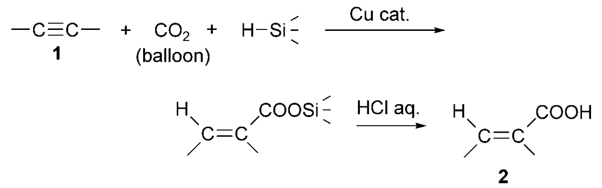
Angewandte Chemie International Edition

DOI: 10.1002/anie.201006292

Copper-Catalyzed Hydrocarboxylation of Alkynes Using Carbon Dioxide and Hydrosilanes**

*Tetsuaki Fujihara, Tinghua Xu, Kazuhiko Semba, Jun Terao, and Yasushi Tsuji**

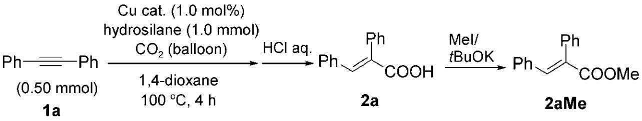
Carbon dioxide (CO_2) is a readily available and renewable chemical feedstock, although thermodynamic considerations limit its widespread use in chemical reactions.[1] For effective utilization of CO_2, transition-metal catalysts are required.[2] Useful transformations of CO_2 such as 1) cycloaddition via a metallacycle[3] and 2) carboxylation of organozinc and organoboron compounds[4] have been reported to date. Besides these reactions, the hydrocarboxylation[5] of C–C multiple bonds using CO_2 is also very promising. The first example of hydrocarboxylation using CO_2 was achieved using a nickel-catalyzed electrochemical reaction with alkynes,[5a] 1,3-diynes,[5b] and 1,3-enynes[5c] as substrates. Later, in supercritical CO_2, palladium-catalyzed hydrocarboxylation of terminal alkenes was reported.[5d,e] As for more efficient hydrocarboxylations, recent nickel-catalyzed reaction of styrenes[5f] and palladium-catalyzed reaction of allenes[5g] were reported with either $ZnEt_2$[5f,g] or $AlEt_3$[5g] as reducing agents. These reactions are very useful, but such strong and extremely air-sensitive reducing agents were indispensable in the reactions. Herein we report the copper-catalyzed hydrocarboxylation of alkynes using CO_2 (balloon).[6,7] The use of mild and easy-to-handle hydrosilane[8] as a reducing agent realizes highly efficient hydrocarboxylation of alkynes to afford α,β-unsaturated carboxylic acids (**2**; Scheme 1).



Scheme 1. Hydrocarboxylation of alkynes using CO_2 and hydrosilanes.

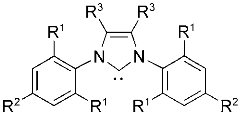
The hydrocarboxylation of diphenylacetylene (**1a**) with CO_2 (balloon) was carried out using $HSi(OEt)_3$ as a reducing agent in 1,4-dioxane (Table 1). The yield of (*E*)-2,3-diphenyl-2-propenoic acid (**2a**) was determined by GC methods after derivatization[9] to the corresponding methyl ester **2aMe**. By employing [IPrCuCl] + *t*BuONa (Table 1, entry 1) or [IMesCuCl] + *t*BuONa (Table 1, entry 2) as a catalyst, **2aMe** was obtained in only trace amounts and 49 % yield, respectively. In the latter case, a considerable amount (19 % yield) of *cis*-stilbene (**3a**) was observed as a by-product. When [IPrCuF][10] was used as a catalyst, **2aMe** was obtained in 41 % yield while reducing the formation of **3a** to 3 % (Table 1, entry 3). The new complex [IMesCuF] was synthesized from [IMesCuCl] similar to the synthesis of [IPrCuF], and its structure was confirmed by X-ray crystallography (Scheme 2).[9] As a result, [IMesCuF] was a much more

Table 1: Hydrocarboxylation of diphenylacetylene (**1a**) using a hydrosilane and carbon dioxide.[a]

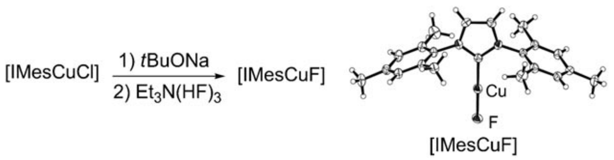


Entry	Catalyst System	Silane	Yield [%][b] **2aMe**	 **3a**[c]
1	[IPrCuCl] + *t*BuONa[d]	$HSi(OEt)_3$	trace	4
2	[IMesCuCl] + *t*BuONa[d]	$HSi(OEt)_3$	49	19
3	[IPrCuF]	$HSi(OEt)_3$	41	3
4	[IMesCuF]	$HSi(OEt)_3$	86 (72)[e]	3
5	[IMesCuF]	PMHS	80	6
6	[IMesCuF]	$HSi(OiPr)_3$	52	12
7	[IMesCuF]	H_2SiPh_2	32	10

[a] Reaction conditions: Diphenylacetylene (**1a**, 0.50 mmol), hydrosilane (1.0 mmol), Cu catalyst (0.0050 mmol, 1.0 mol %), 1,4-dioxane (2.0 mL), CO_2 (balloon), 100 °C, 4 h. [b] Yield determined by GC methods. [c] *cis*-Stilbene. [d] A mixture of [LCuCl] (L = IPr or IMes, 0.0050 mmol) and *t*BuONa (0.025 mmol). [e] Yield of isolated **2a**.



IPr: $R^1 = iPr, R^2 = R^3 = H$
IMes: $R^1 = R^2 = Me, R^3 = H$
Cl_2IPr: $R^1 = iPr, R^2 = H, R^3 = Cl$



Scheme 2. Synthesis and X-ray structure of [IMesCuF].

---

[*] Prof. Dr. T. Fujihara, Dr. T. Xu, K. Semba, Prof. Dr. J. Terao,
Prof. Dr. Y. Tsuji
Department of Energy and Hydrocarbon Chemistry Graduate
School of Engineering, Kyoto University
Kyoto 615-8510 (Japan)
Fax: (+81) 75-383-2514
E-mail: ytsuji@scl.kyoto-u.ac.jp
Homepage: http://twww.ehcc.kyoto-u.ac.jp/

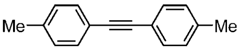
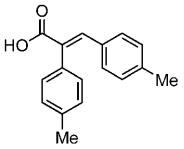
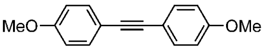
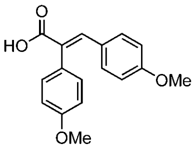
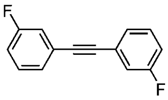
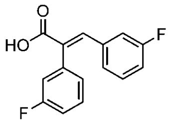
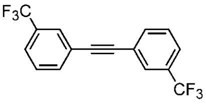
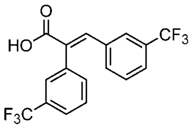
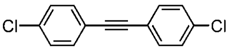
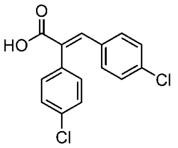
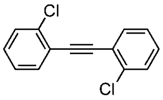
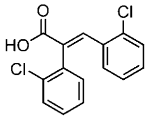
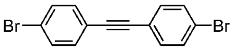
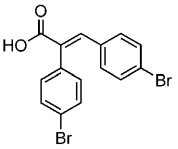
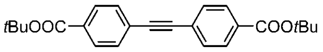
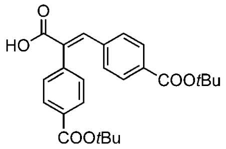
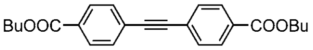
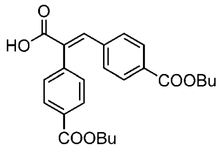
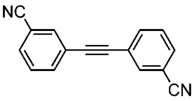
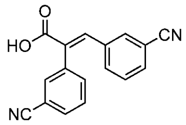
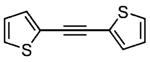
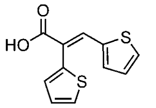
[**] This work was supported by a Grant-in-Aid for Scientific Research on Priority Areas ("Synergy of Elements" and "Chemistry of Concerto Catalysis") from the Ministry of Education, Culture, Sports, Science and Technology (Japan). T.X. is grateful for a Postdoctral Fellowship from JSPS for Foreign Researchers.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201006292.

effective catalyst providing **2aMe** in 86% yield with a small amount of **3a** (Table 1, entry 4). The reaction is stereoselective and affords only the *E* isomer as confirmed by X-ray crystal structure of **2a**.[9] The reaction proceeds smoothly at 100°C, but yields decreased to 42% and 27% at 70°C and 50°C, respectively (see Table S1, entries 2 and 3 in the Supporting Information). In toluene as a solvent, **2aMe** was obtained in 81% yield under the same reaction conditions as used for entry 4 of Table 1, but **2a** was not obtained when using DMF (see entries 4 and 7 in Table S1 in the Supporting Information). Polymethylhydrosiloxane (PMHS), a by-product of the silicone industry, is a cheap, easy-to-handle, and environmentally friendly reducing agent. When $HSi(OEt)_3$ was replaced with PMHS, **2aMe** was obtained in 80% yield (Table 1, entry 5). Other hydrosilanes such as $HSi(O\textit{i}Pr)_3$ and H_2SiPh_2 afforded **2aMe** in 52% and 32% yields, respectively (Table 1, entries 6 and 7), whereas $HSiEt_3$ and H_3SiPh did not provide **2aMe** at all.

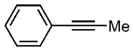
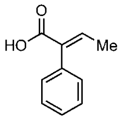
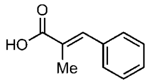
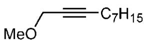
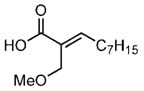
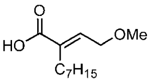
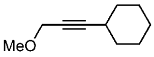
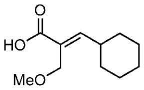
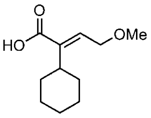
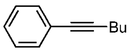
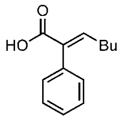
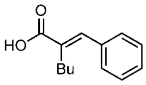
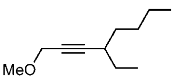
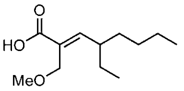
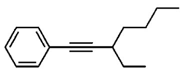
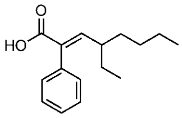
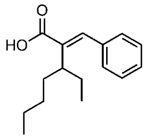
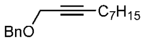
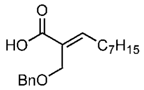
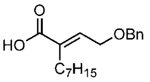
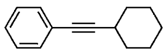
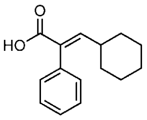
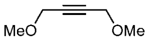
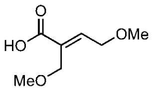
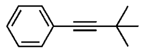
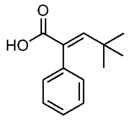
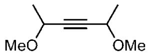
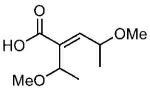
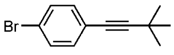
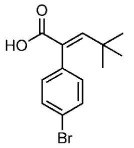
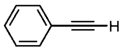
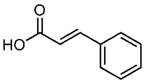
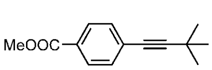
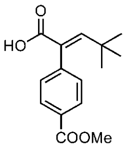
The hydrocarboxylation of a variety of symmetrical aromatic alkynes (**1b**–**l**) was carried out in the presence of [IMesCuF] as a catalyst (Table 2). From all the alkynes listed, the corresponding α,β-unsaturated carboxylic acids (**2b**–**l**) were obtained in good yields with *E* stereochemistry. The stereochemistry was confirmed by NOESY measurements after converting **2b**–**l** into the corresponding allylic alcohols **4b**–**l**.[9] Alkynes bearing both electron-rich (Table 2, entries 1 and 2) and electron-poor (Table 2, entries 3–10) aryl moieties gave the corresponding products (**2b**–**k**) in good yields. Importantly, chloro (Table 2, entries 5 and 6), bromo (Table 2, entry 7), alkoxycarbonyl (Table 2, entries 8 and 9), and cyano (Table 2, entry 10) functionalities were tolerated under the reaction conditions and provided the corresponding products in good yields. An alkyne bearing thiophene rings (**1l**) stereoselectively afforded the corresponding product **2l** in 78% yield (Table 2, entry 11).

Table 2: Hydrocarboxylation of symmetrical aromatic alkynes.[a]

Entry	Substrate		Product		Yield [%][b]
1		**1b**		**2b**	67
2		**1c**		**2c**	58
3		**1d**		**2d**	78 (71)[c]
4		**1e**		**2e**	75 (72)[c]
5		**1f**		**2f**	75
6[d]		**1g**		**2g**	64 (62)[c]
7		**1h**		**2h**	65
8[d]		**1i**		**2i**	71
9[d]		**1j**		**2j**	64
10		**1k**		**2k**	52
11		**1l**		**2l**	78

[a] Reaction conditions: Alkyne (0.50 mmol), $HSi(OEt)_3$ (1.0 mmol), [IMesCuF] (0.0050 mmol, 1.0 mol%), 1,4-dioxane (2.0 mL), CO_2 (balloon), 100°C, 12 h. [b] Yield of isolated **2**. [c] PMHS (2.0 mmol) was used in place of $HSi(OEt)_3$. [d] [IMesCuF] (0.010 mmol, 2.0 mol%) was used.

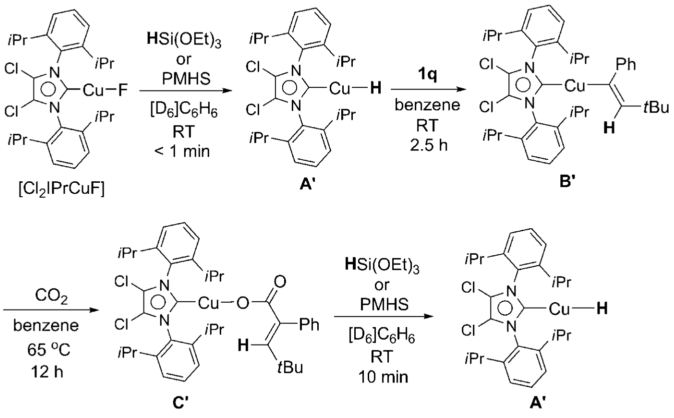
Table 3: Hydrocarboxylation of various alkynes.[a]

Entry	Substrate	Product		Yield [%][b]	Entry	Substrate	Product		Yield [%][b]
1[c]	 **1m**	 **2m**	 **2m′**	trace	10	 **1t**	 **2t**	 **2t′**	63 (93:7)[e]
2[d]	**1m**	**2m**	**2m′**	18 (66:34)[e]					
3	**1m**	**2m**	**2m′**	86 (75:25)	11	 **1u**	 **2u**	 **2u′**	70 (90:10)[e]
4	 **1n**	 **2n**	 **2n′**	91 (88:12)[e] 76[f]	12	 **1v**	 **2v**		74
5	 **1o**	 **2o**	 **2o′**	85 (93:7)[e], 75[f]	13	 **1w**	 **2w**	 **2w′**	75 (85:15)[e], 48[h]
6	 **1p**	 **2p**		88	14[d]	 **1x**	 **2x**		66
7[g]	 **1q**	 **2q**		71	15[d]	 **1y**	 **2y**		61
8[g]	 **1r**	 **2r**		68	16[d]	 **1z**	 **2z**		44
9[g]	 **1s**	 **2s**		63					

[a] Reaction conditions: Alkyne (1.0 mmol), $HSi(OEt)_3$ (2.0 mmol), $[Cl_2IPrCuF]$ (0.025 mmol, 2.5 mol%), *n*-hexane (2.0 mL), CO_2 (balloon), 70 °C, 14 h. [b] Isolated yield. [c] [IMesCuF] (0.025 mmol) in 1,4-dioxane at 100 °C. [d] [IPrCuF] (0.025 mmol) in 1,4-dioxane at 100 °C. [e] A ratio of **2** and **2′** was determined by ^1H NMR analysis. [f] Yield of isolated **2n** or **2o**. [g] $[Cl_2IPrCuF]$ (0.050 mmol). [h] Yield of isolated **2w** as the corresponding methyl ester.

PMHS could be used in place of $HSi(OEt)_3$ as an effective reducing reagent and the products were obtained in comparable yields (Table 2, entries 3, 4, and 6).

The hydrocarboxylation of other alkynes were carried out as shown in Table 3. The best catalyst in Tables 1 and 2, [IMesCuF], provided only a trace amount of the product for the hydroxycarboxylation of 1-phenyl-1-propyne (**1m**) in 1,4-dioxane at 100 °C (Table 3, entry 1), whereas using [IPrCuF] as the catalyst under the same reaction conditions afforded a mixture of regioisomers (**2m** and **2m′**) in low yield with poor



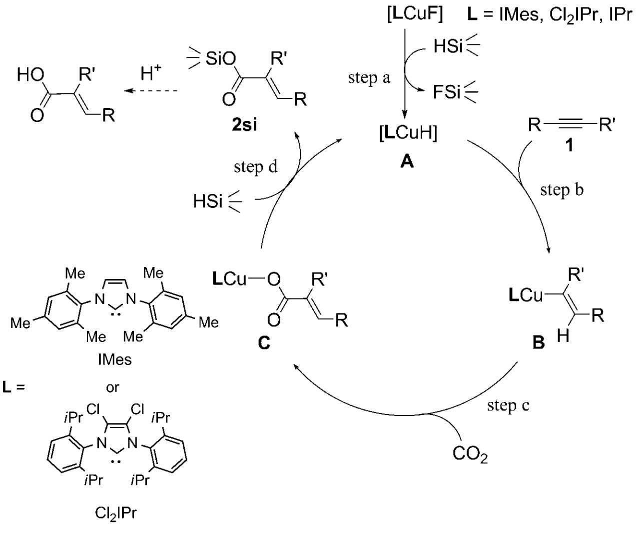
Scheme 3. Stoichiometric reactions relevant to the catalysis.

regioselectivity (Table 3, entry 2). Thus, [Cl_2IPrCuF] was synthesized[9] in a similar way to [IPrCuF][10] using the known NHC ligand Cl_2IPr.[11] The reaction of **1m** in the presence of [Cl_2IPrCuF] (2.5 mol%) in *n*-hexane as a solvent afforded **2m** and **2m′** in much higher yield (88%) even at 70°C with moderate regioselectivity (Table 3, entry 3). The regioselectivity was considerably improved by replacing the methyl group of **1m** with a butyl group (**1n**) or secondary alkyl groups (**1o**). In these cases, the major regioisomers (**2n** and **2o**) were readily isolated in analytically pure form by column chromatography on silica gel. Gratifyingly, alkynes with cyclohexyl (**1p**) and *tert*-butyl groups (**1q–s**) afforded single regioisomers in good to high yields (Table 3, entries 6–9). Here, bromo (Table 3, entry 8) and alkoxycarbonyl (entry 9) functionalities on the phenyl ring were tolerated in the reaction. In the present reaction, simple internal aliphatic alkynes such as 5-decyne were much less reactive (conv. $<5\%$) and did not give the corresponding carboxylic acid under the present reaction conditions. However, it was found that 1-methoxy-2-decyne (**1t**) gave a product in good yield with high regioselectivity (Table 3, entry 10). A similar effect was evident for the β-methoxy (**1u** and **1v**) and benzyloxy groups (**1w**; Table 3, entries 11–13), suggesting that coordination of the ether moieties to a copper center would be important in the reaction. 1,4-Dimethoxy-2-butyne (**1x**) and 2,5-dimethoxy-3-hexyne (**1y**) bearing the two β-ether functionalities also afforded the corresponding products (**2x** and **2y**, respectively) in good yields (Table 3, entries 14 and 15). As for terminal alkynes, phenylacetylene (**1z**) afforded cinnamic acid (**2z**) in 44% yield using [IPrCuF] as the catalyst at 100°C in 1,4-dioxane (Table 3, entry 16). The yield was modest owing to considerable formation of the styrene in 28% yield.

To gain insight into reaction mechanism, fundamental catalytic steps in the present hydrocarboxylation were examined by stoichiometric reactions (Scheme 3). When [Cl_2IPrCuF], the catalyst precursor used the examples shown in Table 3, was treated with an excess of the silane (4 equiv), such as PMHS or $HSi(OEt)_3$ in [D_6]C_6H_6, an immediate color change from colorless to bright orange was observed. The ^1H NMR spectrum indicated clean formation of [Cl_2IPrCuH] (**A′**) with a diagnostic proton resonance of Cu-H at $\delta = 2.39$ ppm (see Figure S2 in the Supporting Information), which is consistent with a reported value of [IPrCuH] at $\delta = 2.63$ ppm.[12]

An aromatic alkyne such as **1q** reacted with **A′** smoothly in 2.5 hours at room temperature to afford the corresponding copper alkenyl complex (**B′**). In contrast, an aliphatic alkyne such as 5-decyne did not react with **A′**, which was decomposed rapidly under the reaction conditions. This low reactivity of the internal aliphatic alkyne is very reminiscent of the catalytic reaction. The copper alkenyl complex **B′** was isolated in 70% yield and fully characterized by ^1H and ^{13}C NMR methods (see Figures S3 and S4 in the Supporting Information). The reaction of **B′** with CO_2 (balloon) was very slow at room temperature, but took place smoothly at a higher reaction temperature (65°C) after 12 hours. The copper carboxylato complex **C′** was also isolated in 84% yield and fully characterized by ^1H and ^{13}C NMR analysis (see Figures S5 and S6 in the Supporting Information). Finally, **C′** reacted with an excess (4 equiv) of $HSi(OEt)_3$ at room temperature and the copper hydride complex **A′** was afforded cleanly. The isolated **B′** and **C′** were active catalysts, affording **2q** in 80% and 74% yields, respectively, under the same reaction condition as those used in entry 7, Table 3.

On the basis of the stoichiometric reactions shown in Scheme 3, a possible catalytic cycle is shown in Scheme 4. A copper(I) hydride species (**A**)[13] is generated in situ from [LCuF] (L = IMes, IPr, or Cl_2IPr) and a hydrosilane by the aid of the strong silicon–fluorine interaction[10] (step a). *Syn* addition of **A** to an alkyne (**1**) initiates the catalytic cycle and affords a copper alkenyl intermediate (**B**) stereoselectively (step b).[12] Then, insertion of CO_2 takes place to provide the corresponding copper carboxylate intermediate **C**[4c,14] (step c). Finally, σ-bond metathesis of **C** with a hydrosilane provides the corresponding silyl ester **2si** and regenerates **A** (step d). All the catalytic were confirmed by the stoichiometric reactions in Scheme 3, in which only the insertion of CO_2 requires the higher reaction temperature (65°C), whereas other stoichiometric reactions proceeded at room



Scheme 4. Plausible catalytic cycle.

temperature. Thus, step c in Scheme 4 must be a rate-determining step.

In conclusion, copper-catalyzed hydrocarboxylation of alkynes (**1**) using carbon dioxide (balloon) has been developed. [IMesCuF] and [Cl_2IPrCuF] complexes show high catalytic activity when using a hydrosilane as a reducing agent. Additional studies on application and reaction mechanism of the reaction are now in progress.

Received: October 7, 2010

Keywords: carbon dioxide · copper · hydrocarboxylation · N-heterocyclic carbene · silanes

---

[1] a) *Carbon Dioxide as Chemical Feedstock* (Ed.: M. Aresta), Wiley-VCH, Weinheim, **2010**; b) T. Sakakura, J.-C. Choi, H. Yasuda, *Chem. Rev.* **2007**, *107*, 2365 – 2387.

[2] a) M. Aresta, A. Dibenedetto, *Dalton Trans.* **2007**, 2975 – 2992; b) D. J. Darensbourg, *Chem. Rev.* **2007**, *107*, 2388 – 2410; c) P. Braunstein, D. Matt, D. Nobel, *Chem. Rev.* **1988**, *88*, 747 – 764; d) S. N. Riduan, Y. Zhang, *Dalton Trans.* **2010**, *39*, 3347 – 3357; e) I. I. F. Boogaerts, S. P. Nolan, *J. Am. Chem. Soc.* **2010**, *132*, 8858 – 8859; f) A. Correa, R. Martin, *J. Am. Chem. Soc.* **2009**, *131*, 15974 – 15975; g) I. I. Boogaerts, G. C. Fortman, M. R. L. Furst, C. S. J Cazin, S. P. Nolan, *Angew. Chem.* **2010**, *122*, 8856 – 8859; *Angew. Chem. Int. Ed.* **2010**, *49*, 8674 – 8677; h) L. Zhang, J. Cheng, T. Ohishi, Z. Hou, *Angew. Chem.* **2010**, *122*, 8852 – 8855; *Angew. Chem. Int. Ed.* **2010**, *49*, 8670 – 8673.

[3] a) T. Tsuda, S. Morikawa, R. Sumiya, T. Saegusa, *J. Org. Chem.* **1988**, *53*, 3140 – 3145; b) J. Louie, J. E. Gibby, M. V. Farnworth, T. N. Tekavec, *J. Am. Chem. Soc.* **2002**, *124*, 15188 – 15189; c) M. Takimoto, M. Mori, *J. Am. Chem. Soc.* **2002**, *124*, 10008 – 10009.

[4] a) C. S. Yeung, V. M. Dong, *J. Am. Chem. Soc.* **2008**, *130*, 7826 – 7827; b) H. Ochiai, M. Jang, K. Hirano, H. Yorimitsu, K. Oshima, *Org. Lett.* **2008**, *10*, 2681 – 2683; c) T. Ohishi, M. Nishiura, Z. Hou, *Angew. Chem.* **2008**, *120*, 5876 – 5879; *Angew. Chem. Int. Ed.* **2008**, *47*, 5792 – 5795; d) J. Takaya, S. Tadami, K. Ukai, N. Iwasawa, *Org. Lett.* **2008**, *10*, 2697 – 2700; e) K. Ukai, M. Aoki, J. Takaya, N. Iwasawa, *J. Am. Chem. Soc.* **2006**, *128*, 8706 – 8707; f) A. Correa, R. Martín, *Angew. Chem.* **2009**, *121*, 6317 – 6320; *Angew. Chem. Int. Ed.* **2009**, *48*, 6201 – 6204.

[5] a) S. Dérien, E. Duñach, J. Périchon, *J. Am. Chem. Soc.* **1991**, *113*, 8447 – 8454; b) S. Dérien, J.-C. Clinet, E. Duñach, J. Périchon, *J. Chem. Soc. Chem. Commun.* **1991**, 549 – 550; c) S. Dérien, J.-C. Clinet, E. Duñach, J. Périchon, *J. Organomet. Chem.* **1992**, *424*, 213 – 224; d) C. Tortosa-Estorach, N. Ruiz, A. M. Masdeu-Bultó, *Chem. Commun.* **2006**, 2789 – 2791; e) C. Tortosa-Estorach, A. Orejón, N. Ruiz, A. M. Masdeu-Bultó, G. Laurenczy, *Eur. J. Inorg. Chem.* **2008**, 3524 – 3531; f) C. M. Williams, B. Jeffrey, J. B. Johnson, T. Rovis, *J. Am. Chem. Soc.* **2008**, *130*, 14936 – 14937; g) J. Takaya, N. Iwasawa, *J. Am. Chem. Soc.* **2008**, *130*, 15254 – 15255.

[6] Hydrocarboxylation of alkynes with CO_2 in the presence of a stoichiometric amount of [$Ni(cod)_2$] (cod = 1,5-cyclooctadiene) has been known: a) M. Aoki, M. Kaneko, S. Izumi, K. Ukai, N. Iwasawa, *Chem. Commun.* **2004**, 2568 – 2569; b) S. Saito, S. Nakagawa, T. Koizumi, K. Hirayama, Y. Yamamoto, *J. Org. Chem.* **1999**, *64*, 3975 – 3978.

[7] For Ni^0-catalyzed or Ni^0-mediated alkylative carboxylation of alkynes using CO_2 and R_2Zn, see: a) K. Shimizu, M. Takimoto, Y. Sato, M. Mori, *Org. Lett.* **2005**, *7*, 195 – 197; b) M. Takimoto, K. Shimizu, M. Mori, *Org. Lett.* **2001**, *3*, 3345 – 3347.

[8] As for a highly active copper catalyst for hydrosilylation of bulky ketones, see: T. Fujihara, K. Semba, J. Terao, Y. Tsuji, *Angew. Chem.* **2010**, *122*, 1514–1518; *Angew. Chem. Int. Ed.* **2010**, *49*, 1472 – 1476.

[9] See the Supporting Information for details.

[10] J. R. Herron, Z. T. Ball, *J. Am. Chem. Soc.* **2008**, *130*, 16486 – 16487.

[11] A. J. Arduengo III, R. Krafczyk, R. Schmutzler, H. A. Craig, J. R. Goerlich, W. J. Marshall, M. Unverzagt, *Tetrahedron* **1999**, *55*, 14523 – 14534.

[12] N. P. Mankad, D. S. Laitar, J. P. Sadighi, *Organometallics* **2004**, *23*, 3369 – 3371.

[13] C. Deutsch, N. Krause, B. H. Lipshutz, *Chem. Rev.* **2008**, *108*, 2916 – 2927.

[14] a) N. P. Mankad, T. G. Gray, D. S. Laitar, J. P. Sadighi, *Organometallics* **2004**, *23*, 1191 – 1193; b) L. Dang, Z. Lin, *Organometallics* **2010**, *29*, 917 – 927.