Synthetic Methods

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Palladium-Catalyzed Hydroaminocarbonylation of Alkenes with Amines: A Strategy to Overcome the Basicity Barrier Imparted by Aliphatic Amines**

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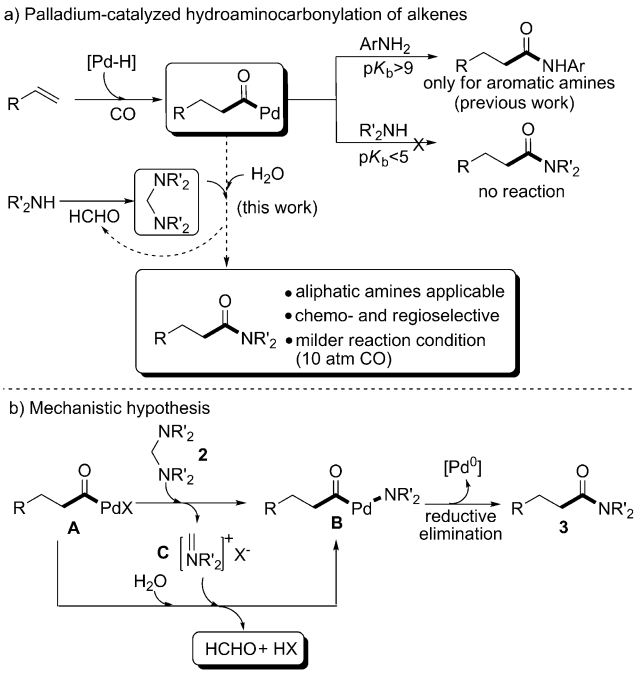
Abstract: *A novel and efficient palladium-catalyzed hydroaminocarbonylation of alkenes with aminals has been developed under mild reaction conditions, and allows the synthesis of a wide range of N-alkyl linear amides in good yields with high regioselectivity. On the basis of this method, a cooperative catalytic system operating by the synergistic combination of palladium, paraformaldehyde, and acid was established for promoting the hydroaminocarbonylation of alkenes with both aromatic and aliphatic amines, which do not react well under conventional palladium-catalyzed hydroaminocarbonylation.*

Amides are not only recognized as fundamental structural motifs in myriad of natural products, pharmaceuticals, functional materials, and agrochemicals,[1] but also serve as attractive precursors in a variety of organic transformations.[2] As such, the development of efficient methods toward amides is of great significance to chemical, medicinal, and material science and has attracted a great deal of attention over the past decades.[3,4] In particular, the focal point is the creation of catalytic protocols which possess the ability to transform abundant, ideally renewable, feedstocks into amides in the absence of stoichiometric by-products.[5–7] This goal can be realized by alkene hydroaminocarbonylation with amines and CO, and provides access to amides directly from alkenes without formation of by-products. To date, however, only a few catalytic systems dealing with hydroaminocarbonylation of alkenes have been reported.[6,7]

Early studies on hydroaminocarbonylation largely relied on the use of Co, Ni, Fe, and Ru complexes as catalysts, which not only suffered from requiring harsh reaction conditions (> 70 atm CO, over 150 °C) but also resulted in intricately poor chemoselectivity.[6] This poor chemoselectivity stems from the inherent preference for the generation of carbamoyl metal complexes, which are prone to the formation of significant amount of formamides as by-products. As a means of addressing this problem, a mechanistically distinct strategy with palladium complexes as catalysts has been developed by the groups of Beller and Liu.[7] Although the synthesis of a wide range of amides with high regioselectivity and chemoselectivity is achievable, a high pressure of CO (40 atm) is still required. The palladium hydride was considered to be a key reactive species in these processes, and is preferentially trapped by alkenes to generate palladium alkyl species, thus suppressing the formation of formamide by-products. However, one common feature of these reactions is the requisite use of aromatic amines as coupling partners (Scheme 1 a), which significantly limits the substrate scope of the amines and reduces the appeal of these reactions. The underlying reasons for the dependence of reactivity on the nature of the amines might be attributed to the fact that the key palladium hydride species only can be formed under relatively acidic conditions.[8] Aliphatic amines which are more basic ($pK_b < 5$) may inhibit the generation of the key palladium hydride species, thus preventing the N-alkyl-substituted amides being formed. Thus, the development of solutions to overcome the inherent side effect incurred by the strong basicity of aliphatic amines would be highly desirable to increase the range of amides which may be accessed.



Scheme 1. Proposed palladium-catalyzed hydroaminocarbonylation of alkenes with aminals.

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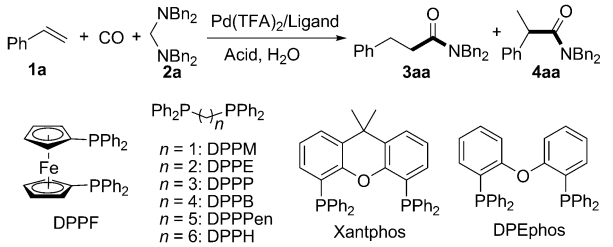
Recently, we identified that aminals can react with a copper complex to generate a copper amide species by C–N bond cleavage under mild reaction conditions.[9] This result together with our progress on the use of aminals as electrophiles for palladium-catalyzed coupling reactions[10] prompted us to envision that aminals might be used as surrogates of aliphatic amines to circumvent the inherent substrate inhibition in the palladium-catalyzed hydroaminocarbonylation reaction with aliphatic amines. Specifically, we postulated that the palladium hydride species might be generated in the presence of a catalytic amount of acid and aminal since the basicity of the aminal is lower, and would allow subsequent migratory insertion of the alkene and CO into the palladium hydride species to generate the acyl palladium species **A.** The interaction of **A** with an aminal would allow generation of the key intermediate **B** together with the iminium **C** through C–N bond cleavage. The iminium **C** would quickly react with another molecule of **A**, facilitated by water, to afford the second molecule of **B** together with paraformaldehyde and acid (HX). Reductive elimination of **B** leads to the final hydroaminocarbonylation products (Scheme 1b). On the basis of this mechanistic assumption, we recognized that cooperative catalysis consisting of palladium, paraformaldehyde, and acid might be also feasible to promote the hydroaminocarbonylation with simple amines as coupling partners, and the paraformaldehyde and acid cocatalyst may act as temporary masking groups to eliminate the side effect resulting from the basicity of aliphatic amines. Herein, we describe a new and efficient protocol for the successful implementation of the palladium-catalyzed hydroaminocarbonylation of alkenes with a variety of aminals by C–N bond cleavage, and it allows synthesis of a variety of N-alkyl-substituted amides under mild reaction conditions. Furthermore, a cooperative catalytic system combined with palladium, paraformaldehyde, and acid was also established for promoting the hydroaminocarbonylation of alkenes with both aliphatic and aromatic amines.

To validate our hypothesis, the hydroaminocarbonylation reaction was initially investigated with styrene (**1a**) and the aminal **2a** in the presence of a catalytic amount of $Pd(TFA)_2$, acid, and H_2O (0.55 equiv) under 10 atm of CO in anisole at 120 °C (Table 1). Low yield of the hydroaminocarbonylation product was obtained with most of the styrene remaining when DPPF served as a ligand (entry 1). The probable reason for the lower conversion could be attributed to the nature of the palladium catalyst. Evaluation of various phosphine ligands revealed that the transformation was sensitive to the bite angle of the bisphosphine ligand and found that DPPPen, which possesses a larger bite angle, afforded the product in good yield (87% yield) and high regioselectivity (entry 6). It should be noted that the two amino moieties of the aminal were successfully incorporated into the desired amide, thus suggesting that our strategy is feasible. The structure of the main product **3aa** was confirmed by X-ray single-crystal diffraction analysis.[11] Furthermore, the impact of acid on the reactivity and regioselectivity of the process was investigated (entries 10–16). $NH_2CH_2CO_2Me{\cdot}HCl$ emerged as the acid of choice to give the desired product in 87% yield, while a comparable result was obtained in the presence of other amino hydrochlorides. As anticipated, control reactions demonstrated that only trace amounts of the amide product were obtained in the absence of acid. In addition, we examined the effect of the palladium source and observed that other palladium precursors provided unsatisfactory results in terms of reactivity and selectivity (see the Supporting Information).

Table 1: Optimization of reaction conditions.[a]

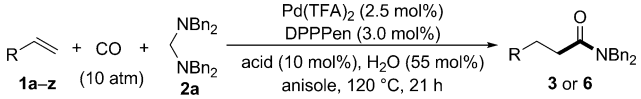


Entry	Ligand	Acid	**3aa** + **4aa** [%][b]	**3aa**/**4aa**[c]
1	DPPF	$NH_2CH_2CO_2Me{\cdot}HCl$	13	80:20
2	DPPM	$NH_2CH_2CO_2Me{\cdot}HCl$	trace	–
3	DPPE	$NH_2CH_2CO_2Me{\cdot}HCl$	0	–
4	DPPP	$NH_2CH_2CO_2Me{\cdot}HCl$	0	–
5	DPPB	$NH_2CH_2CO_2Me{\cdot}HCl$	trace	–
6	DPPPen	$NH_2CH_2CO_2Me{\cdot}HCl$	87	83:17
7	DPPH	$NH_2CH_2CO_2Me{\cdot}HCl$	57	61:39
8	Xantphos	$NH_2CH_2CO_2Me{\cdot}HCl$	trace	–
9	DPEphos	$NH_2CH_2CO_2Me{\cdot}HCl$	trace	–
10	DPPPen	TsOH	trace	–
11	DPPPen	$NH_2CH_2CO_2H$	trace	–
12	DPPPen	$NH_2OH{\cdot}HCl$	47	82:18
13	DPPPen	$NEt_3{\cdot}HCl$	63	81:19
14	DPPPen	$NH_2CH_2CO_2H{\cdot}HCl$	69	84:16
15	DPPPen	$NH_2CH_2CO_2Et{\cdot}HCl$	82	82:18
16	DPPPen	$NH_2CH(Ph)CO_2Me{\cdot}HCl$	69	83:17

[a] General conditions: **1a** (0.8 mmol), **2a** (0.2 mmol), $Pd(TFA)_2$ (0.01 mmol), ligand (0.012 mmol), acid (0.04 mmol), H_2O (0.22 mmol), anisole (1.0 mL), and CO (10 atm), at 120 °C for 21 h. [b] Yields were determined by GC analysis using *n*-cetane as the internal standard. [c] The ratios of **3aa**/**4aa** (linear/branched; l/b) were determined by GC analysis. TFA = trifluoroacetate, Ts = 4-toluenesulfonyl.

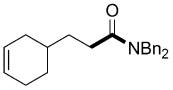
Our hypothesis was amenable to a wide range of alkene substrates, thus allowing preparation of one-carbon elongated amides from olefins in high yields and good to excellent selectivities (Table 2). It was even more intriguing that generally no formamide byproduct was observed, and in most cases, more than 70% yield was isolated for linear adducts. Both electron-rich and electron-deficient aromatic alkenes could be employed efficiently in our protocol (**3ba**–**ka**). For styrenes, a series of functional groups, such as methyl, methoxy, fluoro, and chloro contained in the phenyl ring were compatible with the present catalytic system, and the desired products were isolated in good to excellent yields, which indicated that the present reaction had a good functional-group tolerance. Preference for the formation of linear adducts soared upon increase of steric demand in the substrates as exemplified by *ortho*-substituted styrenes (**3da**, **3ea**, **3ja**, **3ka**). 4-Vinylpyridine underwent the desired reaction to give the branched product in a relatively lower

Table 2: Substrate scope of alkenes.[a]

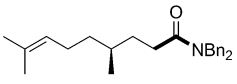


1a–z (10 atm) **2a** **3** or **6**

Entry	R	Product	Yield [%][b]	l/b[c]
1	C_6H_5	**3aa**	72	83:17
2	4-$CH_3C_6H_4$	**3ba**	73	81:19
3	3-$CH_3C_6H_4$	**3ca**	80	87:13
4	2-$CH_3C_6H_4$	**3da**	90	95:5
5	2,6-$(CH_3)_2C_6H_3$	**3ea**	90	95:5
6	4-*t*BuC_6H_4	**3fa**	69	82:18
7	4-$CH_3OC_6H_4$	**3ga**	42	83:17
8	4-FC_6H_4	**3ha**	62	88:12
9	4-ClC_6H_4	**3ia**	70	88:12
10	2,6-$Cl_2C_6H_3$	**3ja**	62	94:6
11	2,3-$Cl_2C_6H_3$	**3ka**	68	94:6
12	4-pyridinyl	**4la**	34	1:99
13	H	**3ma**	89[d]	–
14	$CH_3(CH_2)_5$	**3na**	80	96:4
15	$CH_3(CH_2)_7$	**3oa**	82	95:5
16	$CH_3(CH_2)_9$	**3pa**	85	90:10
17	$CH_3(CH_2)_{11}$	**3qa**	84 (83)[e]	94:6
18	$CH_3(CH_2)_{13}$	**3ra**	80	94:6
19	$CH_3(CH_2)_{15}$	**3sa**	82	93:7
20	$C_6H_5CH_2$	**3ta**	85	93:7
21	4-$CH_3OC_6H_4CH_2$	**3ua**	82	93:7
22	$C_6H_5(CH_2)_2$	**3va**	86	95:5
23	$CyCH_2$	**3wa**	83	92:8
24	$Cl(CH_2)_4$	**3xa**	79	91:9
25	$CH_3CO(CH_2)_2$	**3ya**	88	92:8
26	$EtOOC(CH_2)_2$	**3za**	73	86:14
27	$CH_3COO(CH_2)_4$	**6aa**	73	90:10



6ba, 80%, (91:9)



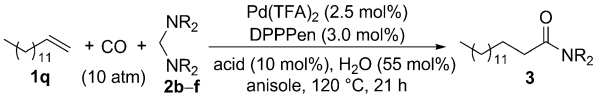
6ca, 92%, (>99:1)

[a] General conditions: **1** (0.8 mmol), **2a** (0.2 mmol), CO (10 atm), $Pd(TFA)_2$ (0.01 mmol), DPPPen (0.012 mmol), $NH_2CH_2CO_2Me{\cdot}HCl$ (0.04 mmol), and H_2O (0.22 mmol) in anisole (1.0 mL) at 120 °C for 21 h. [b] Yield of isolated linear product based on amino moiety. [c] The l/b ratios were determined by GC and GC-MS analysis. [d] Ethene (5 atm). [e] Gram scale.

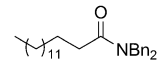
yield with complete regioselectivity under the current reaction conditions. Next, we turned our attention to more challenging aliphatic alkenes. Ethene was initially surveyed and the reaction proceeded smoothly to give the desired amide **3ma** in 89% yield with 5 atm of ethene and 10 atm of CO. Furthermore, similar results were obtained in the reactions of terminal aliphatic alkenes with long chains to deliver the linear amides efficiently in 80–86% yields with high regioselectivities (**3na**–**sa**). Allylbenzene and 3-butenylbenzene were compatible for the reaction conditions, thus affording the corresponding products in excellent yields with high regioselectivities (**3ta–3va**). Typical functional groups on the aliphatic alkenes, such as cyclohexyl, chloro, ketone, and ester, were also well tolerated by the reaction conditions, thereby affording the corresponding linear adducts in 73–88% yields with high regioselectivities (entries 23–27). The reaction was not applicable to internal alkenes, as demonstrated by reactions of 4-vinylcyclohex-1-ene and (+)-β-citronellene, in which the reactions took place exclusively at the terminal double bond to give the corresponding linear amides **6ba** (80%) and **6ca** (92%), respectively, while the internal double bond remained intact. To further demonstrate the robustness of our system, we were able to run experiments on gram scale in the presence of 1 mol% of the palladium catalyst to produce the linear amide **3qa** in 83% yield (3.49 g; entry 17).

Having demonstrated that the process is compatible with a wide range of alkenes, investigation of the scope with respect to the aminal was undertaken (Table 3). Several

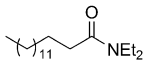
Table 3: Substrate scope of aminals.[a]



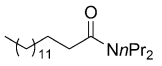
1q (10 atm) **2b–f** **3**



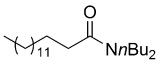
3qa, 84%, (94:6)



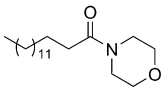
3qb, 70%[b], (95:5)



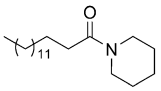
3qc, 71%[b], (93:7)



3qd, 80%[b], (93:7)



3qe, 89%, (92:8)



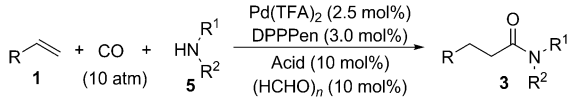
3qf, 55%[b], (94:6)

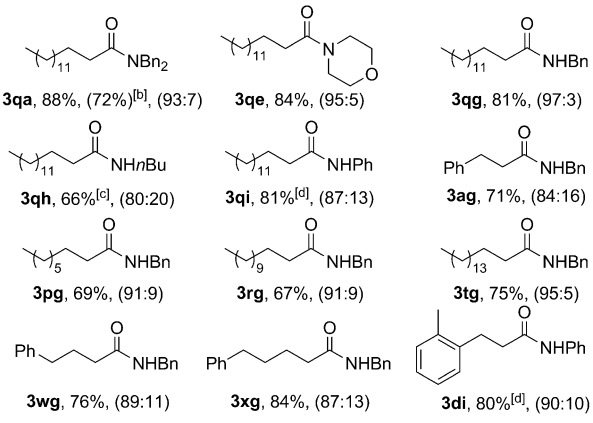
[a] General conditions: **1q** (0.8 mmol), **2** (0.2 mmol), CO (10 atm), $Pd(TFA)_2$ (0.01 mmol), DPPPen (0.012 mmol), $NH_2CH_2CO_2Me{\cdot}HCl$ (0.04 mmol), and H_2O (0.22 mmol) in anisole (1.0 mL) at 120 °C for 21 h. Yield of isolated linear product based on amino moiety; the l/b ratios within parentheses were determined by GC and GC-MS analysis. [b] Acid (0.2 mmol).

aminals (**2b**–**e**) derived from diethylamine, dipropylamine, dibutylamine, and morpholine were effective substrates for reacting with tetradec-1-ene smoothly to provide the products **3qb**–**qe** in 70–89% yields with high regioselectivity. However, the aminal **2f** derived from piperidine was less reactive, and the linear adduct **3qf** was obtained in only 55% yield upon isolation.

As the proposed design was partially realized by successfully employing aminals as aliphatic amine sources for the hydroaminocarbonylation of alkenes, we wanted to further investigate whether cooperative catalysis by the combination of palladium, paraformaldehyde, and acid could promote the desired carbonylation with free primary or secondary amines as coupling partners. To our delight, the combination of 2.5 mol% of $Pd(TFA)_2$, 3 mol% of DPPPen, 10 mol% of acid, and 10 mol% of paraformaldehyde was identified as an efficient cooperative catalytic system for promoting the desired hydroaminocarbonylation. Control reactions demonstrated that only trace amounts of the amide product were obtained in the absence of paraformaldehyde. By using the procedure in Table 4, the hydroaminocarbonylation of tetradec-1-ene with aliphatic and aromatic amines, such as dibenzylamine, morpholine, benzylamine, butylamine, and aniline, proceeded smoothly to generate the desired linear amides in moderate to excellent yields (**3qa**–**qi**). Similar

Table 4: Hydroaminocarbonylation with aliphatic and aromatic amines by a cooperative catalysis with paraformaldehyde.[a]





[a] General conditions: **1** (0.8 mmol), **5** (0.4 mmol), CO (10 atm), $Pd(TFA)_2$ (0.01 mmol), DPPPen (0.012 mmol), $NH_2CH_2CO_2Me{\cdot}HCl$ (0.04 mmol), and $(HCHO)_n$ (0.04 mmol) in anisole (1.0 mL) at 120 °C for 21 h. Yield of isolated linear product based on amino moiety; the l/b ratios shown within parentheses were determined by GC and GC-MS analysis. [b] Gram scale. [c] Acid (0.2 mmol), CO (40 atm). [d] No $(HCHO)_n$.

results were obtained in the reactions of other aliphatic alkenes and styrene to give rise to a variety of linear amides in good yields with high regioselectivity under the current reaction conditions (**3ag**–**xg**). Notably, the aniline **5i** can be applied to this process in the absence of paraformaldehyde, thus giving the desired products **3qi** and **3di** in good yields. The structure of **3ag** was confirmed by X-ray single-crystal diffraction analysis.[11] The gram-scale reaction was successfully realized with 1 mol% of the palladium catalyst in the presence of 10 mol% $(HCHO)_n$ and a catalytic amount of acid, thus affording **3qa** in 72% (3.03 g) yield (see the Supporting Information).

In summary, we have developed a new and efficient protocol for implementation of the palladium-catalyzed hydroaminocarbonylation of simple alkenes with a variety of aminals, which successfully overcomes the difficulty of using aliphatic amines and allows synthesis of a broad range of N-alkyl-substituted amides under mild reaction conditions. On the basis of this method, a cooperative catalytic system through the synergistic combination of palladium, paraformaldehyde, and acid was also established for promoting the hydroaminocarbonylation of alkenes with both aliphatic and aromatic amines. This study not only provides an efficient method to realize the hydroaminocarbonylation with both aliphatic and aromatic amines under mild reaction conditions, but also paves the way for establishing new C–N bond-formation reactions by using this cooperative catalysis. Studies aimed at gaining a detailed mechanistic understanding of this reaction and the application of this strategy in other reactions are currently in progress.

Keywords: alkenes · amines · aminals · palladium · synthetic methods

[1] a) J. W. Clader, *J. Med. Chem.* **2004**, *47*, 1; b) J. W. Bode, *Curr. Opin. Drug Discovery. Dev.* **2006**, *9*, 765; c) W. Wu, Z. Zhang, L. S. Liebeskind, *J. Am. Chem. Soc.* **2011**, *133*, 14256; d) S. Eichner, T. Eichner, H. G. Floss, J. Fohrer, E. Hofer, F. Sasse, C. Zeilinger, A. Kirschning, *J. Am. Chem. Soc.* **2012**, *134*, 1673; e) X. Wang, F. Meng, Y. Wang, Z. Han, Y.-J. Chen, L. Liu, Z. Wang, K. Ding, *Angew. Chem. Int. Ed.* **2012**, *51*, 9276; *Angew. Chem.* **2011**, *123*, 9410; f) H. Noda, G. Erős, J. W. Bode, *J. Am. Chem. Soc.* **2014**, *136*, 5611.

[2] a) L. Crespo, G. Sanclimens, M. Pons, E. Giralt, M. Royo, F. Albericio, *Chem. Rev.* **2005**, *105*, 1663; b) M. A. Mintzer, E. E. Simanek, *Chem. Rev.* **2009**, *109*, 259; c) U. Boas, J. Brask, K. J. Jensen, *Chem. Rev.* **2009**, *109*, 2092; d) D. W. Zhang, X. Zhao, J. L. Hou, Z. T. Li, *Chem. Rev.* **2012**, *112*, 5271; e) E. B. Divito, M. Cascio, *Chem. Rev.* **2013**, *113*, 7343; f) X. Guo, A. Facchetti, T. J. Marks, *Chem. Rev.* **2014**, *114*, 8943; g) D.-W. Zhang, X. Zhao, Z.-T. Li, *Acc. Chem. Res.* **2014**, *47*, 1961.

[3] For reviews, see: a) J. M. Humphrey, A. R. Chamberlin, *Chem. Rev.* **1997**, *97*, 2243; b) G. Kiss, *Chem. Rev.* **2001**, *101*, 3435; c) S.-Y. Han, Y.-A. Kim, *Tetrahedron* **2004**, *60*, 2447; d) F. Albericio, *Curr. Opin. Chem. Biol.* **2004**, *8*, 211; e) C. A. G. N. Montalbetti, V. Falque, *Tetrahedron* **2005**, *61*, 10827; f) E. Valeur, M. Bradley, *Chem. Soc. Rev.* **2009**, *38*, 606; g) A. Brennführer, H. Neumann, M. Beller, *Angew. Chem. Int. Ed.* **2009**, *48*, 4114; *Angew. Chem.* **2009**, *121*, 4176; h) V. R. Pattabiraman, J. W. Bode, *Nature* **2011**, *480*, 471; i) C. L. Allen, J. M. J. Williams, *Chem. Soc. Rev.* **2011**, *40*, 3405; j) X.-F. Wu, H. Neumann, M. Beller, *Chem. Soc. Rev.* **2011**, *40*, 4986; k) Q. Liu, H. Zhang, A. Lei, *Angew. Chem. Int. Ed.* **2011**, *50*, 10788; *Angew. Chem.* **2011**, *123*, 10978; l) X.-F. Wu, H. Neumann, M. Beller, *Chem. Rev.* **2013**, *113*, 1; m) X.-F. Wu, X. Fang, L. Wu, R. Jackstell, H. Neumann, M. Beller, *Acc. Chem. Res.* **2014**, *47*, 1041.

[4] For selected examples of amides from carboxylic acids or esters, see: a) C. Han, J. P. Lee, E. Lobkovsky, J. A. Porco, *J. Am. Chem. Soc.* **2005**, *127*, 10039; b) M. Hosseini-Sarvari, H. Sharghi, *J. Org. Chem.* **2006**, *71*, 6652; Amides from aldehydes or alcohols: c) C. Gunanathan, Y. Ben-David, D. Milstein, *Science* **2007**, *317*, 790; d) L. U. Nordstrøm, H. Vogt, R. Madsen, *J. Am. Chem. Soc.* **2008**, *130*, 17672; e) T. Zweifel, J.-V. Naubron, H. Grützmacher, *Angew. Chem. Int. Ed.* **2009**, *48*, 559; *Angew. Chem.* **2009**, *121*, 567; f) M. W. Leighty, B. Shen, J. N. Johnston, *J. Am. Chem. Soc.* **2012**, *134*, 15233; g) B. Kang, Z. Fu, S. H. Hong, *J. Am. Chem. Soc.* **2013**, *135*, 11704; h) J. Dong, E. C. Harvey, M. Fañanás-Mastral, W. R. Browne, B. L. Feringa, *J. Am. Chem. Soc.* **2014**, *136*, 17302; For selected examples of aminocarbonylation, see: i) P. Hermange, A. T. Lindhardt, R. H. Tanning, K. Bjerglund, D. Lupp, T. Skrydstrup, *J. Am. Chem. Soc.* **2011**, *133*, 6061; j) X.-F. Wu, H. Neumann, M. Beller, *Chem. Eur. J.* **2012**, *18*, 419; k) M. V. Khedkar, T. Sasaki, B. M. Bhanage, *ACS Catal.* **2013**, *3*, 287; l) W. Li, C. Liu, H. Zhang, K. Ye, G. Zhang, W. Zhang, Z. Duan, S. You, A. Lei, *Angew. Chem. Int. Ed.* **2014**, *53*, 2443; *Angew. Chem.* **2014**, *126*, 2475.

[5] a) S.-I. Murahashi, Y. Imada, K. Nishimura, *J. Chem. Soc. Chem. Commun.* **1988**, 1578; b) S.-I. Murahashi, Y. Imada, K. Nishimura, *Tetrahedron* **1994**, *50*, 453; c) H. Yu, G. Zhang, Z.-J. Liu, H. Huang, *RSC Adv.* **2014**, *4*, 64235.

[6] a) P. Pino, P. Paleari, *Gazz. Chim. Ital.* **1951**, *81*, 64; b) W. Reppe, H. Kroper, *Ger. Pat.* **1951**, *149*, 868; c) P. Pino, R. Magri, *Chim. Ind.* **1952**, *34*, 511; d) G. Natta, P. Pino, R. Ercoli, *J. Am. Chem. Soc.* **1952**, *74*, 4496; e) W. Reppe, H. Main, *Chem. Abstr.* **1953**, *47*, 5428; f) B. F. Crowe, O. C. Elmer, *Chem. Abstr.* **1956**, *50*,

16849; g) T. J. Kealy, R. E. Benson, *J. Org. Chem.* **1961**, *26*, 3126; h) A. Striegler, J. Weber, *J. Prakt. Chem.* **1965**, *29*, 281; i) N. S. Imyanitov, D. M. Rudkvsku, *Chem. Abstr.* **1967**, *66*, 10530; j) B. K. Nefedov, N. S. Sergeeva, Y. T. Eidus, *Chem. Abstr.* **1975**, *83*, 205731; k) Y. Tsuji, T. Ohsumi, T. Kondo, Y. Watanabe, *J. Organomet. Chem.* **1986**, *309*, 333; l) S. I. Lee, S. U. Son, Y. K. Chung, *Chem. Commun.* **2002**, 1310.

[7] a) X. Fang, R. Jackstell, M. Beller, *Angew. Chem. Int. Ed.* **2013**, *52*, 14089; *Angew. Chem.* **2013**, *125*, 14339; b) H. Liu, N. Yan, P. J. Dyson, *Chem. Commun.* **2014**, *50*, 7848; c) X. Fang, H. Li, R. Jackstell, M. Beller, *J. Am. Chem. Soc.* **2014**, *136*, 16039; d) J. Cheng, X. Qi, M. Li, P. Chen, G. Liu, *J. Am. Chem. Soc.* **2015**, *137*, 2480.

[8] a) B. M. Trost, W. Pfrengle, H. Urabe, J. Dumas, *Acc. Chem. Res.* **1990**, *23*, 34; b) V. V. Grushin, *Chem. Rev.* **1996**, *96*, 2011; c) B. M. Trost, *Chem. Eur. J.* **1998**, *4*, 2405; d) F. Alonso, I. P. Beletskaya, M. Yus, *Chem. Rev.* **2004**, *104*, 3079.

[9] a) Y. Xie, B. Qian, P. Xie, H. Huang, *Adv. Synth. Catal.* **2013**, *355*, 1315; b) Y. Zhou, H. Huang, *Tetrahedron Lett.* **2013**, *54*, 2713.

[10] a) Y. Xie, J. Hu, Y. Wang, C. Xia, H. Huang, *J. Am. Chem. Soc.* **2012**, *134*, 20613; b) Y. Xie, J. Hu, P. Xie, B. Qian, H. Huang, *J. Am. Chem. Soc.* **2013**, *135*, 18327; c) J. Hu, Y. Xie, H. Huang, *Angew. Chem. Int. Ed.* **2014**, *53*, 7272; *Angew. Chem.* **2014**, *126*, 7400.

[11] CCDC 1048178 (**3aa**) and 1048179 (**3ag**) contain the supplementary crystallographic data for this paper. This data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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Communications

Synthetic Methods

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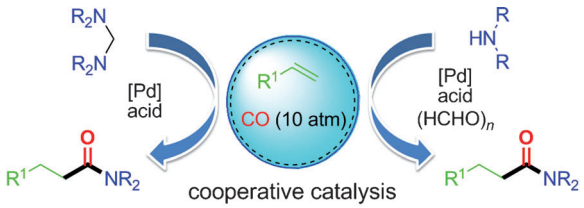
Palladium-Catalyzed Hydroaminocarbonylation of Alkenes with Amines: A Strategy to Overcome the Basicity Barrier Imparted by Aliphatic Amines



Back to basics: The basicity of aliphatic amines precludes their use in the palladium-catalyzed hydroaminocarbonylation. This issue was overcome by using aminals as surrogates of aliphatic amines. A cooperative catalytic system was discovered to operate by the synergistic combination of palladium, paraformaldehyde, and acid for promotion of the hydroaminocarbonylation of alkenes with both aromatic and aliphatic amines.

