Alkene Difunctionalization

International Edition: DOI: 10.1002/anie.201608729
German Edition: DOI: 10.1002/ange.201608729

Unnatural Amino Acid Synthesis Enabled by the Regioselective Cobalt(III)-Catalyzed Intermolecular Carboamination of Alkenes

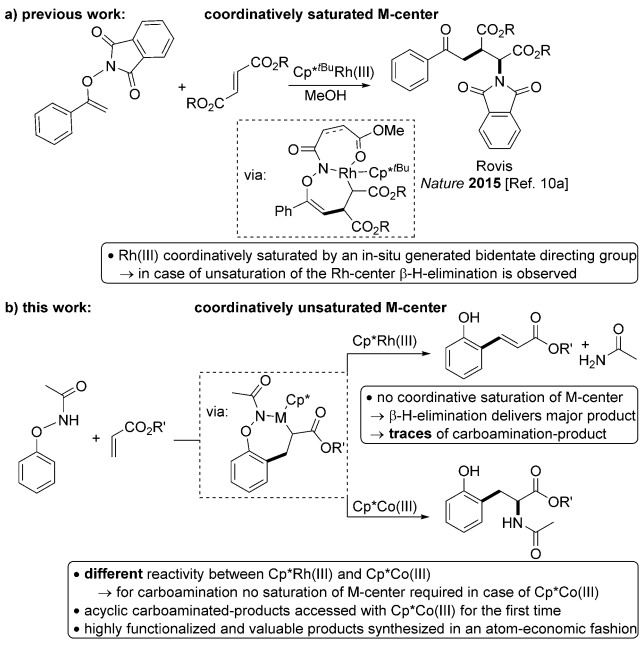
*Andreas Lerchen[+], Tobias Knecht[+], Constantin G. Daniliuc, and Frank Glorius**

Abstract: *Herein, we report an unprecedented regioselective and entirely atom-economic cobalt(III)-catalyzed method for the non-annulative, intermolecular carboamination of alkenes. The methodology enables the direct synthesis of unnatural amino acid derivatives and proceeds under redox-neutral conditions with a completely regioselective C–C bond and C–N bond formation. Furthermore, this reaction exemplifies the inherently different mechanistic behavior of the Cp*Co^{III} catalyst and its Cp*Rh^{III} counterpart, especially towards β-H-elimination.*

Transition-metal catalyzed C–H bond functionalization has proven to be a powerful and straightforward strategy for the synthesis of a variety of complex core structures that are present in natural products as well as pharmaceuticals.[1] Besides the widely established transition-metal catalysts (palladium, rhodium, iridium, ruthenium) that are associated with low abundance and high costs, the utilization of earth-abundant metal catalysts, such as cobalt has received considerable attention.[2] Inspired by the seminal reports of Kanai and Matsunaga,[3] several groups showed that the Cp*Co^{III} catalyst (Cp* = C_5Me_5) is comparable to its Cp*Rh^{III} counterpart considering its analogous reactivity.[4] Nevertheless, only a few reports have appeared to date describing a complementary reactivity of the Cp*Co^{III} catalyst to its Cp*Rh^{III} congener.[5] Reactivity differences have, however, been exploited in the case of other first- and second-row transition metals.[6] It therefore seems promising to further investigate the complementary reactivity of Cp*Co^{III} to Cp*Rh^{III} to address the limitations found with its heavier counterpart.

Alkenes are amongst the most readily available and cheapest chemical feedstocks. Despite their great synthetic potential, the metal-catalyzed difunctionalization of alkenes is still a formidable and rarely explored challenge because 1) the rate of difunctionalization versus β-H-elimination of the resulting C(sp^3)–metal-species is competitive and 2) the selective addition needs to be carefully controlled.[7] Considering the potential as well as the limitations of several alkene difunctionalizations, we became interested in the selective carboamination of alkenes. Although a variety of annulative intramolecular[8] as well as annulative intermolecular[9] carboamination reactions of alkenes have been examined, the non-annulative intermolecular carboamination of alkenes have been far less investigated.[10] Our particular focus was to explore the regioselective, non-annulative intermolecular carboamination of alkenes, since this reaction can provide highly valuable unnatural amino acid derivatives. To our knowledge no report on any non-annulative Cp*Co^{III}-catalyzed carboamination reaction has been reported to date. Additionally, given the generally higher propensity for β-H-elimination with rhodium, this reaction offers an opportunity to demonstrate the inherently divergent mechanistic behavior of the Cp*Co^{III} catalyst and its Cp*Rh^{III} counterpart, with the result that both catalysts give completely different product selectivity.

Recently the Rovis group published a Cp*Rh^{III}-catalyzed route for the intermolecular carboamination of alkenes.[10a] They reported that the β-H-elimination could be inhibited by coordinatively saturating the C(sp^3)-rhodium-intermediate with an in situ generated bidentate directing group (Scheme 1 a). Subsequently, a similar approach was reported by Liu and co-workers using a bidentate coupling partner instead of a bidentate directing group.[10b] However, both concepts essentially require the coordinative saturation of the metal center to achieve the carboamination,[11] which brings signifi-



Scheme 1. Cp*Rh^{III}- and Cp*Co^{III}-catalyzed carboamination strategies.

[*] A. Lerchen,[+] T. Knecht,[+] 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

[+] These authors contributed equally to this work.

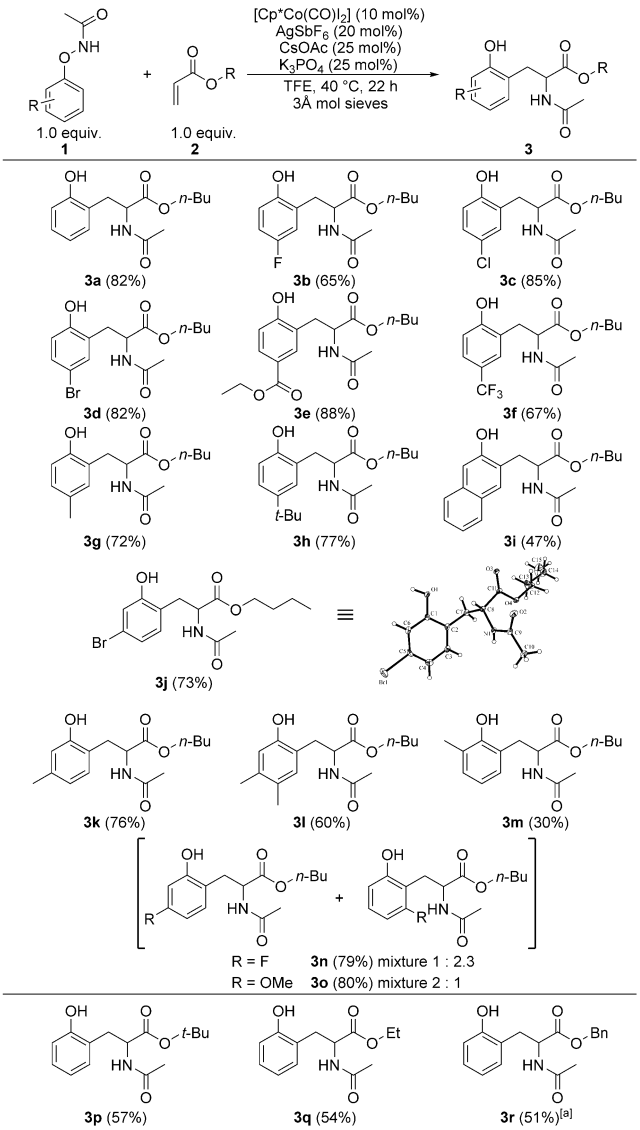
Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under http://dx.doi.org/10.1002/anie.201608729.

cant limitations in the reaction scope and further ligand-modifications as well as inconvenient multi-step substrate syntheses are necessary.

Inspired by these reports we designed the first regioselective intermolecular Cp*Co^{III}-catalyzed carboamination of alkenes. The unique properties of the catalyst system obviate the need for either a bidentate directing group or a bidentate coupling partner (Scheme 1b). In this conceptually and mechanistically distinct reaction, the Cp*Co^{III}-catalyst led to a different product than its Cp*Rh^{III}-counterpart. For the rhodium catalyst, if the saturation of the nascent C(sp^3)–metal center is not achieved, β-H-elimination predominates and the oxidative Heck product is formed. In the case of cobalt, no saturation of the C(sp^3)–metal center is required and the carboamination is inherently favored over the β-H-elimination.

We began our studies using phenoxyacetamide (**1**) as it features a redox-active directing group and *n*-butylacrylate (**2**) as coupling partner. After an extensive screening, (see the Supporting Information) we could achieve a completely regioselective addition to the double bond and isolate the desired product **3a** in 82% yield using stoichiometric amounts of **1** and **2** in the presence of catalytic amounts of [Cp*Co(CO)I$_2$], AgSbF$_6$, CsOAc, and K$_3$PO$_4$ (Scheme 2 and see the Supporting information). When the same conditions were applied with the [(Cp*RhCl$_2$)$_2$] catalyst instead of the [Cp*Co(CO)I$_2$] catalyst, the oxidative Heck product was isolated in 53% yield and only trace amounts of the carboamination product could be detected in the crude reaction mixture by ESI-MS (see the Supporting Information).

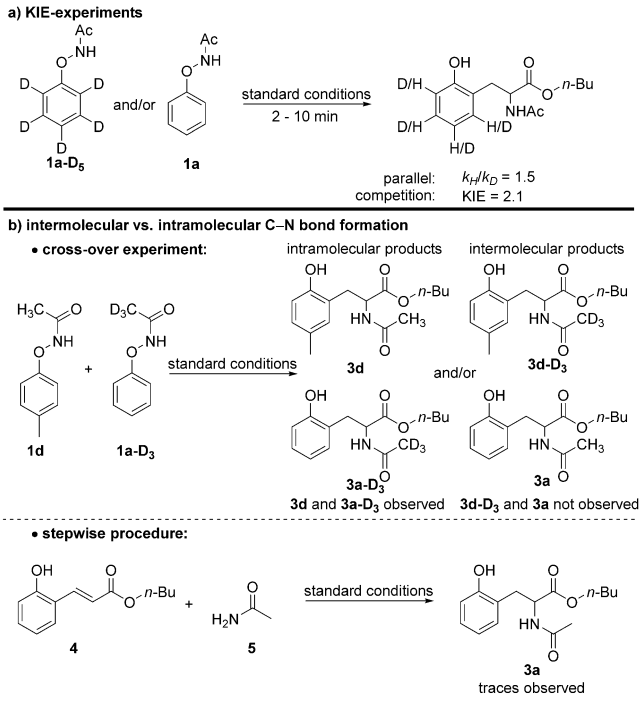
With the optimized reaction conditions in hand, we investigated the scope of the carboamination reaction (Scheme 2). *Para*-substituted phenoxyacetamides with electron-withdrawing functional groups, such as halogens (**3b**–**3d**), esters (**3e**), or even the CF$_3$ substituent (**3f**), delivered the desired amino acid derivatives in good to excellent yields. Similar results could be obtained for *para*-substituted phenoxyacetamides bearing electron-donating functional groups (**3g**, **3h**). Using the disubstituted 3,4-dimethylphenoxyacetamide, the corresponding product could be isolated in good yield (60%) and excellent regioselectivity (**3l**). Furthermore, 2-*N*-(naphthalen-2-yloxy)acetamide could deliver the desired amino acid derivative in a moderate yield of 47% (**3i**). *Meta*-substituted electron-withdrawing (*m*-Br) as well as electron-donating (*m*-Me) phenoxyacetamides delivered the corresponding products in good yields and a single regioisomer was obtained (**3j**, **3k**). The absolute molecule structures for **3j** and **3c** were confirmed by X-ray crystallography (see Scheme 2 and the Supporting Information).[12] For the *meta*-methoxy- and the *meta*-fluorophenoxyacetamides excellent yields could be obtained, although a mixture of regioisomers was observed (**3n**, **3o**). The *ortho*-methylphenoxyacetamide delivered the corresponding product in 30% yield (**3m**). The poor reactivity is attributed to the great steric demand of the Cp*Co^{III} catalyst, which results in sensitivity to steric bulk on the substrates. No product formation was observed in the absence of the Cp*Co^{III} catalyst. We further investigated the scope of the *N*-protecting group. However, benzyloxycarbonyl- (Cbz), benzoyl- (Bz), tosyl- (Ts), and pivaloyl- (Piv) protected substrates were unsuccessful under the optimized reaction conditions (see Supporting Information).



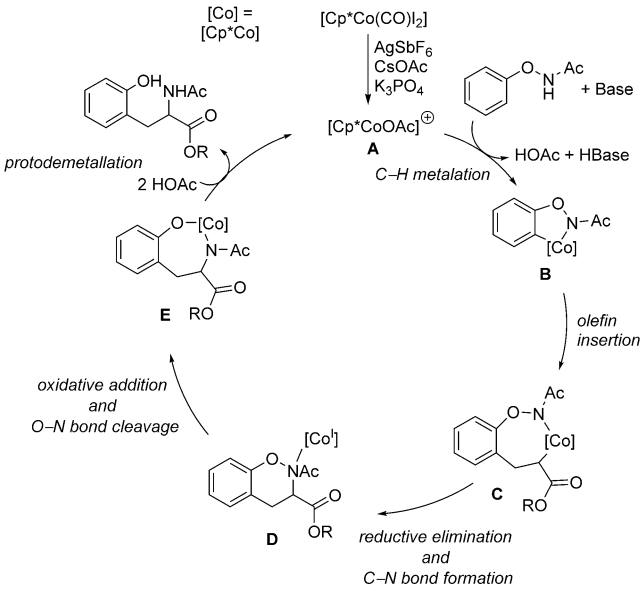
Scheme 2. Variation of the phenoxyacetamide and acrylate. Isolated yields are given. **1** (0.2 mmol), **2** (1.0 equiv), [Cp*Co(CO)I$_2$] (10 mol%), AgSbF$_6$ (20 mol%), CsOAc (25 mol%), K$_3$PO$_4$ (25 mol%), 3 Å MS (40 mg) in TFE (1 mL) at 40°C for 22 h; [a] 0.4 mmol of **2** was used. For crystallographic data see: Ref. [12].

Several acrylates also led to the formation of the corresponding amino acid derivatives. *tert*-Butylacrylate and ethylacrylate delivered the desired products in reasonable yields (**3p**, **3q**). Moreover, using benzylacrylate the carboaminated product (**3r**) was formed in a synthetically useful yield of 51%.

Further experiments were carried out to elucidate a possible reaction mechanism (Scheme 3). First, the kinetic isotope effect was studied in competition and parallel experiments (Scheme 3a). A KIE of 2.1 (competition experiment) and $k_H/k_D = 1.5$ (parallel experiment) were observed. Based on these results, we propose that the C–H activation step is



Scheme 3. Mechanistic experiments.



Scheme 4. Proposed reaction mechanism.

partly rate determining in the reaction.[13] Second, we investigated the reaction process after the C–H activation event for the distinction between an intermolecular and an intramolecular reaction pathway for the C–N bond formation (Scheme 3b). Towards this goal we first synthesized the compounds **1d** and **1a-D$_3$** and treated them in a cross-over experiment. The results indicate that the C–N bond formation proceeds via an intramolecular pathway. The products **3d-D$_3$** and **3a** that would result from an intermolecular cross-over were not detected by ESI-MS of the crude reaction mixture, whereas only the products resulting from the intramolecular cross-over reaction **3d** and **3a-D$_3$** were detected.

Next, we investigated whether the reaction mechanism could proceed in a stepwise manner. Towards this end compound **4** was synthesized and treated with acetamide (**5**). The reaction was performed under the standard reaction conditions and only traces of the amino acid derivative were detected in the crude reaction mixture by ESI-MS (see the Supporting Information). This result is in accordance with the mechanistic cross-over experiment. Based on these results we propose that after the intermolecular formation of the C–C bond, the reaction proceeds via an intramolecular pathway to form the C–N bond.

Based on these experimental results we propose a reaction mechanism (Scheme 4). After the formation of the catalytically active species **A**, the C–H activation occurs under elimination of HOAc and formation of intermediate **B**. Intermediate **B** can then undergo an olefin-coordination followed by an olefin-insertion leading to the 7-membered intermediate **C**. The C(sp^3)–metal-species **C** undergoes reductive elimination thus forming the desired C–N bond under the concomitant generation of Co^{I} (species **D**). Afterwards, the O–N bond undergoes an oxidative addition to the cobalt(I) species to form the 7-membered Co^{III} intermediate **E**. Finally, intermediate **E** delivers the desired amino acid derivative and regenerates the active catalyst species **A** through a proto-demetallation.

In conclusion, we have developed the first non-annulative Cp*Co^{III}-catalyzed carboamination approach for the direct difunctionalization of alkenes. The reaction proceeds in an intermolecular fashion with a completely regioselective C–C bond and then an intramolecular C–N bond formation. Additionally, we could demonstrate for the first time that this reaction proceeds in the absence of a bidentate directing group or a bidentate coupling partner and that the reaction outcome is solely attributed to the unique reactivity of the Cp*Co^{III} catalyst. The results show the complementary nature of the Cp*Co^{III} catalyst and its Cp*Rh^{III} counterpart, since two completely different products are formed under otherwise identical conditions. Moreover, this methodology enables the direct synthesis of unnatural amino acid derivatives that are highly valuable for industrial research as well as for academia.

Acknowledgements

We gratefully thank A. Rühling, T. Gensch, J. B. Ernst, L. Rakers, M. Wiesenfeldt, Dr. E. A. Standley, Dr. K. M. Chepiga, and Dr. M. van Gemmeren for fruitful discussions and K. Gottschalk for technical assistance (all WWU). We gratefully acknowledge generous financial support by the Deutsche Forschungsgemeinschaft (Leibniz award).

Keywords: alkene difunctionalization · carboamination · Cp*Co(III) catalysis · redox-neutral conditions · unnatural amino acids

[1] Selected Reviews: a) P. B. Arockiam, C. Bruneau, P. H. Dixneuf, *Chem. Rev.* **2012**, *112*, 5879; b) G. Song, X. Li, *Acc. Chem. Res.* **2015**, *48*, 1007; c) L. Ackermann, *Chem. Rev.* **2011**, *111*, 1315; d) L. Ackermann, *Acc. Chem. Res.* **2014**, *47*, 281; e) T. Gensch, M. N. Hopkinson, F. Glorius, J. Wencel-Delord, *Chem. Soc. Rev.* **2016**, *45*, 2900; f) N. Kuhl, N. Schröder, F. Glorius, *Adv. Synth. Catal.* **2014**, *356*, 1443; g) T. Satoh, M. Miura, *Chem. Eur. J.* **2010**, *16*, 11212; h) D. Zhao, J. You, C. Hu, *Chem. Eur. J.* **2011**, *17*, 5466; i) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624; j) L. McMurray, F. O'Hara, M. J. Gaunt, *Chem. Soc. Rev.* **2011**, *40*, 1885; k) S. H. Cho, J. Y. Kim, J. Kwak, S. Chang, *Chem. Soc. Rev.* **2011**, *40*, 5068; l) J. Yamaguchi, A. D. Yamaguchi, K. Itami, *Angew. Chem. Int. Ed.* **2012**, *51*, 8960; *Angew. Chem.* **2012**, *124*, 9092; m) X.-S. Zhang, K. Chen, Z.-J. Shi, *Chem. Sci.* **2014**, *5*, 2146; n) T. Cernak, K. D. Dykstra, S. Tyagarajan, P. Vachal, S. W. Krska, *Chem. Soc. Rev.* **2016**, *45*, 546; o) M. Zhang, Y. Zhang, X. Jie, H. Zhao, G. Li, W. Su, *Org. Chem. Front.* **2014**, *1*, 843; p) J. Mo, L. Wang, Y. Liu, X. Cui, *Synthesis* **2015**, 439; q) H. Huang, X. Ji, W. Wu, H. Jiang, *Chem. Soc. Rev.* **2015**, *44*, 1155.

[2] Selected Reviews on earth-abundant metal-catalyzed C–H bond activation: a) M. Moselage, J. Li, L. Ackermann, *ACS Catal.* **2016**, *6*, 498; b) K. Gao, N. Yoshikai, *Acc. Chem. Res.* **2014**, *47*, 1208; c) W. Liu, L. Ackermann, *ACS Catal.* **2016**, *6*, 3743; d) A. A. Kulkarni, O. Daugulis, *Synthesis* **2009**, 4087; e) S. Z. Tasker, E. A. Standley, T. F. Jamison, *Nature* **2014**, *509*, 299; f) J. J. Mousseau, A. B. Charette, *Acc. Chem. Res.* **2013**, *46*, 412; g) E. Nakamura, N. Yoshikai, *J. Org. Chem.* **2010**, *75*, 6061.

[3] a) T. Yoshino, H. Ikemoto, S. Matsunaga, M. Kanai, *Angew. Chem. Int. Ed.* **2013**, *52*, 2207; *Angew. Chem.* **2013**, *125*, 2263; b) T. Yoshino, H. Ikemoto, S. Matsunaga, M. Kanai, *Chem. Eur. J.* **2013**, *19*, 9142.

[4] For selected examples, see: a) D. Zell, Q. Bu, M. Feldt, L. Ackermann, *Angew. Chem. Int. Ed.* **2016**, *55*, 7408; *Angew. Chem.* **2016**, *128*, 7534; b) J. Li, L. Ackermann, *Angew. Chem. Int. Ed.* **2015**, *54*, 8551; *Angew. Chem.* **2015**, *127*, 8671; c) J. Li, L. Ackermann, *Angew. Chem. Int. Ed.* **2015**, *54*, 3635; *Angew. Chem.* **2015**, *127*, 3706; d) H. Wang, J. Koeller, W. Liu, L. Ackermann, *Chem. Eur. J.* **2015**, *21*, 15525; e) H. Wang, M. Moselage, M. J. González, L. Ackermann, *ACS Catal.* **2016**, *6*, 2705; f) N. Sauermann, M. J. González, L. Ackermann, *Org. Lett.* **2015**, *17*, 5316; g) A. Lerchen, S. Vásquez-Céspedes, F. Glorius, *Angew. Chem. Int. Ed.* **2016**, *55*, 3208; *Angew. Chem.* **2016**, *128*, 3261; h) T. Gensch, F. J. R. Klauck, F. Glorius, *Angew. Chem. Int. Ed.* **2016**, *55*, 11287; *Angew. Chem.* **2016**, *128*, 11457; i) X. Wang, A. Lerchen, F. Glorius, *Org. Lett.* **2016**, *18*, 2090; j) D.-G. Yu, T. Gensch, F. de Azambuja, S. Vásquez-Céspedes, F. Glorius, *J. Am. Chem. Soc.* **2014**, *136*, 17722; k) J. R. Hummel, J. A. Ellman, *J. Am. Chem. Soc.* **2015**, *137*, 490; l) J. R. Hummel, J. A. Ellman, *Org. Lett.* **2015**, *17*, 2400; m) B. Sun, T. Yoshino, S. Matsunaga, M. Kanai, *Adv. Synth. Catal.* **2014**, *356*, 1491; n) M. Sen, D. Kalsi, B. Sundararaju, *Chem. Eur. J.* **2015**, *21*, 15529; o) M. Sen, B. Emayavaramban, N. Barsu, J. R. Premkumar, B. Sundararaju, *ACS Catal.* **2016**, *6*, 2792; p) S. Prakash, K. Muralirajan, C.-H. Cheng, *Angew. Chem. Int. Ed.* **2016**, *55*, 1844; *Angew. Chem.* **2016**, *128*, 1876; q) L. Kong, S. Yu, X. Zhou, X. Li, *Org. Lett.* **2016**, *18*, 588; r) Y. Liang, N. Jiao, *Angew. Chem. Int. Ed.* **2016**, *55*, 4035; *Angew. Chem.* **2016**, *128*, 4103; s) X.-G. Liu, S.-S. Zhang, C.-Y. Jiang, J.-Q. Wu, Q. Li, H. Wang, *Org. Lett.* **2015**, *17*, 5404; t) Z.-Z. Zhang, B. Liu, C.-Y. Wang, B.-F. Shi, *Org. Lett.* **2015**, *17*, 4094; u) Z.-Z. Zhang, B. Liu, J.-W. Xu, S.-Y. Yan, B.-F. Shi, *Org. Lett.* **2016**, *18*, 1776.

[5] For selected examples, see: a) H. Ikemoto, T. Yoshino, K. Sakata, S. Matsunaga, M. Kanai, *J. Am. Chem. Soc.* **2014**, *136*, 5424; b) Y. Suzuki, B. Sun, K. Sakata, T. Yoshino, S. Matsunaga, M. Kanai, *Angew. Chem. Int. Ed.* **2015**, *54*, 9944; *Angew. Chem.* **2015**, *127*, 10082; c) B. Sun, T. Yoshino, M. Kanai, S. Matsunaga, *Angew. Chem. Int. Ed.* **2015**, *54*, 12968; *Angew. Chem.* **2015**, *127*, 13160; d) D. Zhao, J. H. Kim, L. Stegemann, C. A. Strassert, F. Glorius, *Angew. Chem. Int. Ed.* **2015**, *54*, 4508; *Angew. Chem.* **2015**, *127*, 4591; e) Q. Lu, S. Vásquez-Céspedes, T. Gensch, F. Glorius, *ACS Catal.* **2016**, *6*, 2352; f) J. H. Kim, S. Greßies, F. Glorius, *Angew. Chem. Int. Ed.* **2016**, *55*, 5577; *Angew. Chem.* **2016**, *128*, 5667; g) J. Park, S. Chang, *Angew. Chem. Int. Ed.* **2015**, *54*, 14103; *Angew. Chem.* **2015**, *127*, 14309; h) H. Wang, M. M. Lorion, L. Ackermann, *Angew. Chem. Int. Ed.* **2016**, *55*, 10386; *Angew. Chem.* **2016**, *128*, 10542; i) D. Kalsi, R. A. Laskar, N. Barsu, J. R. Premkumar, B. Sundararaju, *Org. Lett.* **2016**, *18*, 4198; j) J. A. Boerth, J. R. Hummel, J. A. Ellman, *Angew. Chem. Int. Ed.* **2016**, *55*, 12650; *Angew. Chem.* **2016**, *128*, 12840.

[6] V. P. Ananikov, *ACS Catal.* **2015**, *5*, 1964.

[7] a) K. H. Jensen, M. S. Sigman, *Org. Biomol. Chem.* **2008**, *6*, 4083; b) R. I. McDonald, G. Liu, S. S. Stahl, *Chem. Rev.* **2011**, *111*, 2981; c) for dihydroxylation, see: H. C. Kolb, M. S. VanNieuwenhze, K. B. Sharpless, *Chem. Rev.* **1994**, *94*, 2483; d) for diamination, see: Y. Zhu, R. G. Cornwall, H. Du, B. Zhao, Y. Shi, *Acc. Chem. Res.* **2014**, *47*, 3665; e) F. Cardona, A. Goti, *Nat. Chem.* **2009**, *1*, 269; f) K. Muñiz, *Chem. Soc. Rev.* **2004**, *33*, 166; g) for dihalogenation, see; A. J. Cresswell, S. T.-C. Eey, S. E. Denmark, *Angew. Chem. Int. Ed.* **2015**, *54*, 15642; *Angew. Chem.* **2015**, *127*, 15866; h) U. Hennecke, *Chem. Asian J.* **2012**, *7*, 456; i) for aminohalogenation, see: S. R. Chemler, M. T. Bovino, *ACS Catal.* **2013**, *3*, 1076; j) for carboamination, see: D. M. Schultz, J. P. Wolfe, *Synthesis* **2012**, 351.

[8] a) S. R. Chemler, *Org. Biomol. Chem.* **2009**, *7*, 3009; for selected annulative intramolecular carboamination reactions, see: b) A. Faulkner, J. S. Scott, J. F. Bower, *J. Am. Chem. Soc.* **2015**, *137*, 7224; c) B. A. Hopkins, J. P. Wolfe, *Chem. Sci.* **2014**, *5*, 4840; d) B. A. Hopkins, J. P. Wolfe, *Angew. Chem. Int. Ed.* **2012**, *51*, 9886; *Angew. Chem.* **2012**, *124*, 10024; e) J. D. Neukom, N. S. Perch, J. P. Wolfe, *J. Am. Chem. Soc.* **2010**, *132*, 6276; f) G. Zhang, L. Cui, Y. Wang, L. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 1474; g) C. F. Rosewall, P. A. Sibbald, D. V. Liskin, F. E. Michael, *J. Am. Chem. Soc.* **2009**, *131*, 9488; h) N. C. Giampietro, J. P. Wolfe, *J. Am. Chem. Soc.* **2008**, *130*, 12907; i) K.-T. Yip, M. Yang, K.-L. Law, N.-Y. Zhu, D. Yang, *J. Am. Chem. Soc.* **2006**, *128*, 3130; j) J. S. Nakhla, J. W. Kampf, J. P. Wolfe, *J. Am. Chem. Soc.* **2006**, *128*, 2893. Intramolecular: the olefin is preinstalled and the first step of the reaction proceeds in an intramolecular fashion.

[9] For selected intermolecular annulative carboamination reactions, see: a) D. R. White, J. T. Hutt, J. P. Wolfe, *J. Am. Chem. Soc.* **2015**, *137*, 11246; b) M. K. Manna, A. Hossian, R. Jana, *Org. Lett.* **2015**, *17*, 672; c) C. E. Houlden, C. D. Bailey, J. G. Ford, M. R. Gagné, G. C. Lloyd-Jones, K. I. Booker-Milburn, *J. Am. Chem. Soc.* **2008**, *130*, 10066; d) C. C. Scarborough, S. S. Stahl, *Org. Lett.* **2006**, *8*, 3251; e) D. Zhao, S. Vásquez-Céspedes, F. Glorius, *Angew. Chem. Int. Ed.* **2015**, *54*, 1657; *Angew. Chem.* **2015**, *127*, 1677. Intermolecular: the first step of the reaction proceeds in an intermolecular fashion.

[10] For intermolecular non-annulative carboamination reactions, see: a) T. Piou, T. Rovis, *Nature* **2015**, *527*, 86; b) Z. Hu, X. Tong, G. Liu, *Org. Lett.* **2016**, *18*, 1702. Intermolecular: the olefin is not preinstalled and the first step of the reaction proceeds in an intermolecular fashion.

[11] For results with coordinatively non-saturated Cp^*Rh^{III} species, see: a) for the Rovis work: T. Piou, T. Rovis, *J. Am. Chem. Soc.* **2014**, *136*, 11292; b) for the Liu work: Y. Shen, G. Liu, Z. Zhou, X. Lu, *Org. Lett.* **2013**, *15*, 3366.

[12] CCDC 1501392 and 1501393 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.
[13] a) E. M. Simmons, J. F. Hartwig, *Angew. Chem. Int. Ed.* **2012**, *51*, 3066; *Angew. Chem.* **2012**, *124*, 3120; b) G. Bellucci, R. Bianchini, C. Chiappe, D. Lenoir, A. Attar, *J. Am. Chem. Soc.* **1995**, *117*, 6243.

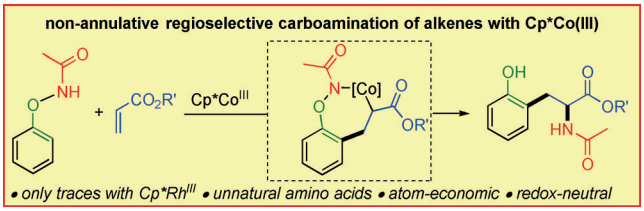
Received: September 6, 2016
Published online: ■■ ■■, ■■■■

Communications

Alkene Difunctionalization

A. Lerchen, T. Knecht, C. G. Daniliuc, F. Glorius* ——— ■■■■–■■■■

Unnatural Amino Acid Synthesis Enabled by the Regioselective Cobalt(III)-Catalyzed Intermolecular Carboamination of Alkenes



It's cobaltastic: An unprecedented regioselective and entirely atom-economic cobalt(III)-catalyzed method for the non-annulative, intermolecular carboamination of alkenes enables the direct synthesis of acyclic unnatural amino acid derivatives in a redox-neutral fashion. Moreover Cp^*Co^{III} and Cp^*Rh^{III} catalysts gave different products under otherwise identical conditions.

