Article

Rh(I)-Catalyzed Hydroamidation of Olefins via Selective Activation of N-H Bonds in Aliphatic Amines

Kaiwu Dong, Xianjie Fang, Ralf Jackstell, Gabor Laurenczy, Yuehui Li, and Matthias Beller

J. Am. Chem. Soc., **Just Accepted Manuscript** • Publication Date (Web): 12 Apr 2015

Rh(I)-Catalyzed Hydroamidation of Olefins via Selective Activation of N-H Bonds in Aliphatic Amines

Kaiwu Dong,[†] Xianjie Fang,[†] Ralf Jackstell,[†] Gabor Laurenczy,[‡] Yuehui Li,*[,†] and Matthias Beller*[,†]

[†]Leibniz-Institut für Katalyse e.V. an der Universität Rostock, Albert-Einstein Str. 29a, 18059 Rostock, Germany

[‡]Institut des Sciences et Ingénierie Chimiques, Ecole Polytechnique Fédérale de Lausanne, 1015 Lausanne, Switzerland

KEYWORDS: Olefins, Aliphatic Amines, Hydroamidation, Rhodium, Ligand-free

Supporting Information Placeholder

ABSTRACT: Hydroamidation of olefins constitutes an ideal, atom-efficient method to prepare carboxylic amides from easily available olefins, CO and amines. So far, aliphatic amines are not suitable for these transformations. Here, we present a ligand- and additive-free Rh(I) catalyst as solution to this problem. Various amides are obtained in good yields and excellent regioselectivities. Notably, chemoselective amidation of aliphatic amines takes place in the presence of aromatic amines and alcohols. Mechanistic studies reveal the presence of Rh-acyl species as crucial intermediates for the selectivity and rate-limiting step in the proposed Rh(I)-catalytic cycle.

INTRODUCTION

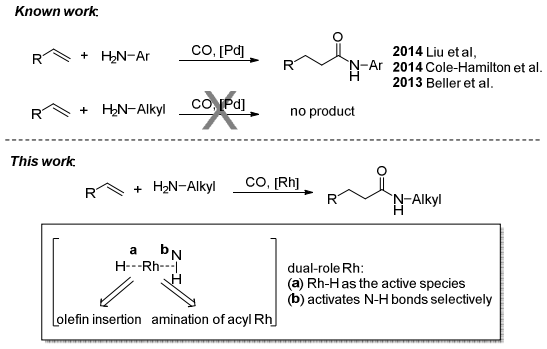
Carbonylation reactions constitute the most important and largest examples of industrially applied homogeneous catalytic reactions.[1] In addition to hydroformylation,[1b,2] the transition-metal catalyzed addition of carbon monoxide to alkenes, alkynes or aryl/vinyl halides in the presence of a suitable nucleophile, such as water, alcohols, and amines, leads to the formation of saturated or unsaturated carboxylic acid derivatives which are valuable products for the chemical industry.[3] Compared with the well-explored alkoxycarbonylation of alkenes and alkynes, related hydroamidations leading to amides are still in their infancy.

Amides represent important intermediates, building blocks and products in organic synthesis, the chemical and life science industries as well as biological systems.[4] Hence, efficient and selective construction of amide bonds is a long-standing task for chemists.[5] Traditional methods involve condensation of carboxylic acids and their derivatives with amines in the presence of activation reagents.[6] Recently, several interesting catalytic methods were reported such as oxidative amidation of amines,[7] hydrocarbamoylation of alkenes/alkynes,[8] oxidative coupling of α-bromo nitroalkanes with amines,[9] transamidation reactions,[10] and acylation of amine surrogates.[11] However, most of these procedures suffer from several drawbacks such as harsh conditions, generation of (over)stoichiometric amounts of by-products or/and limited substrate scope.

In general, carbonylation of alkenes, alkynes,[12] 1,3-dienes,[13] or aryl/vinyl halides[1e,14] with amines represents a straightforward tool for the synthesis of saturated or unsaturated amides. In hydroamidations of alkenes, cobalt-carbonyl complexes,[15] nickel cyanide,[16] iron carbonyl complexes,[17] and ruthenium chloride[18] were used as catalysts at an early stage. However, all these reactions are carried out under severe conditions (>200 °C; >150 atm CO). Since the 1980s, ruthenium-carbonyl complexes[19] and cobalt on charcoal[20] proved to be more efficient catalysts. Nevertheless, the unavoidable formation of formamide by-products and the limited substrate scope impeded further applications of these processes.

Recently, Cole-Hamilton[21] and Liu[22] and co-workers as well as our group[23] independently developed palladium-based catalysts for aminocarbonylation of alkenes. Notably, in all these works aromatic amines were employed. Unfortunately, when using aliphatic amines as substrates, no desired reaction occurred due to the stronger basicity of aliphatic amines. Hence, the generation of catalytically active palladium hydrides is retarded. Thus, the development of alternative catalytic systems for the hydroamidation of olefins with aliphatic amines continues to be a challenging goal.

Scheme 1. Catalytic hydroamidation of olefins



Although rhodium phosphine complexes dominate as catalysts in alkene hydroformylation reactions,[2,24] to the best of our

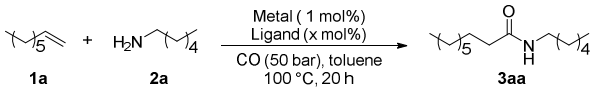
knowledge there is no systematic study on related rhodium-catalyzed aminocarbonylations of alkenes.[19] Despite the apparent simplicity of the required aminolysis of Rh-acyl intermediates, no formation of amides was observed in previous reports on Rh-catalyzed hydroaminomethylations (hydroformylation/reductive amination) of olefins.[25] Nevertheless, here we report an efficient, convenient and general hydroamidation of alkenes with a variety of aliphatic amines in the presence of "phosphine-free" rhodium catalysts.

RESULTS AND DISCUSSION

Model Studies. Initial attempts of the hydroamidation of 1-octene **1a** with hexylamine **2a** were carried out at 100 °C with 1 mol% of different metal complexes under 50 bar pressure of CO. As shown in Table 1, no desired product *N*-hexylnonanamide **3aa** was detected when $PdCl_2$, $Ru_3(CO)_{12}$, $CoCl_2$, or $Ni(OTf)_2$ was used as the catalyst (Table 1, entries 1-4). To our surprise, the desired **3aa** was obtained in moderate yield with excellent regioselectivity in the presence of $Rh(acac)(CO)_2$ (Table 1, entry 5: 35% yield, *n*/*iso* = 93/7). Encouraged by this result, the addition of different ligands was investigated (see SI, Table S2). However, no positive effect was observed and the reactivity was almost fully suppressed in many cases (Table 1, entries 6-10). As shown in Table S2 stronger coordinating ligands led to lower activity. For example, when using electron-rich ligands such as **L1, L5** and bidentate ligands, no product could be obtained. These results indicated that hexylamine **2a** might need effective coordination to the vacant site on Rh center for generation of the Rh-H intermediates and/or cleavage of the N-H bonds.

To our delight, the yield of **3aa** was improved significantly to 86% (*n*/*iso*: 94/6) when excess amounts of 1-octene **1a** were used (Table 1, entries 11-12). Next, we studied the influence of different rhodium precursors in the aminocarbonylation of 1-octene **1a**. Here, rhodium complexes in different oxidation states were examined. Among the tested complexes, Rh(I), Rh(III), and Rh(0) precursors all similarly afforded the desired product **3aa** in high yields with excellent regioselectivities, which implicates that the same/similar active species are formed in all the cases (Table 1, entries 12-14).

Table 1. Catalytic hydroamidation of 1-octene 1a with hexylamine 2a: Investigation of different metals and ligands[a]



Entry	Metal/Ligand (1/x)	Yield/%	*n*/*iso*
1	$PdCl_2$	0	--
2	$Ru_3(CO)_{12}$	0	--
3	$CoCl_2$	0	--
4	$Ni(OTf)_2$	0	--
5	$Rh(acac)(CO)_2$	35	93/7
6	$Rh(acac)(CO)_2/PPh_3$ (1/2)	3	--
7	$Rh(acac)(CO)_2/Ph_2P(2\text{-}Py)$ (1/2)	7	95/5
8	$Rh(acac)(CO)_2$/Xantphos (1/1)	0	--
9	$Rh(acac)(CO)_2$/d^{t}bpx (1/1)	5	--
10	$Rh(acac)(CO)_2$/Naphos (1/1)	0	--
11[b]	$Rh(acac)(CO)_2$	59	94/6
12[c]	$Rh(acac)(CO)_2$	86	94/6
13[c]	$Rh_4(CO)_{12}$	94	92/8
14[c]	$RhCl_3 \cdot 3H_2O$	92	96/4

[a] Reaction conditions: **1a** (1.0 mmol), **2a** (1.0 mmol), metal (1 mol%), CO (50 bar), toluene (2.0 mL), 100 °C, 20 h. Yield of **3aa** was determined by GC analysis using isooctane as internal standard. The ratio of isomers was determined by GC analysis. [b] **1a** (2.0 mmol). [c] **1a** (5.0 mmol), toluene (1.0 mL). Xantphos = (9,9-dimethyl-9*H*-xanthene-4,5-diyl)bis(diphenylphosphane). d^{t}bpx = 1,2-bis((di-*tert*-butylphosphanyl)methyl)benzene. Naphos = 2,2'-bis((diphenylphosphanyl)methyl)-1,1'-binaphthalene.

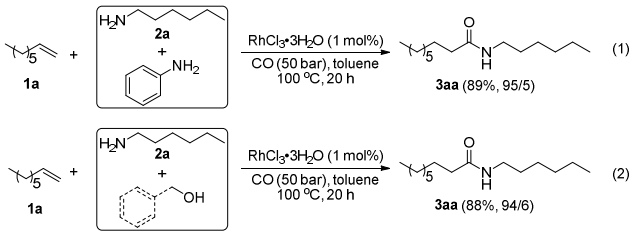
Due to the possible activation effect of bases and acids on N-H bonds, several additives were tested in the benchmark reaction, too (see SI, Table S5). Similar activity is obtained in the presence of the weak base KOAc (Table S5, entry 1). The addition of Brønsted acids yielded slightly lower amounts of **3aa** with the same selectivity (Table S5, entries 2-4). Notably, the reaction was inhibited when BmimCl (1-butyl-3-methylimidazolium chloride) was added as the additive (Table S5, entry 6). The activity of the reaction decreased when Lewis acids were added into the catalytic system (Table S5, entries 7 and 8).

Mechanistic Studies. With the above ligand-free and additive-free Rh-catalytic system in hand, the mechanism was then studied by control experiments, mass spectroscopic investigations and in situ NMR spectroscopy.

First, control experiments were carried out to compare the reactivity of aliphatic amines with other types of nucleophiles.[26] In general, with or without phosphine co-ligands present the active Rh-H species is formed efficiently from the reaction of aliphatic amines and the rhodium precursor complex. In these cases a significant amount of olefin isomerization is observed. However, it was found that in the presence of aromatic amines no desired hydroamidation occurred and only trace amounts of isomerized olefins were detected. This indicates the difficulty of Rh-H formation step from aromatic amines. In agreement with this finding, competition reactions of 1-hexylamine with aniline or benzyl alcohol showed the selective carbonylation with aliphatic amines and no reaction occurred with the aromatic amine or alcohol (Scheme 2). More specifically, when both hexylamine **2a** and aniline were introduced into the reaction system (hexylamine/aniline = 1/1), only hexylamine **2a** was transformed into the desired amide **3aa** in 89% yield with 95/5 selectivity (Scheme 2, eq 1). Simi-

lar results were obtained for methanol and benzyl alcohol (Scheme 2, eq 2). Hence, in contrast to classical carbonylation reactions, here the catalyst does not only allow for the efficient formation of the Rh acyl intermediate but is also responsible for the selective activation of the N-H bonds of aliphatic amines. This dual role of the Rh is a specific feature of this transformation.

Scheme 2. Selective activation of aliphatic N-H bonds: Control experiments using 1-octene with hexylamine, aniline and alcohols.



Previous work on rhodium-catalyzed hydroamination of alkenes, both experimental observations and computational studies, suggest that the direct oxidative addition of an amine H-N bond to an unsaturated rhodium center is possible.[27] However, this route can be excluded under the present (mild) conditions (80-100 °C) due to the absence of ureas or formamides which are known to be formed form the corresponding Rh-N intermediates. Meanwhile, the formation of formamides following by fast of rhodium-catalyzed hydrocarbamoylation can also be excluded due to the difficulty of the direct activation of the C-H bonds in amides by transition metal.[8,28]

Performing MS spectroscopic studies of the reaction solution showed a variety of signals when the reaction was carried out in the absence of CO or CO/olefin. In contrast, in the presence of CO only four major signals (186.2, 229.2, 242.2, 251.2) were obtained for the MS-ESI data of the mixture of the reaction shown in eq. 1-1 including the product peak (241+1).

1-1: n = 5, 0.25 equiv. [Rh(cod)Cl]$_2$, 30 bar CO, toluene, 100 °C, 20 h
1-2: n = 7, 0.2 equiv. $RhCl_3$, 8 bar ^{13}CO, *d*-toluene, 80 °C, 12 h

Next, in situ NMR measurements were carried out to further investigate the reaction pathway (eq. 1-2). During the reaction (12 h at 80 °C), no signals of metal hydrides were observed. However, after three hours the desired amide product could be detected by ^{13}C NMR. After 12 h of reaction, in addition to the product and Rh carbonyl complexes, in situ ^{13}C NMR showed one major peak at 230.3 ppm and one minor broad peak at 234.9 ppm. These signals are assigned to different Rh(I)-acyl species (Figure 1, red).[29a] After the mixture was cooled to 25 °C, the spectrum showed two comparable peaks at 231.3 and 235.9 ppm (Figure 1, blue). Meanwhile, the number of rhodium carbonyl peaks increased at 180-190 ppm as shown in the spectra (Figure 1, red vs blue).

In general, the ligand on the Rh center trans to acyl groups has a significant impact on the chemical shift of the acyl group.[29] Substitution of the ligand (e.g. monophosphines) trans to the acyl group by CO typically results in a downfield shift of the carbon nucleus of the acyl group by ca. 4 ppm.

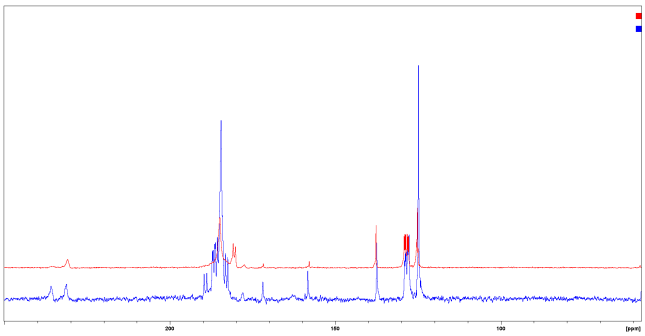


Figure 1. ^{13}C NMR of the reaction in eq. 1-2. Red: at 80 °C; blue: at 25 °C.

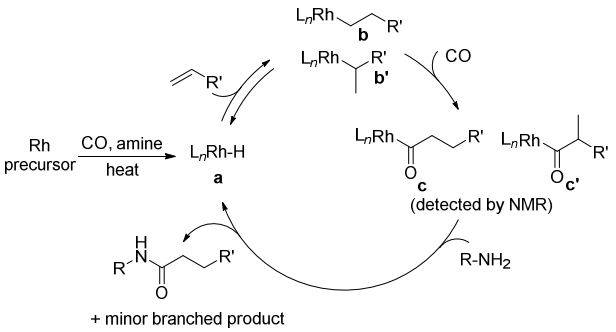
Probably, at 80 °C the various aminorhodium-carbonyl complexes are in fast equilibrium with each other resulting in a major peak at around 230 ppm (CO trans to the acyl group). Meanwhile, peaks around 235 ppm represent the species with CO trans to the acyl group. At 25 °C, the dynamic exchange between the different ligands is slower resulting in an increased amount of Rh-carbonyl signals in between 180-190 ppm. Moreover, substitution of the coordinating amines by CO might occur due to the increased CO concentration in solution at lower temperature. Accordingly, the peak at around 235 ppm increased, which is also consistent with the observation of more Rh-carbonyl signals vide supra.

A preliminary mechanism of the Rh-catalyzed hydroamidation of olefins with aliphatic amines and CO is proposed in Scheme 3. Firstly, under heating conditions [Rh(I)-H] species **a** is formed from the Rh precursor in the presence of amines and CO.[30] Then, insertion of the double bond of olefins into the Rh-H bond of **a** leads to the alkyl Rh species **b** and **b'**. Subsequent insertion of CO generates the acyl Rh(I) species **c** and **c'**, respectively. Notably, rhodium-acyl intermediates **c** and **c'** are detected by in-situ ^{13}C NMR measurements during the reaction using ^{13}C-enriched CO. As the rate determining step, nucleophilic addition of the amine to the rhodium-acyl complexes produces the desired amide products with regeneration of the Rh(I)-H complex. In contrast, such kind of aminolization was shown to be not conceivable in the presence of H_2.[25] Specifically, in catalytic hydroaminomethylation reactions of olefins with CO/H_2 and amines, it is proposed that Rh-acyl complexes as key intermediates are formed following by the much more favored hydrogenolysis to generate aldehydes. The aldehydes proceed via reductive amination to provide the corresponding products.

This proposal is supported by experimental results shown in Tables 1 and S2 (ligand effect). Specifically, in the presence of phosphine ligands, efficient isomerization of olefins via Rh-H insertion and β-hydride elimination was observed which indicates formation of [Rh-H] and the related alkyl-Rh species. Considering the easy formation of Rh-acyl intermediates during hydroformylation reactions in the presence of phosphine ligands, it is suggested that the amidation step is difficult and will be retarded by addition of phosphine ligands. Apparently, in the presence of such additional ligands the crucial amine coordination/N-H bond cleavage on Rh center is blocked.[31]

Hence, the most effective catalyst system for hydroamidation consists of simple rhodium carbonyl complexes.

Scheme 3. Proposed catalytic cycle



Meanwhile, the CO gas consumption-time profile was recorded for the hydroamidation of 1-octene **1a**. As shown in Figure 2, the reaction showed almost no induction period, which indicated that active Rh-H species are generated immediately at 100 °C. Due to the fast isomerization of 1-octene **1a**, the rate of hydroamidation decreased significantly after 2 h. The product **3aa** was obtained in 87% yield with 95/5 selectivity after 12 h. To our delight the catalyst loading could be lowered to 0.1 mol% and **3aa** was obtained in 70% yield with 96/4 selectivity after 20 h.

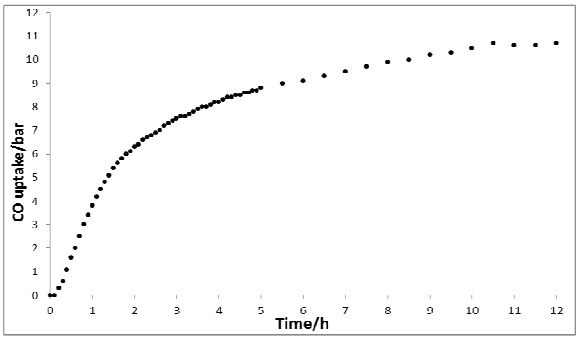
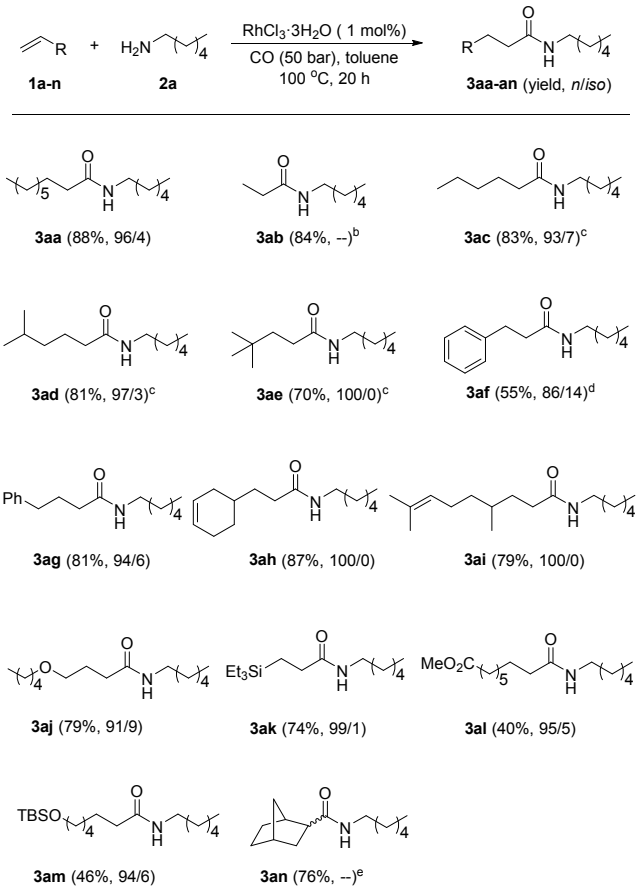


Figure 2. **CO gas uptake for rhodium-catalyzed hydroamidation of 1a with 2a.**

Substrate Scope. Next, the compatibility and limitations of alkenes in our rhodium-catalyzed hydroamidation were tested. Firstly, we studied the reaction of hexylamine **2a** with different alkenes (Scheme 4). Applying standard aliphatic terminal olefins such as 1-octene, ethylene, 1-pentene, and 4-methyl-1-pentene, the corresponding products **3aa**−**ad** were obtained in good yields with high regioselectivities. Bulky group substituted alkene **1e** could also be tolerated and gave the product in moderate yield with excellent linear selectivity. When using styrene as an example of an aromatic substrate, the desired product **3af** was achieved too, albeit in lower yield and selectivity. However, when a-methylstyrene was employed, no desired product was detected even at increased temperature (130 °C). On the other hand, allylbenzene and alkenes containing functional groups such as additional alkenyl, ether, silyl, and ester groups reacted smoothly, affording the corresponding products **3ag-am** in moderate to good yields with excellent regioselectivities. Interestingly, norbornene **1n** worked well with our catalytic system and the product **3an** was obtained in 76% yield.

Then, the rhodium-catalyzed hydroamidation of 1-octene **1a** with different aliphatic amines was investigated. As shown in Scheme 5, both primary amines (butylamine, hexylamine, octylamine, cyclohexylamine, and phenethylamine) and secondary amines (*N*-hexylmethylamine, piperidine and morpholine) were smoothly transformed into the desired amides in high yields with excellent regioselectivities. As expected, when benzylamines **2g-i** were used as substrates, similar good results were obtained in all cases. Interestingly, **3ja** represents a potential drug for the treatment of erectile dysfunction as α2-blocker,[32] which was prepared efficiently from easily available tryptamine **2j** via our methodology. It is worth mentioning that functionalized amine with non-protected hydroxyl group can be chemoselectively transformed into the desired amide with excellent regioselectivity. Futhermore, diamines with aliphatic and aromatic amine moieties could be chemoselectively transformed, too.[33] Meanwhile, the chiral center in (*S*)-1-phenylethylamine **2p** was not influenced using this catalytic method, providing the optically pure **3pa** in 75% yield and 98/2 regioselectivity. At last, glycine *tert*-butyl ester was also proven to be suitable substrate and the corresponding *N*-acylated product **3qa** was obtained in 51% yield.

Scheme 4. Rhodium-catalyzed hydroamidation of alkenes 1a-n with hexylamine 2a[a]



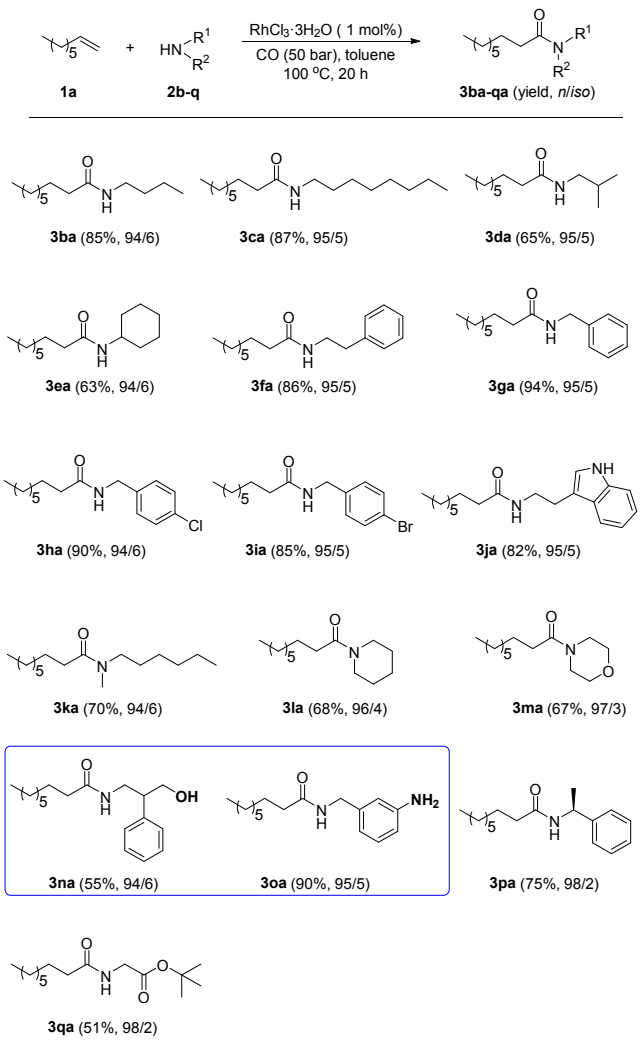
[a] Reaction conditions: **1** (5.0 mmol), **2a** (1.0 mmol), $RhCl_3·3H_2O$ (1 mol%), CO (50 bar), toluene (1.0 mL), 100 °C, 20 h. The isolated yields of **3aa-an** were based on **2a**. The ratios of isomers were determined by

GC analysis. [b] **1b** (ethylene, 25 mmol), **2a** (5.0 mmol), toluene (5.0 mL). [c] **1c-e** (15.0 mmol), **2a** (3.0 mmol), toluene (3.0 mL). [d] 120 °C. [e] **1n** (2.0 mmol).

CONCLUSION

In conclusion, we have developed a general and efficient rhodium-catalyzed hydroamidation of olefins with aliphatic amines. In the presence of easily available rhodium pre-catalysts, various olefins and aliphatic amines are transformed into the desired *N*-alkyl amides in medium to high yields with excellent regioselectivities. Notably, even in the presence of aryl amines and alcohols the straightforward hydroamidation of olefins with aliphatic amines was realized selectively. Preliminary mechanistic studies reveal the formation of [Rh(I)-H] complexes as active species and the aminolysis of the rhodium-acyl complexes as the crucial reaction step.

Scheme 5. Rhodium catalyzed hydroamidation of 1-octene 1a with amines 2a-q[a]



[a] Reaction conditions: **1a** (5.0 mmol), **2b-q** (1.0 mmol), $RhCl_3 \cdot 3H_2O$ (1 mol%), CO (50 bar), toluene (1.0 mL), 100 °C, 20 h. The isolated yields were based on amines **2**. The ratios of isomers were determined by GC analysis.

METHODS

General procedure for hydroamidation: Under argon atmosphere, $RhCl_3 \cdot 3H_2O$ (2.6 mg, 1.0 mol%) and a stirring bar were added into a vial (4 mL). Then, toluene (1.0 mL), **1** (**1a** or **1f-m**, 5.0 mmol) and **2a** (0.14 mL, 1.0 mmol) were injected by syringe. The vial was placed in an alloyed plate, which was transferred into an autoclave (300 mL) under argon atmosphere. At room temperature, the autoclave was flushed with CO gas three times and pressurized with CO gas to 50 bar. The reaction was performed at 100 °C for 20 h. After the reaction was finished, the autoclave was cooled to room temperature and the pressure was carefully released. The regioselectivity was measured by GC analysis. Removal of the solvent under vacuum and purification of the remaining residue by flash chromatography on silica gel (eluent: heptane/ethyl acetate = 5/1–3/1) gave the desired amide **3**.

ASSOCIATED CONTENT

Supporting Information

Additional experimental results and procedures and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

Matthias.Beller@catalysis.de
Yuehui.Li@catalysis.de

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

The Federal Ministry of Education and Research (BMBF) and Evonik Industries are gratefully acknowledged for their general support. K. Dong thanks Shanghai Institute of Organic Chemistry-Zhejiang Medicine joint fellowship for financial support. We thank the analytical department of Leibniz-Institute for Catalysis, Rostock for their excellent analytical service.

REFERENCES

(1) (a) *Applied Homogeneous Catalysis with Organometallic Compounds*; Wiley-VCH: Weinheim, 2002. (b) Beller, M. *Catalytic Carbonylation Reactions*; Springer: Berlin, 2006. (c) Kollár, L. *Modern Carbonylation Methods*; Wiley-VCH: Weinheim, 2008. (d) Hartwig, J. In *Organotransition Metal Chemistry*; University Science Books: Sausalito, CA, 2010, pp. 745–824. (e) Wu, X.-F.; Neumann, H.; Beller, M. *Chem. Soc. Rev.* **2011**, *40*, 4986-5009. (f) Wu, X.-F.; Neumann, H.; Beller, M. *Chem. Rev.* **2012**, *113*, 1-35. (g) Diebolt, O.; van Leeuwen, P. W. N. M.; Kamer, P. C. J. *ACS Catalysis* **2012**, *2*, 2357-2370. (h) Wu, X.-F.; Fang, X.; Wu, L.; Jackstell, R.; Neumann, H.; Beller, M. *Acc. Chem. Res.* **2014**, *47*, 1041-1053. (i) Sam, B.; Breit, B.; Krische, M. J. *Angew. Chem. Int. Ed.* **2015**, *54*, 3267-3274.

(2) (a) Beller, M.; Cornils, B.; Frohning, C. D.; Kohlpaintner, C. W. *J. Mol. Catal. A: Chem.* **1995**, *104*, 17-85. (b) van Leeuwen, P. W. N. M.; Claver, C. *Rhodium Catalyzed Hydroformylation*; Springer: Berlin Heidelberg, 2000. (c) Breit, B. In *Metal Catalyzed Reductive C-C Bond Formation*; Krische, M., Ed.; Springer: Berlin Heidelberg, 2007, pp. 139-172. (d) Rivillo, D.; Gulyás, H.; Benet-Buchholz, J.; Escudero-Adán, E. C.; Freixa, Z.; van Leeuwen, P. W. N. M. *Angew. Chem. Int. Ed.* **2007**, *46*, 7247-7250. (e) Zhao, B.; Peng, X.; Wang, Z.; Xia, C.; Ding, K. *Chem. Eur. J.* **2008**, *14*, 7847-7857. (f) Casey, C. P.; Hartwig, J. In *Organotransition Metal Chemistry: From Bonding to Catalysis*; Palgrave Macmillan: 2009, pp. 751-769. (g) Franke, R.; Selent, D.; Börner, A. *Chem. Rev.* **2012**, *112*, 5675-5732. (h) Jia, X.; Wang, Z.; Xia, C.; Ding, K. *Chem. Eur. J.* **2012**, *18*, 15288-

15295. (i) Obrecht, L.; Kamer, P. C. J.; Laan, W. *Catal. Sci. Technol.* **2013**, *3*, 541-551.

(3) (a) El Ali, B.; Alper, H.; Beller, M.; Bolm, C. In *Transition Metals for Organic Synthesis*; Wiley-VCH: Weinheim: Germany, 2008, pp. 49-67. (b) Brennführer, A.; Neumann, H.; Beller, M. *ChemCatChem* **2009**, *1*, 28-41. (c) Nunez Magro, A. A.; Robb, L.-M.; Pogorzelec, P. J.; Slawin, A. M. Z.; Eastham, G. R.; Cole-Hamilton, D. J. *Chem. Sci.* **2010**, *1*, 723-730. (e) Kiss, G. *Chem. Rev.* **2001**, *101*, 3435-3456.

(4) (a) Humphrey, J. M.; Chamberlin, A. R. *Chem. Rev.* **1997**, *97*, 2243-2266. (b) Bode, J. W. *Curr. Opin. Drug Discovery Dev.* **2006**, *9*, 765-775. (c) Cupido, T.; Tulla-Puche, J.; Spengler, J.; Albericio, F. *Curr. Opin. Drug Discovery Dev.* **2007**, *10*, 768-783.

(5) Pattabiraman, V. R.; Bode, J. W. *Nature* **2011**, *480*, 471-479.

(6) (a) Montalbetti, C. A. G. N.; Falque, V. *Tetrahedron* **2005**, *61*, 10827-10852. (b) Han, S.-Y.; Kim, Y.-A. *Tetrahedron* **2004**, *60*, 2447-2467. (c) Valeur, E.; Bradley, M. *Chem. Soc. Rev.* **2009**, *38*, 606-631.

(7) (a) Prechtl, M. H. G.; Wobser, K.; Theyssen, N.; Ben-David, Y.; Milstein, D.; Leitner, W. *Catal. Sci. Technol.* **2012**, *2*, 2039-2042. (b) Liu, Q.; Zhang, H.; Lei, A. *Angew. Chem. Int. Ed.* **2011**, *50*, 10788-10799. (c) Shi, R.; Lu, L.; Zhang, H.; Chen, B.; Sha, Y.; Liu, C.; Lei, A. *Angew. Chem. Int. Ed.* **2013**, *52*, 10582-10585. (d) Li, W.; Liu, C.; Zhang, H.; Ye, K.; Zhang, G.; Zhang, W.; Duan, Z.; You, S.; Lei, A. *Angew. Chem. Int. Ed.* **2014**, *53*, 2443-2446. (e) Li, W.; Duan, Z.; Zhang, X.; Zhang, H.; Wang, M.; Jiang, R.; Zeng, H.; Liu, C.; Lei, A. *Angew. Chem. Int. Ed.* **2015**, *54*, 1893-1896. (f) Ferguson, J.; Zeng, F.; Alwis, N.; Alper, H. *Org. Lett.* **2013**, *15*, 1998-2001.

(8) (a) Tsuji, Y.; Yoshii, S.; Ohsumi, T.; Kondo, T.; Watanabe, Y. *J. Organomet. Chem.* **1987**, *331*, 379-385. (b) Kobayashi, Y.; Kamisaki, H.; Yanada, K.; Yanada, R.; Takemoto, Y. *Tetrahedron Lett.* **2005**, *46*, 7549-7552. (c) Nakao, Y.; Idei, H.; Kanyiva, K. S.; Hiyama, T. *J. Am. Chem. Soc.* **2009**, *131*, 5070-5071. (d) Fujihara, T.; Katafuchi, Y.; Iwai, T.; Terao, J.; Tsuji, Y. *J. Am. Chem. Soc.* **2010**, *132*, 2094-2098. (e) Miyazaki, Y.; Yamada, Y.; Nakao, Y.; Hiyama, T. *Chem. Lett.* **2012**, *41*, 298-300. (f) Li, B.; Park, Y.; Chang, S. *J. Am. Chem. Soc.* **2013**, *136*, 1125-1131. (g) Huang, L.; Arndt, M.; Gooßen, K.; Heydt, H.; Gooßen, L. J. *Chem. Rev.* **2015**, DOI: 10.1021/cr300389u.

(9) Shen, B.; Makley, D. M.; Johnston, J. N. *Nature* **2010**, *465*, 1027-1032.

(10) Stephenson, N. A.; Zhu, J.; Gellman, S. H.; Stahl, S. S. *J. Am. Chem. Soc.* **2009**, *131*, 10003-10008.

(11) (a) Shangguan, N.; Katukojvala, S.; Greenberg, R.; Williams, L. J. *J. Am. Chem. Soc.* **2003**, *125*, 7754-7755. (b) Li, X.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2008**, *130*, 5446-5448. (c) Rao, Y.; Li, X.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2009**, *131*, 12924-12926.

(12) For recent reviews and compendia on carbonylation of alkynes, see: (a) Doherty, S.; Knight, J. G.; Smyth, C. H. *Recent developments in alkyne carbonylation.* In *Modern Carbonylation Methods*; Kollár, L., Ed.; Wiley-VCH: Weinheim, Germany, 2008. (b) Brennführer, A.; Neumann, H.; Beller, M. *ChemCatChem* **2009**, *1*, 28-41. (c) Chinchilla, R.; Nájera, C. *Chem. Rev.* **2014**, *114*, 1783-1826.

(13) Fang, X.; Li, H.; Jackstell, R.; Beller, M. *J. Am. Chem. Soc.* **2014**, *136*, 16039-16043.

(14) (a) Brennführer, A.; Neumann, H.; Beller, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 4114-4133. (b) Wu, X.-F.; Neumann, H.; Beller, M. *Chem. Eur. J.* **2010**, *16*, 9750-9753. (c) Wu, X.-F.; Schranck, J.; Neumann, H.; Beller, M. *ChemCatChem* **2012**, *4*, 69-71. (d) Reeves, D. C.; Rodriguez, S.; Lee, H.; Haddad, N.; Krishnamurthy, D.; Senanayake, C. H. *Org. Lett.* **2011**, *13*, 2495-2497. (e) Hermange, P.; Lindhardt, A. T.; Taaning, R. H.; Bjerglund, K.; Lupp, D.; Skrydstrup, T. *J. Am. Chem. Soc.* **2011**, *133*, 6061-6071. (f) Nielsen, D. U.; Neumann, K.; Taaning, R. H.; Lindhardt, A. T.; Modvig, A.; Skrydstrup, T. *J. Org. Chem.* **2012**, *77*, 6155-6165. (g) de la Fuente, V.; Godard, C.; Claver, C.; Castillón, S. *Adv. Synth. Catal.* **2012**, *354*, 1971-1979. (c) Xu, T.; Alper, H. *Tetrahedron Lett.* **2013**, *54*, 5496-5499.

(15) (a) Pino, P.; Paleari, P. *Gazz. Chim. Ital.* **1951**, *81*, 64. (b) Pino, P.; Magri, R. *Chim. Ind.* **1952**, *34*, 511-517.

(16) Reppe, W.; Kroper, H. *Ger. Pat.* **1951**, 868.

(17) Striegler, A.; Weber, J. *J. Prakt. Chem.* **1965**, *29*, 281-295.

(18) Kealy, T. J.; Benson, R. E. *J. Org. Chem.* **1961**, *26*, 3126-3130.

(19) (a) For ruthenium-catalyzed hydroamidation of olefins, [RhCl(CO)2]2 and $Rh_6(CO)_{16}$ were tested for the hydroamidation of 1-octene with benzylamine and low yields were achieved (55% and 47% yield, respectively), see: Tsuji, Y.; Ohsumi, T.; Kondo, T.; Watanabe, Y. *J. Organomet. Chem.* **1986**, *309*, 333-344. (b) After the submission of our paper, the related work by Behr et al was published online, see: Behr, A.; Levikov, D.; Nürenberg, E. *Catal. Sci. Technol.* **2015**, DOI: 10.1039/C5CY00168D.

(20) Lee, S. I.; Son, S. U.; Chung, Y. K. *Chem. Commun.* **2002**, 1310-1311.

(21) Jimenez-Rodriguez, C.; Nunez-Magro, A. A.; Seidensticker, T.; Eastham, G. R.; Furst, M. R. L.; Cole-Hamilton, D. J. *Catal. Sci. Technol.* **2014**, *4*, 2332-2339.

(22) Liu, H.; Yan, N.; Dyson, P. J. *Chem. Commun.* **2014**, *50*, 7848-7851.

(23) Fang, X.; Jackstell, R.; Beller, M. *Angew. Chem. Int. Ed.* **2013**, *52*, 14089-14093.

(24) For selected examples of related rhodium catalyzed hydroacylation, methanol carbonylation, or reductive coupling reactions, see: (a) Willis, M. C. *Chem. Rev.* **2009**, *110*, 725-748. (b) Leung, J. C.; Krische, M. J. *Chem. Sci.* **2012**, *3*, 2202-2209. (c) Forster, D. *J. Am. Chem. Soc.* **1976**, *98*, 846-848. (d) Freixa, Z.; Kamer, P. C. J.; Lutz, M.; Spek, A. L.; van Leeuwen, P. W. N. M. *Angew. Chem. Int. Ed.* **2005**, *44*, 4385-4388. (e) Thomas, C. M.; Süss-Fink, G. *Coord. Chem. Rev.* **2003**, *243*, 125-142. (f) Kong, J.-R.; Cho, C.-W.; Krische, M. J. *J. Am. Chem. Soc.* **2005**, *127*, 11269-11276. (g) Skucas, E.; Kong, J. R.; Krische, M. J. *J. Am. Chem. Soc.* **2007**, *129*, 7242-7243. (h) Komanduri, V.; Grant, C. D.; Krische, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 12592-12593.

(25) (a) Seayad, A.; Ahmed, M.; Klein, H.; Jackstell, R.; Gross, T.; Beller, M. *Science* **2002**, *297*, 1676-1678. (b) Ahmed, M.; Seayad, A. M.; Jackstell, R.; Beller, M. *J. Am. Chem. Soc.* **2003**, *125*, 10311-10318. (c) Crozet, D.; Gual, A.; McKay, D.; Dinoi, C.; Godard, C.; Urrutigoïty, M.; Daran, J.-C.; Maron, L.; Claver, C.; Kalck, P. *Chem. Eur. J.* **2012**, *18*, 7128-7140.

(26) For Pd-catalyzed chemoselective carbonylation of aminophenols with Iodoarenes, see: Xu, T.; Alper, H. *J. Am. Chem. Soc.* **2014**, *136*, 16970-16973.

(27) (a) Baker, R.; Onions, A.; Popplestone, R. J.; Smith, T. N. *J. Chem. Soc., Perkin Trans. 2* **1975**, 1133-1138. (b) Brunet, J.-J.; Commenges, G.; Neibecker, D.; Philippot, K. *J. Organomet. Chem.* **1994**, *469*, 221-228. (c) Musaev, D. G.; Morokuma, K. *J. Am. Chem. Soc.* **1995**, *117*, 799-805. (d) Müller, T. E.; Beller, M. *Chem. Rev.* **1998**, *98*, 675-704.

(28) Jo, Y.; Ju, J.; Choe, J.; Song, K. H.; Lee, S. *J. Org. Chem.* **2009**, *74*, 6358-6361.

(29) The observed trans effect of CO on the chemical shift of Rh(I)-acyl species is consistent with literature reports, see: (a) Kamer, P. C. J.; Reek, J. N. H.; van Leeuwen, P. W. N. M. In *Mechanisms in Homogeneous Catalysis*; Wiley-VCH Verlag GmbH & Co. KGaA: 2005, pp. 231-269. (b) McCleverty, J. A.; Wilkinson, G.; Lipson, L. G.; Maddox, M. L.; Kaesz, H. D. In *Inorg. Synth.*; John Wiley & Sons, Inc.: 2007, pp. 211-214.

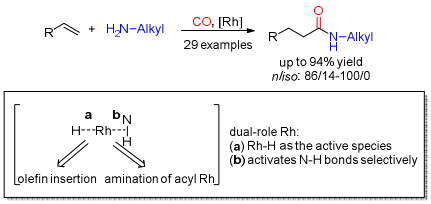
(30) The signals of carbonyl groups in rhodium imido complexes may show around 202-206 ppm in ^{13}C NMR, see: Ge, Y. W.; Sharp, P. R. *Inorg. Chem.* **1992**, *31*, 379-384.

(31) In contrast to the results of aliphatic amines, no hydroamidation occurs and only trace amounts of olefin isomerization were detected under standard conditions. This indicates that the effective interaction between Rh-complexes and N-H bonds in aliphatic amines selectively produces Rh-H species and promotes the aminolization step during the catalytic procedure.

(32) Yamada, K.; Tanaka, Y.; Somei, M. *Heterocycles* **2009**, *79*, 635-645.

(33) Especially, such kind of chemoselectivity is not achievable in known Pd-catalyzed carbonylation reactions of olefins.

TOC


R
+ H2N–Alkyl
CO, [Rh]
29 examples
R
N–Alkyl
H
up to 94% yield
n/iso: 86/14-100/0
a
b
N
H···Rh···H
H
olefin insertion
amination of acyl Rh
dual-role Rh:
(a) Rh-H as the active species
(b) activates N-H bonds selectively