CHEMISTRY
A EUROPEAN JOURNAL

ChemPubSoc
Europe

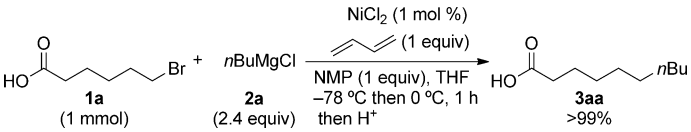
DOI: 10.1002/chem.201204222

Nickel–Butadiene Catalytic System for the Cross-Coupling of Bromoalkanoic Acids with Alkyl Grignard Reagents: A Practical and Versatile Method for Preparing Fatty Acids

Takanori Iwasaki,[a] Kiyokazu Higashikawa,[a] Vutukuri P. Reddy,[a] Willbe W. S. Ho,[a] Yukari Fujimoto,[b] Koichi Fukase,[b] Jun Terao,[c] Hitoshi Kuniyasu,[a] and Nobuaki Kambe*[a]

Fatty acids are essential to natural life because they act as key components in biological membranes and glycerides, as well as in various biologically active agents, such as prostaglandins and endocannabinoids.[1] For the construction of structurally diverse carbon frameworks of fatty acids, transition-metal-catalyzed cross-coupling reactions appear to be the most straightforward and efficient methods for carbon–carbon bond formation and they have been employed in the synthesis of a wide variety of fatty acids with unsaturated bonds.[2–4] However, these methods are limited to reactions at sp^2[3] or sp carbon atoms,[4] in which the stereochemistry of the olefinic moieties that are being introduced must be controlled. In contrast to these reactions, cross-coupling reactions between sp^3-hybridized carbon centers[5] appear to be a useful and, potentially, more-promising tool, because they are applicable to the synthesis of both saturated and unsaturated fatty acids and they are free from the problems associated with double-bond stereochemistry.[6–8] However, owing to the lower tolerance of the carboxylic group toward organometallic reagents, including transition-metal complexes,[9,10] protected carboxy groups[3c,4b,8,11] or their synthetic equivalents[3a,d,4c] are often employed. Herein, we report a convenient and efficient one-pot procedure for the construction of carbon frameworks of fatty acids by using the nickel-catalyzed cross-coupling of alkyl halides that contain a carboxy functionality with Grignard reagents in the presence of 1,3-butadiene as an additive,[8e,12,13] in combination with an in situ protection procedure.[14] As an example of a synthetic application of this method, the regioisomers of elaidic acid were synthesized through an iterative cross-coupling procedure.

In our previous studies, we reported that the Ni-catalyzed cross-coupling reactions of alkyl halides with alkyl Grignard reagents in the presence of butadienes[8e,12] were effective for the construction of hydrocarbon skeletons that contained aprotic polar functionalities, such as ketones, esters, and nitriles.[8e,12f] When alkyl halides that contained a carboxylic acid group are subjected to this cross-coupling reaction, without employing tedious protection-deprotection processes, the deprotonation of the carboxylic acid group is unavoidable. Thus, to develop a simple and straightforward route to fatty acids with various carbon chains, we examined the Ni-catalyzed cross-coupling reactions of 6-bromohexanoic acid (**1a**) with excess amounts of *n*BuMgCl under various conditions and we found that the expected decanoic acid was obtained in quantitative yield as the sole product, with no evidence of any undesirable side reactions, when the reaction was conducted at 0 °C for 1 h in the presence of 2.4 equivalents of *n*BuMgCl (Scheme 1). In this reaction, a



Scheme 1. Cross-coupling of bromoalkanoic acid **1a** with *n*BuMgCl in the presence of a Ni catalyst.

stoichiometric amount of *n*BuMgCl acted as base to form the magnesium carboxylate salt of compound **1a**, which then underwent cross-coupling at the other terminal carbon atom with the remaining *n*BuMgCl.

To avoid consuming the Grignard coupling partner during the deprotonation process, we tested other Grignard reagents for use as the base in the cross-coupling of bromohexanoic acid (**1a**) with *n*OctMgCl (**2b**). The in situ protection of compound **1a** by deprotonation with the base was

[a] Dr. T. Iwasaki, K. Higashikawa, Dr. V. P. Reddy, W. W. S. Ho, Prof. Dr. H. Kuniyasu, Prof. Dr. N. Kambe
Department of Applied Chemistry
Graduate School of Engineering
Osaka University, Suita, Osaka 565-0871 (Japan)
Fax: (+81) 6-6879-7390
E-mail: kambe@chem.eng.osaka-u.ac.jp

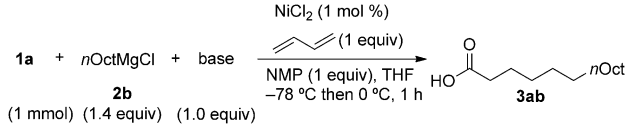
[b] Prof. Dr. Y. Fujimoto, Prof. Dr. K. Fukase
Department of Chemistry, Graduate School of Science
Osaka University, Toyonaka, Osaka 560-0043 (Japan)

[c] Prof. Dr. J. Terao
Department of Energy and Hydrocarbon Chemistry
Graduate School of Engineering
Kyoto University, Katsura
Nishikyo-ku, Kyoto 615-8510 (Japan)

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201204222.

performed by stirring compound **1a** with one equivalent of a Grignard reagent at −78 °C for 10 min in a THF solution that contained one equivalent of *N*-methyl-2-pyrrolidone (NMP). When methyl- and phenyl Grignard reagents were used, compound **3ab** was obtained in 84 % and 56 % yield, respectively (Table 1, entries 1 and 2). In contrast to these

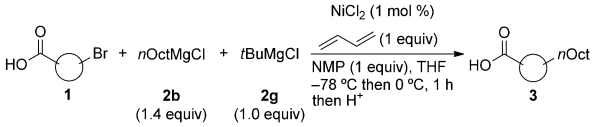
Table 1. Ni-catalyzed cross-coupling of 6-bromohexanoic acid (**1a**) with octylmagnesium chloride by using different Grignard reagents as the base.[a]

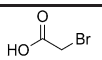
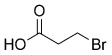
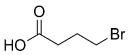
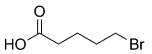
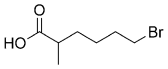
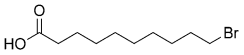
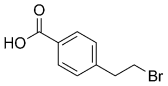


Entry	Base	2	Yield [%][b]
1	MeMgBr	**2c**	84
2	PhMgBr	**2d**	56
3	*n*BuMgCl	**2a**	95
4	*i*BuMgCl	**2e**	>99
5	*s*BuMgCl	**2f**	>99
6	*t*BuMgCl	**2g**	>99

[a] Reaction conditions: 6-Bromohexanoic acid (195 mg, 1.0 mmol), THF (1.5 mL), NMP (95 μL, 1.0 mmol), $C_{12}H_{26}$ as an internal standard, RMgCl (in THF, 1.0 mmol), −78 °C, 10 min; then, *n*OctMgCl (in THF, 1.4 mmol), gaseous 1,3-butadiene (22 mL, 1.0 mmol), $NiCl_2$ (1 mol %, 1.3 mg), 0 °C, 1 h. [b] GC yield after conversion into the corresponding methyl ester.

Table 2. Cross-coupling of alkyl bromides that contain a carboxy group (**1**) with *n*-octyl Grignard reagent **2b**.[a]



Entry	Bromocarboxylic acid	1	Yield [%][b]
1		**1b**	54
2		**1c**	n.i.[c]
3		**1d**	>99
4		**1e**	95
5		**1f**	>99
6		**1g**	97
7		**1h**	97

[a] Reaction conditions: Compound **1** (1.0 mmol), THF (1.5 mL), NMP (95 μL, 1.0 mmol), *t*BuMgCl (in THF, 1.0 mmol), −78 °C, 10 min; then, *n*OctMgCl (in THF, 1.4 mmol), gaseous 1,3-butadiene (22 mL, 1.0 mmol), $NiCl_2$ (1 mol %, 1.3 mg), 0 °C, 1 h. [b] Yield of isolated product. [c] Not isolated (n.i.).

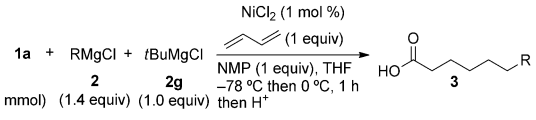
unsatisfactory results, quantitative yields were obtained when *n*-, *i*-, *s*-, and *t*BuMgCl were used as the base (Table 1, entries 3–6). Among these reagents, *t*BuMgCl was found to be a more-suitable base than *n*-, *i*-, and *s*BuMgCl, because the latter three reagents, when they remained, competed with the different Grignard reagents that were subsequently added for the cross-coupling reaction with bromide **1** (see below). Unfortunately, metal hydrides, such as NaH and CaH_2, were not suitable and resulted in lower yields of the cross-coupling products. In the absence of NMP, the yield decreased slightly (by about 5 %).

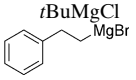
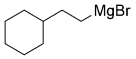
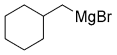
Next, we performed the Ni-catalyzed cross-coupling reactions of various bromocarboxylic acids (**1**) under our optimized conditions. As shown in Table 2, when α-bromoacetic acid (**1b**) was used as the substrate, coupling product **3bb** was obtained in 54 % yield (Table 2, entry 1). β-Bromopropionic acid (**1c**) gave a complex mixture and no coupling product was isolated (Table 2, entry 2). This result is in sharp contrast to the successful cross-coupling of the corresponding nickelalactones, which suggests that the mechanisms for these two reactions are different from each other.[7] Carboxylic acids that contained a longer methylene tether could be coupled with Grignard reagent **2b** in good-to-excellent yields (Table 2, entries 3, 4, and 6). Because Ni catalyzes the cross-coupling of alkyl tosylates and fluorides with Grignard reagents,[12d,e] we examined the reactions of decanoic-acid derivatives that contained a TsO group or an F atom on the terminal carbon atom as analogues of compound **1g**; however the expected products were not obtained in either case. The reaction of branched bromocarboxylic acid **1f** proceeded efficiently, thereby affording the product in excellent yield (Table 2, entry 5). An aromatic carboxylic acid moiety also remained intact under the reaction conditions and the corresponding coupling product (**3hb**) was obtained in 97 % yield (Table 2, entry 7).

The results for the cross-coupling of 6-bromohexanoic acid (**1a**) with various Grignard reagents are summarized in Table 3. Primary alkyl Grignard reagents afforded their corresponding carboxylic acids (**3**) in good-to-excellent yields (Table 3, entries 1, 2, and 5–7). Under the same conditions, *i*BuMgCl and *s*BuMgCl yielded their corresponding carboxylic acids in 75 % and 52 % yields, respectively, and no product was obtained with *t*BuMgCl (Table 3, entries 2–4). These results indicate that the steric bulkiness of the carbon chains is an important factor in this reaction. Similar trends were also observed with Grignard reagents **2j**–**2l** (Table 3, entries 6–8). Secondary Grignard reagent **2l** gave the corresponding coupling product in reasonable yield. A more sterically hindered primary Grignard reagent (**2m**) reacted sluggishly, even when 5 mol % of the Ni catalyst was used (Table 3, entry 9). PhMgBr did not give the desired product, but reacted at the carboxy carbon to afford the corresponding ketone as the major product (Table 3, entry 10).

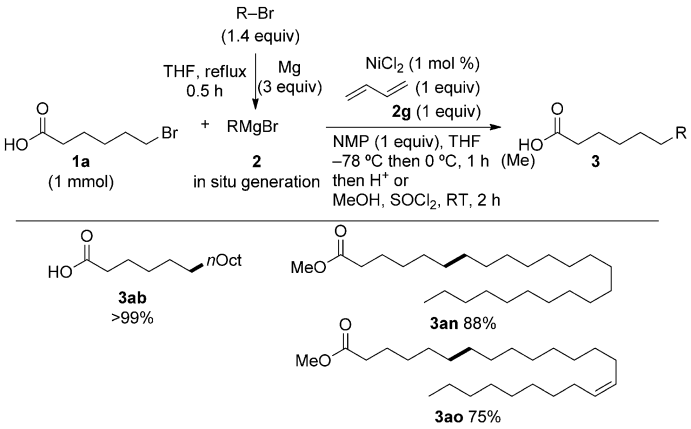
Grignard reagents with long alkyl chains are less easily accessible and are also difficult to handle, owing to their low solubility in THF. Indeed, when octadecylmagnesium bromide was prepared from 1-bromooctadecane and magnesium metal at a concentration of about 1 M in THF by using

Table 3. Cross-coupling of compound **1a** with various Grignard reagents.[a]

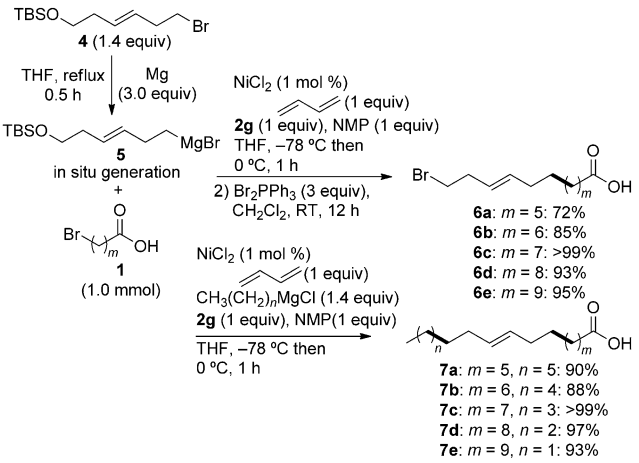


Entry	RMgX	2	Yield [%][b]
1	$CH_3(CH_2)_{13}MgCl$	**2h**	95
2	*i*BuMgCl	**2e**	75
3	*s*BuMgCl	**2f**	52
4	*t*BuMgCl	**2g**	n.d.
5		**2i**	83
6		**2j**	92
7		**2k**	95
8		**2l**	76
9[c]		**2m**	25
10		**2d**	n.d.[d]

[a] Reaction conditions: 6-Bromohexanoic acid (1.0 mmol), THF (1.5 mL), NMP (95 μL, 1.0 mmol), *t*BuMgCl (in THF, 1.0 mmol), −78 °C, 10 min; then, compound **2** (in THF, 1.4 mmol), gaseous 1,3-butadiene (22 mL, 1.0 mmol), $NiCl_2$ (1 mol %, 1.3 mg), 0 °C, 1 h. [b] Yield of isolated product. [c] 5 mol % $NiCl_2$. [d] Not detected (n.d.); 6-bromo-1-phenylhexan-1-one (44 % yield) was obtained as the major product.



Scheme 2. Cross-coupling through a reverse-addition procedure.



Scheme 3. Synthesis of elaidic acid and its regioisomers.

standard procedures, the resulting mixture became a thick slurry and was difficult to handle with a syringe. In such a case, a reverse-addition procedure was found to be effective for carrying out the cross-coupling efficiently: A solution of compound **1a** and *t*BuMgCl in THF was transferred by means of a cannula into a solution of the Grignard reagents (**2b**, **2n**, or **2o**) at −78 °C, which were generated by the reactions of octyl, octadecyl, and *cis*-octadec-9-enyl bromides with two equivalents of magnesium in THF, respectively. The cross-coupling reactions were performed by adding NMP, 1,3-butadiene, and $NiCl_2$ to the mixtures. After stirring at 0 °C for 1 h, the corresponding carboxy acids (**3ab**, **3an**, and **3ao**) were obtained in good-to-excellent yields, as shown in Scheme 2. Notably, the carbon chain of the readily available oleic acid could be incorporated into *cis*-15-tetracosenoic acid (**3ao**, nervonic acid) through the *cis*-octadec-9-enyl bromide that is formed from the successive reduction and bromination of oleic acid with complete retention of the double-bond stereochemistry.

Finally, we attempted the synthesis of the ω-5 to ω-8 regioisomers of elaidic acid[15] by using an iterative cross-coupling approach with (*E*)-1-bromo-6-(*tert*-butyldimethylsiloxy)hex-3-ene (**4**) as a *trans*-olefin building block (Scheme 3). The first cross-coupling reaction was performed by using [6-(*tert*-butyldimethylsiloxy)hex-3-en-1-yl]magnesium bromide (**5**), which was generated in situ from compound **4**, and a series of ω-bromocarboxylic acids with a C_5–C_9 methylene carbon tether. The corresponding coupling products (**6a**–**6e**) were obtained in good-to-excellent yields after the usual work-up, followed by direct bromination of the siloxy group with Br_2PPh_3.[16] The second coupling reactions of compounds **6a**–**6e** with alkyl Grignard reagents that had an appropriate chain length afforded elaidic acid (**7a**), as well as a series of its regioisomers (**7b**–**7e**) that contained a *trans*-olefin unit at the ω-5 to ω-8 positions.

In summary, various fatty acids have been prepared through the alkyl–alkyl cross-coupling of bromoalkyl carboxylic acids with Grignard reagents by using a nickel–butadiene catalytic system. These cross-coupling reactions proceeded efficiently and exclusively in a convenient one-pot procedure, combined with prior deprotonation by *t*BuMgCl as a base. Nervonic acid was synthesized by using this method with the incorporation of the unsaturated carbon skeleton of the easily available oleic acid as part of its carbon framework. The synthetic utility of this procedure was demonstrated in the synthesis of elaidic acid and its regioisomers through sequential Ni-catalyzed three-component cross-coupling reactions by using (*E*)-6-bromohex-3-enyl-1-ol as a synthetic building block of a double-bond unit. This method provides a simple and convenient route to carboxylic acids with various carbon chains and will open up

new fields of fatty acid chemistry in both biological and materials disciplines.

Experimental Section

General procedure for the cross-coupling of bromocarboxylic acid with Grignard reagents: *t*BuMgCl (**2g**; 0.72 M in THF, 1.4 mL, 1.0 mmol) was added into a Schlenk tube that contained a bromocarboxylic acid (**1**; 1.0 mmol), NMP (95 μL, 1.0 mmol), and THF (1.0 mL) at −78 °C and the mixture was stirred for 10 min under a nitrogen atmosphere. The Grignard reagent (**2**; in THF, 1.4 mmol), gaseous 1,3-butadiene (22.4 mL, 1 atm, 1.0 mmol), and $NiCl_2$ (1.3 mg) were added at the same temperature and the mixture was stirred with cooling in an ice-bath for 1 h. The reaction was quenched by the addition of aqueous HCl and the resulting solution was extracted with CH_2Cl_2 (3×30 mL). The combined extract was dried over Na_2SO_4, concentrated under vacuum, and purified by column chromatography on silica gel to afford the desired product.

Acknowledgements

This work was supported by a Grant-in-Aid for Scientific Research (S) (20225004), a Grant-in-Aid for Young Scientists (B) (22750094), and a Grant-in-Aid for Scientific Research on Innovative Areas (2015) from the Ministry of Education, Culture, Sports and Technology, Japan. T.I. acknowledges the NOVARTIS Foundation (Japan) for the Promotion of Science, Asahi Kasei Pharma Co., Ltd., and the Frontier Research Center of Osaka University. We also thank the Instrumental Analysis Center of the Faculty of Engineering, Osaka University, for providing assistance with the HRMS analysis.

Keywords: additives · alkylation · C–C coupling · fatty acids · nickel

[1] For reviews, see: a) M. S. F. Lie, K. Jie, M. K. Pasha, M. S. K. Syed-Rahmatullah, *Nat. Prod. Rep.* **1997**, *14*, 163–189; b) J. A. Hamilton, *Prostaglandins Leukotrienes Essent. Fatty Acids* **2002**, *67*, 65–72; c) P. Yaqoob, *Trends Immunol.* **2003**, *24*, 639–645.

[2] For a review, see: S. Durand, J.-L. Parrain, M. Santelli, *J. Chem. Soc. Perkin Trans. 1* **2000**, 253–273.

[3] For examples, see: a) J. A. Soderquist, I. Rosado, Y. Marrero, *Tetrahedron Lett.* **1998**, *39*, 3115–3116; b) S. J. Lee, K. C. Gray, J. S. Paek, M. D. Burke, *J. Am. Chem. Soc.* **2008**, *130*, 466–468; c) K. M. Graf, M. G. Tabor, M. L. Brown, M. Palge, *Org. Lett.* **2009**, *11*, 5382–5385; d) T. K. Macklin, G. C. Micalizio, *Nat. Chem.* **2010**, *2*, 638–643.

[4] For examples, see: a) M. Abarbri, J.-L. Parrain, J.-C. Cintrat, A. Duchêne, *Synthesis* **1996**, 82–86; b) S. G. Romanov, I. V. Ivanov, V. P. Shevchenko, I. Y. Nagaev, A. A. Pushkov, N. F. Myasoedov, G. I. Myagkova, H. Kuhn, *Chem. Phys. Lipids* **2004**, *130*, 117–126; c) C. Kellersmann, H. Steinhart, W. Francke, *Lipids* **2006**, *41*, 777–788.

[5] For representative reviews, see: a) D. J. Cárdenas, *Angew. Chem.* **2003**, *115*, 398–401; *Angew. Chem. Int. Ed.* **2003**, *42*, 384–387; b) M. R. Netherton, G. C. Fu, *Adv. Synth. Catal.* **2004**, *346*, 1525–1532; c) A. C. Frisch, M. Beller, *Angew. Chem.* **2005**, *117*, 680–695; *Angew. Chem. Int. Ed.* **2005**, *44*, 674–688; d) N. Kambe, T. Iwasaki, J. Terao, *Chem. Soc. Rev.* **2011**, *40*, 4937–4947; e) X. L. Hu, *Chem. Sci.* **2011**, *2*, 1867–1886.

[6] The copper-catalyzed coupling reactions of sodium bromocarboxylates with Grignard reagents have been reported, although subsequent reduction and oxidation processes were required to obtain the desired products in higher yields; see: a) J. Klimentová, P. Kosák, K. Vávrová, T. Holas, A. Hrabálek, *Bioorg. Med. Chem.* **2006**, *14*, 7681–7687. For the stoichiometric reactions of alkylcuprates with ω-iodoalkanoic acids, see: b) E. J. Corey, G. H. Posner, *J. Am. Chem. Soc.* **1968**, *90*, 5615–5616.

[7] Five-membered nickelalactones have a β-metalated propionate structure and have been used as carbon nucleophiles in coupling reactions with alkyl iodides to afford aliphatic carboxylic acids; see: a) B. Schönecker, D. Walther, R. Fischer, B. Nestlar, G. Bräunlich, H. Eibisch, P. Droescher, *Tetrahedron Lett.* **1990**, *31*, 1257–1260; b) R. Fischer, D. Walther, G. Bräunlich, B. Undeutsch, W. Ludwig, H. Bandmann, *J. Organomet. Chem.* **1992**, *427*, 395–407; c) R. Fischer, B. Schönecker, D. Walther, *Synthesis* **1993**, 1267–1270; d) A. M. Castaño, A. M. Echavarren, *Organometallics* **1994**, *13*, 2262–2268.

[8] For cross-coupling reactions between sp^3 carbon atoms that contain a protected carboxylic moiety and alkylzinc reagents, see: a) A. Devasagayaraj, T. Stüdemann, P. Knochel, *Angew. Chem.* **1995**, *107*, 2952–2954; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2723–2725; b) R. Giovannini, T. Stüdemann, G. Dussin, P. Knochel, *Angew. Chem.* **1998**, *110*, 2512–2515; *Angew. Chem. Int. Ed.* **1998**, *37*, 2387–2390; c) R. Giovannini, T. Stüdemann, A. Devasagayaraj, G. Dussin, P. Knochel, *J. Org. Chem.* **1999**, *64*, 3544–3553. With alkylboranes, see: d) T. Hatakeyama, T. Hashimoto, K. K. A. D. S. Kathriarachchi, T. Zenmyo, H. Seike, M. Nakamura, *Angew. Chem.* **2012**, *124*, 8964–8967; *Angew. Chem. Int. Ed.* **2012**, *51*, 8834–8837. With alkyl Grignard reagents, see: e) S. P. Singh, J. Terao, N. Kambe, *Tetrahedron Lett.* **2009**, *50*, 5644–5646.

[9] For the reactions of carboxy groups under transition-metal-catalyzed cross-coupling conditions, see: a) R. Kakino, H. Narahashi, I. Shimizu, A. Yamamoto, *Chem. Lett.* **2001**, 1242–1243; b) S. Raju, V. R. Batchu, N. K. Swamy, R. V. Dev, B. R. Sreekanth, J. M. Babu, K. Vyas, P. R. Kumar, K. Mukkanti, P. Annamalai, M. Pal, *Tetrahedron* **2006**, *62*, 9554–9570; c) L. J. Gooßen, K. Gooßen, N. Rodríguez, M. Blanchot, C. Linder, B. Zimmermann, *Pure Appl. Chem.* **2008**, *80*, 1725–1733.

[10] Transition-metal catalysts also mediate the decarboxylative cross-coupling of benzoic acids; see: O. Baudoin, *Angew. Chem.* **2007**, *119*, 1395–1397; *Angew. Chem. Int. Ed.* **2007**, *46*, 1373–1375.

[11] For synthetic applications of the cross-coupling of compounds that contain protected carboxy groups, see: a) S. M. Kühnert, M. E. Maier, *Org. Lett.* **2002**, *4*, 643–646; b) Y. Zhang, T. Rovis, *J. Am. Chem. Soc.* **2004**, *126*, 15964–15965; c) B. M. Baron, R. J. Cregge, R. A. Farr, D. Friedrich, R. S. Gross, B. L. Harrison, D. A. Janowick, D. Matthews, T. C. McCloskey, S. Meikrantz, P. L. Nyce, R. Vaz, W. A. Metz, *J. Med. Chem.* **2005**, *48*, 995–1018; d) C. Sánchez-Sixto, V. F. V. Prazeres, L. Castedo, H. Lamb, A. R. Hawkins, C. González-Bello, *J. Med. Chem.* **2005**, *48*, 4871–4881; e) A.-L. Gérard, V. Lisowski, S. Rault, *Tetrahedron* **2005**, *61*, 6082–6087; f) A. B. Smith III, A. H. Davulcu, L. Kürti, *Org. Lett.* **2006**, *8*, 1665–1668; g) X. Dai, N. A. Strotman, G. C. Fu, *J. Am. Chem. Soc.* **2008**, *130*, 3302–3303; h) C. Studte, B. Breit, *Angew. Chem.* **2008**, *120*, 5531–5535; *Angew. Chem. Int. Ed.* **2008**, *47*, 5451–5455; i) O. Delgado, H. M. Müller, T. Bach, *Chem. Eur. J.* **2008**, *14*, 2322–2339. For Pd-catalyzed cross-coupling reactions that are affected by the presence of carboxylic acids, see: j) A. S. K. Hashmi, R. Döpp, C. Lothschütz, M. Rudolph, D. Riedel, F. Rominger, *Adv. Synth. Catal.* **2010**, *352*, 1307–1314.

[12] a) J. Terao, N. Kambe, *Bull. Chem. Soc. Jpn.* **2006**, *79*, 663–672; b) J. Terao, H. Todo, H. Watabe, A. Ikumi, Y. Shinohara, N. Kambe, *Pure Appl. Chem.* **2008**, *80*, 941–951; c) J. Terao, N. Kambe, *Acc. Chem. Res.* **2008**, *41*, 1545–1554; d) J. Terao, H. Watanabe, A. Ikumi, H. Kuniyasu, N. Kambe, *J. Am. Chem. Soc.* **2002**, *124*, 4222–4223; e) J. Terao, A. Ikumi, H. Kuniyasu, N. Kambe, *J. Am. Chem. Soc.* **2003**, *125*, 5646–5647; f) J. Terao, H. Todo, H. Watanabe, A. Ikumi, N. Kambe, *Angew. Chem.* **2004**, *116*, 6306–6308; *Angew. Chem. Int. Ed.* **2004**, *43*, 6180–6182; g) S. P. Singh, T. Iwasaki, J. Terao, N. Kambe, *Tetrahedron Lett.* **2011**, *52*, 774–776; h) T. Iwasaki, A. Tsumura, T. Omori, H. Kuniyasu, J. Terao, N. Kambe, *Chem. Lett.* **2011**, *40*, 1024–1024.

[13] a) J. Terao, Y. Naitoh, H. Kuniyasu, N. Kambe, *Chem. Commun.* **2007**, 825–827; b) Y. Naitoh, F. Bando, J. Terao, K. Otsuki, H. Kuniyasu, N. Kambe, *Chem. Lett.* **2007**, *36*, 236–237; c) J. Terao, H. Todo, S. A. Begum, H. Kuniyasu, N. Kambe, *Angew. Chem.* **2007**, *119*, 2132–2135; *Angew. Chem. Int. Ed.* **2007**, *46*, 2086–2089; d) R. Shen, T. Iwasaki, J. Terao, N. Kambe, *Chem. Commun.* **2012**, *48*, 9313–9315.

[14] a) G. Cahiez, C. Chaboche, M. Jézéquel, *Tetrahedron* **2000**, *56*, 2733–2737; b) F. Kopp, S. Wunderlich, P. Knochel, *Chem. Commun.* **2007**, 2075–2077.

[15] a) E. López-García, M. B. Schulze, J. B. Meigs, J. E. Manson, N. Rifai, M. J. Stampfer, W. C. Willett, F. B. Hu, *J. Nutr.* **2005**, 562–566; b) C. Tyburczy, C. Major, A. L. Lock, F. Destaillats, P. Lawrence, J. T. Brenna, A. M. Salter, W. E. Bauman, *J. Nutr.* **2009**, 257–263.

[16] J. M. Aizpurua, F. P. Cossio, C. Palomo, *J. Org. Chem.* **1986**, *51*, 4941–4943.

Received: November 27, 2012
Published online: February 1, 2013

