Coupling Reactions

DOI: 10.1002/anie.201003009

Synthesis of Aryl Ketones by Palladium(II)-Catalyzed Decarboxylative Addition of Benzoic Acids to Nitriles

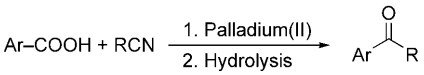
*Jonas Lindh, Per J. R. Sjöberg, and Mats Larhed**

Ketones are a common functionality in many types of organic compounds for example, pharmaceuticals and natural products. In 2004, Larock reported novel reactions of arenes or arylboronic acids with nitriles to generate aryl ketones by hydrolysis of the intermediate ketimine.[1] This pioneering work on carbon–transition-metal bond insertions into polar carbon–nitrogen triple bonds has since been followed by a number of related reports.[2] As useful as the reported transformations are, there are possible drawbacks: all of these reported methods use arenes or arylboronic acids to generate the aryl palladium species and often require relatively harsh reaction conditions.[1] Arenes are generally cheap and widely available, but suffer from poor regiocontrol.[1] Arylboronic acids, on the other hand, offer regiocontrol, but are comparably expensive, are not as widely available, and may be unstable.[3]

Carboxylic acids are cheap, non-toxic, widely commercially available, stable, and are easily prepared.[4] Although metal-mediated decarboxylations have long been known[5] and sporadically reported in the literature,[6] they did not emerge as synthetically useful processes until recently. In the last couple of years, discoveries have shown that it is possible to use certain benzoic acids as direct aryl palladium precursors, thus resulting in the release of gaseous carbon dioxide and the desired aryl palladium complex.[4,7,8] As decarboxylation is an environmentally friendly and efficient way of generating aryl palladium intermediates, this finding is of great importance in the endeavor towards more sustainable chemistry. Using a palladium(II) catalyst, the scope of accessible benzoic acids might be somewhat limited, as they appear to require certain activating *ortho* substituents.[4,7,9] However, work by Goossen et al. has enabled copper- and silver-catalyzed protodecarboxylations of a wide range of benzoic acids by using phenanthroline ligands.[10]

The recent advancements in palladium(II)-catalyzed decarboxylations have been successfully employed in a number of Suzuki- and Heck-type reactions in the last couple of years, foremost by the groups of Goossen[4,11] and Myers.[12,13] Furthermore, a number of reactions employing bimetallic catalysts have been developed, which can efficiently promote the decarboxylation of a broad range of non-activated aryl carboxylates.[14]

Intrigued by the possibility of further broadening the scope of these useful aryl palladium precursors, we decided to investigate the possibility of preparing aryl ketones from benzoic acids and nitriles using palladium(II) catalysis (Scheme 1).



Scheme 1. General reaction scheme.

As the use of the carboxylic acid functional group is very common in organic synthesis, there are reported methods for transforming benzoic acids into aryl ketones.[15] Traditionally, these multistep methods require harsh reaction conditions, are tedious to perform, and generally involve stoichiometric amounts of metal reagents, such as lithium reagents.[16]

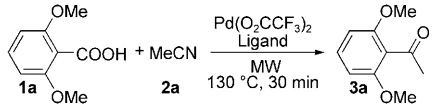
In the last decade, a number of attractive new cross-coupling methods for preparing aryl ketones from carboxylic acid derivatives and boronic acids have been published. These mild procedures require pre-formation of thioesters[17] or in situ activation of the carboxylic acid by stoichiometric additives to form anhydrides[18] and employ relatively expensive boronic acids as coupling partners. Recently, a new method to synthesize aryl ketones from α-oxocarboxylic acid salts and aryl bromides was reported,[19] in which α-oxocarboxylic acid salts are decarboxylated by a copper catalyst to generate acyl copper species and then arylated with aryl bromide using a palladium catalyst. A potential limitation of these methods is the difficulty of using alkylboronic acids or alkyl halides in cross-couplings, which essentially limits the scope to only aryl coupling partners. By utilizing nitriles instead, the reaction scope is extended to afford high yielding and low-cost reactions with both aryl and alkyl coupling partners. Herein, we report our initial results towards developing a facile new catalytic intermolecular one-pot reaction to afford aryl ketones from benzoic acids and nitriles.

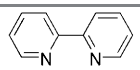
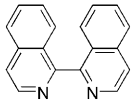
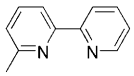
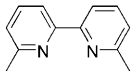
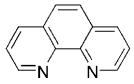
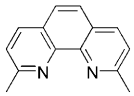
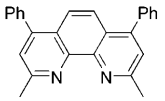
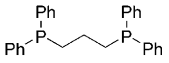
Based on earlier work within our group[20] involving palladium(II)-catalyzed oxidative Heck[21] reactions, a monometallic test reaction was performed using $Pd(O_2CCF_3)_2$ and the dmphen (2,9-dimethyl-1,10-phenanthroline; Table 1, **4f**) ligand as the catalytic system, 2,6-dimethoxybenzoic acid (Table 1, **1a**) as the substrate, and acetonitrile as the reactant/solvent.[22] After 30 minutes of microwave (MW) heating,[23] the results were promising, as the aryl methyl ketone (Table 1,

[*] J. Lindh, Prof. M. Larhed
Organic Pharmaceutical Chemistry
Department of Medicinal Chemistry, Uppsala University
BMC, Box-574, 75123 Uppsala (Sweden)
Fax: (+46) 18-471-4474
E-mail: Mats@orgfarm.uu.se
Dr. P. J. R. Sjöberg
Department of Physical and Analytical Chemistry
Uppsala University (Sweden)

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201003009.

Table 1: Ligand screen.



	Ligand	Yield [%][a]
4a		16
4b		32
4c		73 80[b] 50[c] 71[d] 63[e]
4d		36
4e		18
4f		68
4g		67
4h		0
4i		19[f]
–	–	19

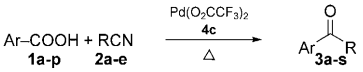
[a] Yield of isolated product, >95% pure by GC/MS. Reaction conditions: A 5 mL Pyrex glass vial was charged with 2,6-dimethoxybenzoic acid (0.5 mmol), $Pd(O_2CCF_3)_2$ (0.02 mmol), ligand (0.024 mmol), H_2O (200 μL), and MeCN (2 mL). The vial was capped in air and exposed to microwave heating for 30 min at 130 °C. [b] $Pd(O_2CCF_3)_2$ (0.04 mmol), 6-methyl-2,2′-bipyridine (0.048 mmol) and exposed to MW heating for 60 min at 130 °C. [c] Heated in a heating block at 100 °C for 48 h. [d] Same as [c] but with $Pd(O_2CCF_3)_2$ (0.04 mmol), 6-methyl-2,2′-bipyridine (0.048 mmol). [e] $Pd(OAc)_2$ (0.04 mmol) used instead of $Pd(O_2CCF_3)_2$. [f] 100 μL dimethyl sulfoxide was added. MW = microwave.

3a) was isolated in 50% yield by in situ hydrolysis of the intermediate ketimine. A few different palladium(II) salts were tested, of which $Pd(O_2CCF_3)_2$ was the most successful.[24] A ligand screen was performed that employed seven different bidentate nitrogen ligands (Table 1, **4a**–**g**), a bidentate phosphine ligand (Table 1, **4h**), dimethyl sulfoxide (**4i**), and a ligand-free reaction. Phosphine ligand **4h** was unsuitable for the transformation and did not provide any of the desired product. Dimethyl sulfoxide, which had been successfully employed by Zhou and Larock in reactions of arenes or arylboronic acids with nitriles to generate aryl ketones,[1] was not an efficient ligand for this transformation, providing only 19% of isolated **3a**. Interestingly, ligandless conditions provided the same low yield as with dimethyl sulfoxide. Among the bidentate nitrogen ligands, 6-methyl-2,2′-bipyridine (**4c**), dmphen (**4f**), and 2,9-dimethyl-4,7-diphenyl-1,10-phenanthroline (**4g**) were superior. In no case was the intermediate imine detected by GC-MS or LC-MS. Based on the yield of isolated product, 6-methyl-2,2′-bipyridine (**4c**) was selected as the optimal ligand for further investigation of the reaction scope. Prolonging the exposure to microwave irradiation from 30 to 60 minutes and increasing the catalyst loading from 4 to 8 mol% improved the yield from 73 to 80%. Increasing the temperature above 130 °C led to formation of palladium black and poor yields. Lowering the reaction temperature led to prolonged reaction times to reach full conversion and very slow product formation was observed at 80 °C. The reactions could be safely carried out in a heating block at 100 °C, whereas higher temperatures required the use of a microwave reactor owing to the build-up of pressure in the sealed vessels. Unfortunately, the results from employing a bimetallic catalyst system (Cu/Pd or Ag/Pd) were disappointing, resulting in very limited product formation.[10,14,25] The addition of 1.2 equivalents of *para*-benzoquinone, as a reoxidant of palladium, had no beneficial effect on the yield, thereby indicating that the formation of palladium(0) is not an issue under these reaction conditions.[26] Addition of 1 equivalent of acid (TFA or HOAc) hindered the reaction and led to formation of palladium black as did the addition of 1 equivalent of base (Et_3N or K_2CO_3).

To optimize the desired formation of the aryl ketones **3**, several different reaction conditions were examined for each nitrile (**2**) and benzoic acid (**1**; Table 2). To investigate the scope of the reaction with respect to the nitrile, four additional nitriles (**2b-e**) were tested. Nitriles **2b** and **2c** worked well, providing **3b** and **3c** respectively (Table 2, entries 2 and 3). Benzonitrile (**2d**) proved to be a poor solvent or reactant for **1a,** and provided only 20% of isolated product **3d** (Table 2, entry 4). Benzyl cyanide (**2e**) gave a satisfying yield of the product **3e** (Table 2, entry 5).

To further investigate the scope of the reaction, a number of different *ortho*-substituted benzoic acids were reacted with acetonitrile to generate the corresponding aryl methyl ketones (Table 2, entries 6–19). Interestingly, acetonitrile, whilst being the simplest and cheapest nitrile, has been scarcely employed in the related couplings of arenes and boronic acids to nitriles.[1] Trisubstituted **1b** worked well, providing a useful 71% of product **3f** (Table 2, entry 6). Ethoxy-substituted **1c** also gave a good yield of product **3g** (74%), as did the corresponding methoxy-substituted **1d**, which afforded 70% of **3h** (Table 2, entries 7 and 8). Bromo-substituted **3i** was isolated in 61%, without any trace of dehalogenation as a result of palladium(0) activation (Table 2, entry 9). Product **3j** was isolated in an excellent yield of 91% (Table 2, entry 10). In an attempt to scale-up the reaction, from 0.5 mmol to 10.0 mmol scale, the yield dropped to 67% (Table 2, entry 10). Benzoic acid **1g** provided a disappointing 26% of product **3k** (Table 2, entry 11). Interestingly, *ortho*-fluoro-substituted **1h** was a useful substrate and provided the isolated product **3l** in 63% yield (Table 2, entry 12).[27] Importantly, **1i** provided a good amount of **3m** (85%) when hydrolyzed with formic acid, but a low yield of only 11% in the absence of an additional hydrolysis step (Table 2, entry 13). Sterically hindered ketimines are known

Table 2: Palladium(II)-catalyzed reactions of benzoic acids and nitriles.



Entry	Ar–COOH	R	Product	Yield [%][a]	Entry	Ar–COOH	R	Product	Yield [%][a]
1	**1a**	Me (**2a**)	**3a**	94[b] 78[c] 90[d] 88[e] 86[f]	11	**1g**	Me (**2a**)	**3k**	26[g] 20[f]
2	**1a**	Et (**2b**)	**3b**	80[g] 77[f]	12	**1h**	Me (**2a**)	**3l**	63[f]
3	**1a**	Pr (**2c**)	**3c**	66[g] 73[f]	13	**1i**	Me (**2a**)	**3m**	11[b] 85[f]
4	**1a**	Ph (**2d**)	**3d**	20[g]	14	**1j**	Me (**2a**)	**3n**	25[g] 27[f]
5	**1a**	CH_2Ph (**2e**)	**3e**	50[g] 73[f]	15	**1k**	Me (**2a**)	**3o**	67[b] 61[g] 90[f]
6	**1b**	Me (**2a**)	**3f**	57[b] 61[g] 62[c] 71[f]	16	**1l**	Me (**2a**)	**3p**	57[b] 57[g] 84[f]
7	**1c**	Me (**2a**)	**3g**	50[b] 66[g] 74[f]	17	**1m**	Me (**2a**)	**3q**	62[f]
8	**1d**	Me (**2a**)	**3h**	60[b] 59[g] 70[f]	18	**1n**	Me (**2a**)	**3r**	51[f]
9	**1e**	Me (**2a**)	**3i**	58[b] 54[g] 61[c] 45[f]	19	**1o**	Me (**2a**)	**3s**	53[f]
10	**1f**	Me (**2a**)	**3j**	63[b] 76[g] 91[f] 67[h]					

[a] Yield of isolated product, >95% pure by GC/MS. [b] A 5 mL Pyrex glass vial was charged with ArCOOH (0.5 mmol), $Pd(O_2CCF_3)_2$ (0.10 mmol), 6-methyl-2,2′-bipyridine (0.12 mmol), H_2O (200 μL), and nitrile (2 mL). The vial was capped in air and heated in a heating block at 100°C for 48 h. [c] Same as [b] but exposed to microwave heating for 60 min at 130°C. [d] Same as [c] with the subsequent addition of 1 mL 2 M HCl and heating at 100°C for 16 h. [e] Same as [c] but with subsequent addition of 1 mL formic acid and heating at 100°C for 1 h. [f] Same as [e] but with $Pd(O_2CCF_3)_2$ (0.04 mmol), 6-methyl-2,2′-bipyridine (0.048 mmol). [g] Same as [c] but with $Pd(O_2CCF_3)_2$ (0.04 mmol), 6-methyl-2,2′-bipyridine (0.048 mmol). [h] A 20 mL Pyrex glass vial was charged with ArCOOH (10.0 mmol), $Pd(O_2CCF_3)_2$ (0.8 mmol), 6-methyl-2,2′-bipyridine (0.96 mmol), H_2O (2.0 mL), and MeCN (10.0 mL). The vial was capped in air and exposed to microwave heating for 60 min at 130°C, with subsequent addition of 5 mL formic acid and heating at 100°C for 60 min.

to be stable and can be difficult to hydrolyze into their corresponding ketones,[1,28] and, as shown in Table 2, additional hydrolysis through the addition of 1 mL of formic acid and heating at 100°C for 1 hour often improved the yields of the isolated aryl methyl ketones. Naphthyl derivative **1j** worked poorly and gave only 27% of product **3n** (Table 2, entry 14). Five different heteroaromatic benzoic acids **1k–o** were tested, and provided their corresponding aryl methyl ketones **3o–s** in 51–90% yield (Table 2, entries 15–19). The fact that only *ortho*-functionalized aromatic acids reacted

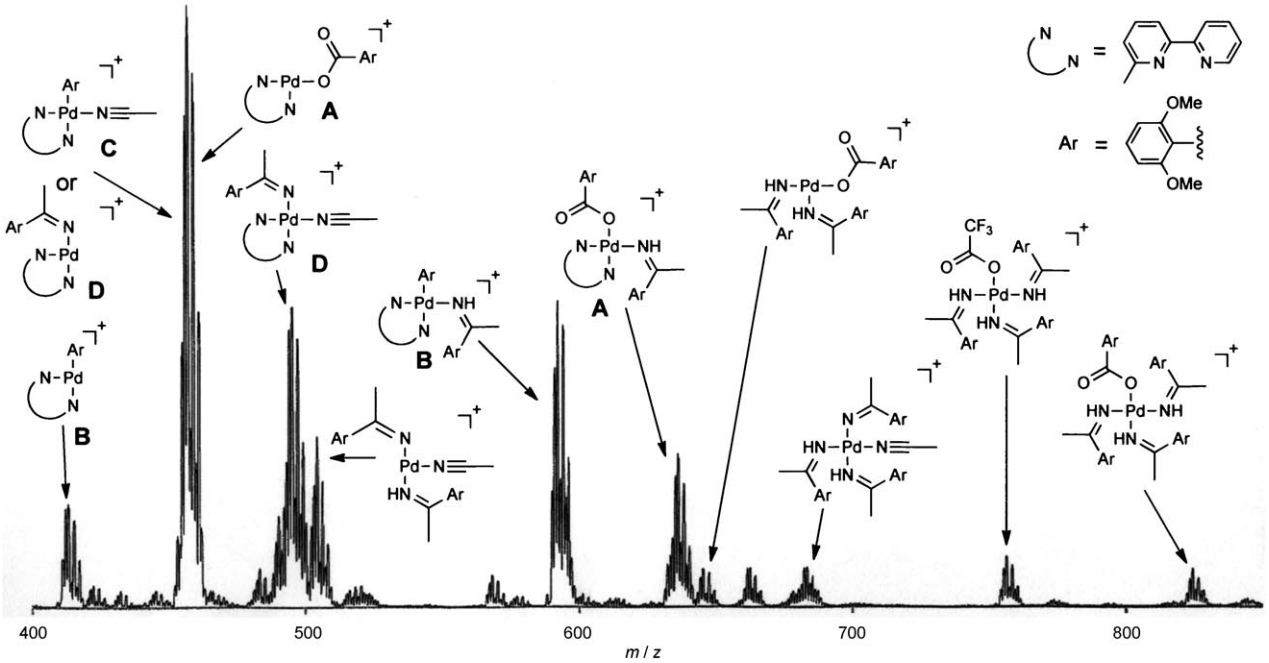


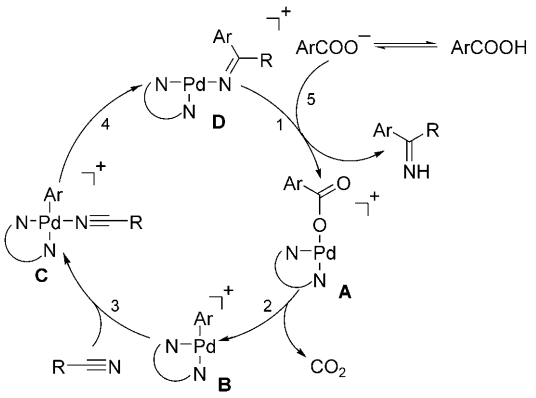
Figure 1. ESI/MS-(+) spectrum for the reaction of **1a** and MeCN with assigned Pd^{II} intermediates.

successfully is in accordance with previous examples of monometallic palladium(II)-catalyzed decarboxylative processes.[4,7]

To examine the reaction mechanism, an electrospray ionization mass spectrometry (ESI/MS)[29] study was performed. ESI/MS is considered a soft MS ionization technique as it promotes few fragmentation products and is therefore a valuable tool in the analysis of catalytic intermediates and organometallic complexes.[30]

In this study, ESI/MS analysis was conducted to detect cationic palladium-containing reaction intermediates in ongoing reactions. The reaction shown in Table 2, entry 1 (100 °C, 48 h) was chosen for our mechanistic investigation. An aliquot was withdrawn from the reaction mixture after 6 hours and then diluted 10-fold with acetonitrile. The ESI/MS-(+) spectrum was immediately recorded by scanning the first quadrupole (Q1) of a triple-quadrupole instrument. Several groups of peaks with m/z signals corresponding to the characteristic isotopic pattern of monopalladium complexes were observed, whilst only a limited number of non-palladium-containing cations were detected (Figure 1). Based on the m/z signals in the MS mode, and MS/MS of the selected signals, structures for the intermediates were proposed.[31] The detected classes of intermediates were assigned letters (**A**–**D**) based on their plausible role in the reaction. The corresponding ESI/MS-(−) study was also performed, but no anionic palladium complexes were observed.

A plausible reaction mechanism, exemplified by incorporating one complex from each category **A**–**D** (Scheme 2), and in agreement with the mechanistic proposals for other related reactions,[1,9,12] involves the following key steps: 1) coordination of the carboxylic acid to the palladium(II) center to generate complex **A**; 2) decarboxylation of the benzoic acid to give the aryl–palladium complex **B**; 3) coordination of the



Scheme 2. Proposed mechanistic hypothesis supported by MS-detected cationic palladium complexes.

nitrile group to form complex **C**, which is probably a fast process given the large excess of nitrile; 4) 1,2-carbopalladation of the nitrile to form ketimine complex **D**; 5) protonation of the ketimine by the benzoic acid to afford the free ketimine and a palladium(II) species.

In conclusion, we have reported a new palladium(II)-catalyzed method that allows for the rapid synthesis of aryl ketone derivatives from *ortho*-functionalized benzoic acids and low-cost nitriles. This efficient and environmentally benign reaction produces gaseous CO_2 and ammonium hydroxide as the sole by-products. ESI/MS and MS/MS analysis detected all key intermediates and suggest that the reaction pathway involves decarboxylation of benzoic acid, to generate the aryl palladium species, followed by addition to the nitrile. This procedure is one of the simplest and most convenient methods described for the small-scale synthesis of

aryl ketones from *ortho*-substituted benzoic acids. Ongoing efforts in our laboratory are devoted to expanding the scope of the reaction and to further investigate the reaction mechanism by comprehensive DFT calculations.

Received: May 18, 2010
Revised: July 14, 2010
Published online: September 13, 2010

Keywords: carboxylic acids · decarboxylation · microwave chemistry · nitriles · palladium

[1] a) C. X. Zhou, R. C. Larock, *J. Am. Chem. Soc.* **2004**, *126*, 2302 – 2303; b) C. X. Zhou, R. C. Larock, *J. Org. Chem.* **2006**, *71*, 3551 – 3558.
[2] a) R. M. Ceder, G. Muller, M. Ordinas, J. I. Ordinas, *Dalton Trans.* **2007**, 83 – 90; b) B. W. Zhao, X. Y. Lu, *Org. Lett.* **2006**, *8*, 5987 – 5990; c) B. W. Zhao, X. Y. Lu, *Tetrahedron Lett.* **2006**, *47*, 6765 – 6768; d) K. Ueura, S. Miyamura, T. Satoh, M. Miura, *J. Organomet. Chem.* **2006**, *691*, 2821 – 2826.
[3] S. Darses, J. P. Genet, *Chem. Rev.* **2008**, *108*, 288 – 325.
[4] L. J. Goossen, N. Rodriguez, K. Goossen, *Angew. Chem.* **2008**, *120*, 3144 – 3164; *Angew. Chem. Int. Ed.* **2008**, *47*, 3100 – 3120.
[5] A. F. Shepard, N. R. Winslow, J. R. Johnson, *J. Am. Chem. Soc.* **1930**, *52*, 2083 – 2090.
[6] a) M. Nilsson, *Acta Chem. Scand.* **1966**, *20*, 423 – 426; b) T. Cohen, R. A. Schambach, *J. Am. Chem. Soc.* **1970**, *92*, 3189 – 3190; c) A. Cairncross, J. R. Roland, R. M. Henderson, W. A. Sheppard, *J. Am. Chem. Soc.* **1970**, *92*, 3187 – 3189.
[7] J. S. Dickstein, C. A. Mulrooney, E. M. O'Brien, B. J. Morgan, M. C. Kozlowski, *Org. Lett.* **2007**, *9*, 2441 – 2444.
[8] P. Hu, J. Kan, W. P. Su, M. C. Hong, *Org. Lett.* **2009**, *11*, 2341 – 2344.
[9] S. L. Zhang, Y. Fu, R. Shang, Q. X. Guo, L. Liu, *J. Am. Chem. Soc.* **2010**, *132*, 638 – 646.
[10] a) L. J. Goossen, R. T. Werner, N. Rodriguez, C. Linder, B. Melzer, *Adv. Synth. Catal.* **2007**, *349*, 2241 – 2246; b) L. J. Goossen, C. Linder, N. Rodriguez, P. P. Lange, A. Fromm, *Chem. Commun.* **2009**, 7173 – 7175.
[11] L. J. Goossen, G. J. Deng, L. M. Levy, *Science* **2006**, *313*, 662 – 664.
[12] D. Tanaka, S. P. Romeril, A. G. Myers, *J. Am. Chem. Soc.* **2005**, *127*, 10323 – 10333.
[13] a) D. Tanaka, A. G. Myers, *Org. Lett.* **2004**, *6*, 433 – 436; b) A. G. Myers, D. Tanaka, M. R. Mannion, *J. Am. Chem. Soc.* **2002**, *124*, 11250 – 11251.
[14] a) L. J. Goossen, B. Zimmermann, T. Knauber, *Angew. Chem.* **2008**, *120*, 7211 – 7214; *Angew. Chem. Int. Ed.* **2008**, *47*, 7103 – 7106; b) L. J. Goossen, N. Rodriguez, P. P. Lange, C. Linder, *Angew. Chem.* **2010**, *122*, 1129 – 1132; *Angew. Chem. Int. Ed.* **2010**, *49*, 1111 – 1114; c) L. J. Goossen, N. Rodriguez, B. Melzer, C. Linder, G. J. Deng, L. M. Levy, *J. Am. Chem. Soc.* **2007**, *129*, 4824 – 4833.
[15] R. Adams, L. O. Binder, *J. Am. Chem. Soc.* **1941**, *63*, 2773 – 2776.
[16] C. K. Bradsher, S. T. Webster, *J. Am. Chem. Soc.* **1957**, *79*, 393 – 395.
[17] L. S. Liebeskind, J. Srogl, *J. Am. Chem. Soc.* **2000**, *122*, 11260 – 11261.
[18] a) L. J. Goossen, K. Ghosh, *Angew. Chem.* **2001**, *113*, 3566 – 3568; *Angew. Chem. Int. Ed.* **2001**, *40*, 3458 – 3460; b) L. J. Goossen, K. Ghosh, *Eur. J. Org. Chem.* **2002**, 3254 – 3267; c) R. Kakino, H. Narahashi, I. Shimizu, A. Yamamoto, *Chem. Lett.* **2001**, *30*, 1242 – 1243; d) L. J. Goossen, L. Winkel, A. Dohring, K. Ghosh, J. Paetzold, *Synlett* **2002**, 1237 – 1240.
[19] L. J. Goossen, F. Rudolphi, C. Oppel, N. Rodriguez, *Angew. Chem.* **2008**, *120*, 3085 – 3088; *Angew. Chem. Int. Ed.* **2008**, *47*, 3043 – 3045.
[20] a) J. Lindh, P. A. Enquist, Å. Pilotti, P. Nilsson, M. Larhed, *J. Org. Chem.* **2007**, *72*, 7957 – 7962; b) P. A. Enquist, J. Lindh, P. Nilsson, M. Larhed, *Green Chem.* **2006**, *8*, 338 – 343; c) M. M. S. Andappan, P. Nilsson, M. Larhed, *Chem. Commun.* **2004**, 218 – 219.
[21] a) K. M. Gligorich, M. S. Sigman, *Chem. Commun.* **2009**, 3854 – 3867; b) J. W. Ruan, X. M. Li, O. Saidi, J. L. Xiao, *J. Am. Chem. Soc.* **2008**, *130*, 2424 – 2425; c) J. H. Delcamp, A. P. Brucks, M. C. White, *J. Am. Chem. Soc.* **2008**, *130*, 11270 – 11271; d) J. A. Schiffer, A. B. Machotta, M. Oestreich, *Synlett* **2008**, 2271 – 2274.
[22] The choice of a monometallic palladium(II)-catalyzed system might limit the scope of usable benzoic acids to activated *ortho*-substituted benzoic acids.
[23] P. Nilsson, K. Olofsson, M. Larhed, *Top. Curr. Chem.* **2006**, *266*, 103 – 144.
[24] Recently, a catalytic asymmetric decarboxylative Mannich-type reaction was reported in which the nucleophile was generated via CuI-catalyzed decarboxylation of cyanocarboxylic acids. The reaction occured without detection of any homocoupled product as a result of carbopalladation of the cyanide substituent, thus indicating that copper might be a poor catalyst for our carboxylic-acid-into-ketone transformation. See: L. Yin, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2009**, *131*, 9610 – 9611.
[25] The bimetallic reactions were evaluated in a 5 mL Pyrex glass vial charged with 2-methoxybenzoic acid (0.5 mmol), Pd-$(O_2CCF_3)_2$ (0.04 mmol), Cu_2O (0.04 mmol) or AgOAc (0.04 mmol), 6-methyl-2,2′-bipyridine (0.088 mmol), H_2O (200 μL), and MeCN (2 mL). The vial was thereafter capped under air and exposed to MW heating for 30 min at 130 °C.
[26] a) J. E. Bäckvall, A. Gogoll, *J. Chem. Soc. Chem. Commun.* **1987**, 1236 – 1238; b) J. Piera, J. E. Bäckvall, *Angew. Chem.* **2008**, *120*, 3558 – 3576; *Angew. Chem. Int. Ed.* **2008**, *47*, 3506 – 3523.
[27] Z. M. Sun, P. J. Zhao, *Angew. Chem.* **2009**, *121*, 6854 – 6858; *Angew. Chem. Int. Ed.* **2009**, *48*, 6726 – 6730.
[28] J. B. Culbertson, *J. Am. Chem. Soc.* **1951**, *73*, 4818 – 4823.
[29] C. M. Whitehouse, R. N. Dreyer, M. Yamashita, J. B. Fenn, *Anal. Chem.* **1985**, *57*, 675 – 679.
[30] a) L. S. Santos, *Eur. J. Org. Chem.* **2008**, 235 – 253; b) P. A. Enquist, P. Nilsson, P. J. R. Sjöberg, M. Larhed, *J. Org. Chem.* **2006**, *71*, 8779 – 8786; c) M. Andaloussi, J. Lindh, J. Sävmarker, P. J. R. Sjöberg, M. Larhed, *Chem. Eur. J.* **2009**, *15*, 13069 – 13074; d) J. Lindh, J. Sävmarker, P. Nilsson, P. J. R. Sjöberg, M. Larhed, *Chem. Eur. J.* **2009**, *15*, 4630 – 4636; e) A. O. Aliprantis, J. W. Canary, *J. Am. Chem. Soc.* **1994**, *116*, 6985 – 6986; f) J. M. Brown, K. K. Hii, *Angew. Chem.* **1996**, *108*, 679 – 682; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 657 – 659; g) A. A. Sabino, A. H. L. Machado, C. R. D. Correia, M. N. Eberlin, *Angew. Chem.* **2004**, *116*, 2568 – 2572; *Angew. Chem. Int. Ed.* **2004**, *43*, 2514 – 2518.
[31] The exact structure of the complexes, that is, the *cis*/*trans* configuration, has not yet been determined.

