usually lower (Table 1)

3. Summary and conclusion

Herein, we have collected a few elements concerning the study of the selectivity in three different Rh catalyzed C–H activation cross-couplings. We think they bring some more perspectives on these works, and clarify some of the issues related with regioselectivity.

Data sets were collected with a Nonius KappaCCD diffractometer. Programs used: data collection COLLECT (Nonius B.V., 1998), data reduction Denzo-SMN (Z. Otwinowski, W. Minor, Methods in Enzymology, 276 (1997) 307–26), absorption correction Denzo (Z. Otwinowski, D. Borek, W. Majewski & W. Minor, Acta Cryst. A59 (2003) 228–34), structure solution SHELXS-97 (G.M.

Table 1
Crystallographic data.

	2b	**4a**	**4b**	**6**	***E*-13**
Formula	$C_{21}H_{19}NO_3$	$C_{20}H_{16}N_2O$	$C_{16}H_{16}N_2O$	$C_{15}H_{17}NO_3$	$C_{14}H_{15}NO_3$
M	333.37	300.35	252.31	259.30	245.27
Crystal size (mm)	0.35 × 0.10 × 0.02	0.25 × 0.20 × 0.10	0.25 × 0.20 × 0.07	0.35 × 0.07 × 0.05	0.35 × 0.05 × 0.03
Color	colorless	colorless	colorless	colorless	colorless
a (Å)	6.5120 (7)	8.3207 (2)	7.4414 (4)	4.0426 (3)	33.2953 (17)
b (Å)	7.5339 (8)	20.3346 (8)	13.5131 (7)	11.7557 (6)	5.8094 (2)
c (Å)	17.536 (2)	9.8166 (5)	14.2305 (5)	14.3134 (12)	13.9664 (8)
α (°)	90	90	90	101.941 (4)	90
β (°)	94.574 (5)	107.628 (2)	103.936 (5)	95.094 (7)	109.925 (7)
γ (°)	90	90	90	91.029 (3	90
V (Å^3)	857.59 (16)	1582.96 (11)	1388.85 (11)	662.42 (8)	2539.7 (2)
λ (Å)	1.54178	1.54178	1.54178	1.54178	1.54178
ρ_{calc} (g cm^{-3})	1.291	1.260	1.207	1.300	1.283
μ (mm^{-1})	0.696	0.621	0.604	0.738	0.741
Z	2	4	4	2	8
Crystal system/space group	Monoclinic/$P2_1$ (No. 4)	Monoclinic/$P2_1$/n (No. 14)	Monoclinic/$P2_1$/c (No. 14)	Triclinic/*P*1 bar (No. 2)	Monoclinic/*C*2/c (No. 15)
Reflections collected	5121	12312	10008	7107	8548
Reflections unique/R_{merge}	2329/0.069	2755/0.037	2412/0.053	2235/0.037	2138/0.046
Reflection observed ($I \geq 2\ \sigma(I)$)	1861	2470	2043	2018	1818
Refined parameter	228	210	176	177	168
R_1 (oberserved data)	0.056	0.038	0.044	0.044	0.054
wR^2 (all data)	0.153	0.107	0.117	0.124	0.155
Flack parameter	0.0(5)	–	–	–	–
Max./min. residual electron density	0.20/–0.16	0.15/–0.17	0.17/–0.18	0.29/–0.19	0.19/–0.21
CCDC	864553	864554	864555	864556	864557

Sheldrick, Acta Cryst. A46 (1990), 467–73), structure refinement SHELXL-97 (G.M. Sheldrick, Acta Cryst. A64 (2008) 112–22), graphics ORTEP.

Acknowledgements

This work was supported by the European Research Council under the European Community's Seventh Framework Program (FP7 2007–2013)/ERC Grant agreement no 25936 and the Alexander von Humboldt Foundation (F.P.). The research of F.G. has been supported by the Alfried Krupp Prize for Young University Teachers of the Alfried Krupp von Bohlen und Halbach Foundation.

References

[1] For recent reviews on C–H activation see:
(a) D.A. Colby, A.S. Tsai, R.G. Bergman, J.A. Ellman, Acc. Chem. Res. (2012), http://dx.doi.org/10.1021/ar200190g;
(b) K.M. Engle, T.S. Mei, M. Wasa, J.Q. Yu, Acc. Chem. Res. (2012), http://dx.doi.org/10.1021/ar200185g;
(c) J. Wencel-Delord, T. Dröge, F. Liu, F. Glorius, Chem. Soc. Rev. 40 (2011) 4740;
(d) C.S. Yeung, V.M. Dong, Chem. Rev. 111 (2011) 1215;
(e) L. McMurray, F. O'Hara, M.J. Gaunt, Chem. Soc. Rev. 40 (2011) 1885;
(f) T. Satoh, M. Miura, Chem. Eur. J. 16 (2010) 11212;
(g) T.W. Lyons, M.S. Sanford, Chem. Rev. 110 (2010) 1147;
(h) D.A. Colby, R.G. Bergman, J.A. Ellman, Chem. Rev. 110 (2010) 624;
(i) L.M. Xu, Z. Yang, Z.J. Shi, Chem. Soc. Rev. 39 (2010) 712;
(j) C.L. Sun, B.J. Li, Z.J. Shi, Chem. Commun. 46 (2010) 677;
(k) L. Ackermann, R. Vicente, A.R. Kapdi, Angew. Chem. Int. Ed. 48 (2009) 9792;
(l) X. Chen, K.M. Engle, D.H. Wang, J.Q. Yu, Angew. Chem. Int. Ed. 48 (2009) 5094;
(m) R. Giri, B.F. Shi, K.M. Engle, N. Maugel, J.Q. Yu, Chem. Soc. Rev. 38 (2009) 3242;
(n) B.J. Li, S.D. Yang, Z.J. Shi, Synlett (2008) 949;
(o) F. Kakiuchi, T. Kochi, Synthesis (2008) 3013;
(p) T. Satoh, M. Miura, Top. Organomet. Chem. 24 (2008) 61;
(q) D. Alberico, M.E. Scott, M. Lautens, Chem. Rev. 107 (2007) 174;
(r) L.C. Campeau, D.R. Stuart, K. Fagnou, Aldrichimica Acta. 40 (2007) 35;
For a comprehensive review on C–C bond forming CDC couplings see:
(s) C.J. Li, Acc. Chem. Res. 42 (2009) 335;
(t) F.W. Patureau, F. Wencel-Delord, F. Glorius, Glorius, Aldrichimica Acta 45 (2012) 31;
(u) G. Song, F. Wang, X. Li, Chem. Soc. Rev. 41 (2012) 3651.
[2] F.W. Patureau, T. Besset, F. Glorius, Preparation of (*E*)-*N*,*N*-Diethyl-2-styrylbenzamide by Rh-catalyzed C-H activation, Synth. 90 (2013) 41.
[3] F.W. Patureau, F. Glorius, J. Am. Chem. Soc. 132 (2010) 9982.
[4] (a) S. Rakshit, F.W. Patureau, F. Glorius, J. Am. Chem. Soc. 132 (2010) 9585;
For a selection of related works:
(b) D.R. Stuart, M. Bertrand-Laperle, K.M.N. Burgess, K. Fagnou, J. Am. Chem. Soc. 130 (2008) 16474;
(c) D.R. Stuart, P. Alsabeh, M. Kuhn, K. Fagnou, J. Am. Chem. Soc. 132 (2010) 18326;
(d) M.P. Huestis, L. Chan, D.R. Stuart, K. Fagnou, Angew. Chem. Int. Ed. 50 (2011) 1338.
[5] F.W. Patureau, T. Besset, F. Glorius, Angew. Chem. Int. Ed. 50 (2011) 1064.
[6] For a related *exo* cyclization in a palladium-catalyzed oxidative Heck reaction using hydroxyl-directing groups, see:
Y. Lu, D.H. Wang, K.M. Engle, J.Q. Yu, J. Am. Chem. Soc. 132 (2010) 5916.
[7] For related Rh(III)Cp* catalyzed cyclizations, see:
(a) K. Ueura, T. Satoh, M. Miura, Org. Lett. 9 (2007) 1407;
(b) K. Ueura, T. Satoh, M. Miura, J. Org. Chem. 72 (2007) 5362;
(c) N. Umeda, K. Hirano, T. Satoh, M. Miura, J. Org. Chem. 74 (2009) 7094;
(d) T. Fukutani, N. Umeda, K. Hirano, T. Satoh, M. Miura, Chem. Commun. (2009) 5141;
(e) K. Morimoto, K. Hirano, T. Satoh, M. Miura, Org. Lett. 12 (2010) 206;
(f) S. Mochida, N. Umeda, K. Hirano, T. Satoh, M. Miura, Chem. Lett. 39 (2010) 744;
(g) K. Morimoto, K. Hirano, T. Satoh, M. Miura, J. Org. Chem. 76 (2011) 9548;
(h) N. Umeda, K. Hirano, T. Satoh, N. Shibata, H. Sato, M. Miura, J. Org. Chem. 76 (2011) 13;
(i) N. Guimond, S.I. Gorelsky, K. Fagnou, J. Am. Chem. Soc. 133 (2011) 6449;
(j) T.K. Hyster, T. Rovis, J. Am. Chem. Soc. 132 (2010) 10565;
(k) T.K. Hyster, T. Rovis, Chem. Sci. 2 (2011) 1606;
(l) G. Song, D. Chen, C.L. Pan, R.H. Crabtree, X. Li, J. Org. Chem. 75 (2010) 7487;
(m) J. Chen, G. Song, C.L. Pan, X. Li, Org. Lett. 12 (2010) 5426;
(n) F. Wang, G. Song, X. Li, Org. Lett. 12 (2010) 5430;
(o) F. Wang, G. Song, Z. Du, X. Li, J. Org. Chem. 76 (2011) 2926;
(p) X. Li, X. Gong, M. Zhao, G. Song, J. Deng, X. Li, Org. Lett. 13 (2011) 5808;
(q) X. Li, M. Zhao, J. Org. Chem. 76 (2011) 8530;
(r) G. Song, X. Gong, X. Li, J. Org. Chem. 76 (2011) 7583;
(s) Y.F. Wang, K.K. Toh, J.Y. Lee, S. Chiba, Angew. Chem. Int. Ed. 50 (2011) 5927;
(t) P.C. Too, S.H. Chua, S.H. Wong, S. Chiba, J. Org. Chem. 76 (2011) 6159;
(u) P.C. Too, Y.F. Wang, S. Chiba, Org. Lett. 12 (2010) 5688;
(v) J. Willwacher, S. Rakshit, F. Glorius, Org. Biomol. Chem. 9 (2011) 4736;
For the addition of a Rh(III)-C–H activated species to imines, see:
(w) Y. Li, B.J. Li, W.H. Wang, W.P. Huang, X.S. Zhang, K. Chen, Z.J. Shi, Angew. Chem. Int. Ed. 50 (2011) 2115;
(x) A.S. Tsai, M.E. Tauchert, R.G. Bergman, J.A. Ellman, J. Am. Chem. Soc. 133 (2011) 1248;
For the recent development of non-chelation assisted Rh(III)Cp* catalyzed C–H activations, see:
(y) F.W. Patureau, C. Nimphius, F. Glorius, Org. Lett. 13 (2011) 6346;
(z) J. Wencel-Delord, C. Nimphius, F.W. Patureau, F. Glorius, Angew. Chem. Int. Ed. 51 (2012) 2247;
(aa) J. Wencel-Delord, C. Nimphius, F.W. Patureau, F. Glorius, Chem. Asian J. 7 (2012) 1208;
For related recent developments, see:
(ab) N. Kuhl, M.N. Hopkinson, F. Glorius, Angew. Chem. Int. Ed. 51 (2012) 8230;
(ac) Z. Shi, N. Schröder, F. Glorius, Angew. Chem. Int. Ed. 51 (2012) 8092;
(ad) N. Schröder, J. Wencel-Delord, F. Glorius, J. Am. Chem. Soc. 134 (2012) 8298;
(ae) N. Schröder, T. Besset, F. Glorius, Adv. Synth. Catal. 354 (4) (2012) 579;
(af) P. Zhao, R. Niu, F. Wang, K. Han, X. Li, Org. Lett 14 (2012) 4166;
(ag) X. Wei, F. Wang, G. Song, Z. Du, X. Li, Org. Biomol. Chem. 10 (2012) 5521;
(ah) S. Sharma, E. Park, J. Park, I.S. Kim, Org. Lett 14 (2012) 906;
(ai) C. Zhu, J.R. Falck, Chem. Commun. 48 (2012) 1674.
[8] T. Besset, N. Kuhl, F.W. Patureau, F. Glorius, Chem. Eur. J. 17 (2011) 7167.
[9] For selected examples of vinylic C–H functionalization reactions, see:
(a) T. Sato, F. Kakiuchi, N. Chatani, S. Murai, Chem. Lett. 893 (1998);
(b) C.H. Jun, C.W. Moon, Y.M. Kim, H. Lee, J.H. Lee, Tetrahedron Lett. 43 (2002) 4233;
(c) D.A. Colby, R.G. Bergman, J.A. Ellman, J. Am. Chem. Soc. 128 (2006) 5604;
(d) L.J. Gooßen, N. Rodriguez, Angew. Chem. Int. Ed. 46 (2007) 7544;
(e) A.S. Tsai, R.G. Bergman, J.A. Ellman, J. Am. Chem. Soc. 130 (2008) 6316;
(f) K. Parthasarathy, M. Jeganmohan, C.H. Cheng, Org. Lett. 10 (2008) 325;
(g) R. Giri, J.Q. Yu, J. Am. Chem. Soc. 130 (2008) 14082;
(h) M.O. Simon, R. Martinez, J.P. Genet, S. Darses, Adv. Synth. Catal. 351 (2009) 153;
(i) N.M. Neisius, B. Plietker, Angew. Chem. Int. Ed. 48 (2009) 5752;
(j) Y. Shibata, Y. Otake, M. Hirano, K. Tanaka, Org. Lett. 11 (2009) 689;
(k) M.O. Simon, J.P. Genet, S. Darses, Org. Lett. 12 (2010) 3038;
(l) Y. Su, M. Zhao, K. Han, G. Song, X. Li, Org. Lett. 12 (2010) 5462;
(m) D.A. Colby, R.G. Bergman, J.A. Ellman, J. Am. Chem. Soc. 130 (2008) 3645;
(n) A.T. Lindhardt (nee Hansen), M.L.H. Mantel, T. Skrydstrup, Angew. Chem. Int. Ed. 47 (2008) 2668;
(o) J.P. Ebran, A.L. Hansen, T.M. Gøgsig, T. Skrydstrup, J. Am. Chem. Soc. 129 (2007) 6931.