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Palladium-Catalyzed Carbonylative Heck Reaction of Aryl Bromides with Vinyl Ethers to 3-Alkoxy Alkenones and Pyrazoles

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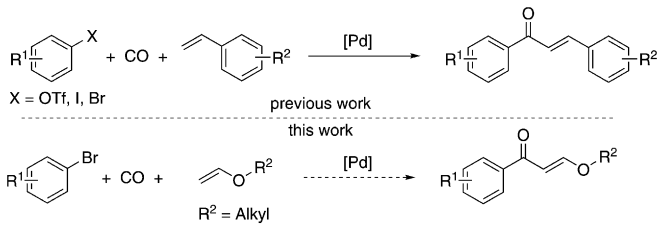
Since their discovery in the 1970s and 80s, palladium-catalyzed coupling reactions of aryl halides have become the most popular tool for the straightforward functionalization of arenes and heteroarenes.[1] Apart from numerous academic developments, palladium catalysts also proved to be successful for the production of intermediates for pharmaceuticals, agrochemicals, and fine chemicals on an industrial scale.[2]

Beside the common two-component C–C bond forming processes, such as Heck and Suzuki reactions, three-component carbonylative palladium-catalyzed coupling reactions became increasingly popular in the last decade.[3] By applying such carbonylations, the synthesis of (hetero)aromatic ketones and alkynones, apart from the well-known esters, amides, and acids, is possible from available (hetero)aryl halides.[4,5,6] In this respect, our group has developed novel carbonylative Heck-type coupling reactions in 2010. More specifically, aryl triflates or aryl halides were reacted with styrenes in the presence of carbon monoxide to give substituted chalcones in high yields (Scheme 1).[7] Based on this work, very recently Skrydstrup and co-workers also described carbonylative Heck reactions with in situ generated CO.[8]



Scheme 1. Palladium-catalyzed carbonylative vinylations.

In our previous work, aromatic olefins reacted well with different types of aryl halides. However, the carbonylative coupling of aryl bromides with vinyl ethers failed under these conditions and, to the best of our knowledge, no such example has been described until to date.

Obviously, the resulting 1-aryl-3-alkoxy propenones represent valuable monoprotected 1,3-dicarbonyl equivalents, which are known to serve as attractive building blocks for a variety of heterocycles.[9] On the other hand, only few synthetic routes for the synthesis of this class of compounds have been published.[10] So far, the most convenient procedure makes use of the palladium-catalyzed aroylation of vinyl ethers with benzoyl chlorides.[10] Owing to the improved stability and commercial availability of aryl bromides compared to benzoyl chlorides, the development of a general procedure for the direct coupling of inexpensive aryl bromides with vinyl ethers still represents a challenging and important goal in coupling chemistry.

Based on our previous work in the field of palladium-catalyzed carbonylations,[11] we initially investigated the reaction of bromobenzene with carbon monoxide and an excess amount of *n*-butyl vinyl ether (Table 1). Applying [{(cinnamyl)PdCl}$_2$]/**L9** as the catalyst system, which was previously optimized for the carbonylative coupling with styrenes, gave only 24% of the desired 3-butoxy-1-phenyl-2(*E*)-propen-1-one (**1**, Table 1, entry 8). Even lower activity was observed in the presence of very simple monodentate ligands, such as triphenylphosphine, tricyclohexylphosphine, tri-*tert*-butylphosphine, or cataCXium A (Table 1, entries 1–4). Next, some pyrrole- and imidazole-based ligands with different electronic and steric properties were tested, but only **L8** gave a moderate yield of the desired product (Table 1, entries 5–7 and 9–11). For comparison, SPhos and Xanthphos were also examined and resulted only in low yields (Table 1, entries 12–13). Notably, the formation of significant amounts of benzoic anhydride, *N*,*N*-diethylbenzamide, and small amounts of benzaldehyde were responsible for the high differences between conversion and yield.

To improve the model system, several different solvents were tested (Table 2, entries 1–4). It is worth noting that changing the solvent from DMF to acetonitrile or 1,4-dioxane increased the yield to 46 and 44%, respectively. At lower temperature (100°C), conversion and yield dropped because the C–Br bond was not activated efficiently (Table 2, entry 5). An increased temperature (130°C) did not show a significant influence on the yield, since full conversion was already achieved at 120°C (Table 2, entries 6 and 9). While the application of different bases in the model reaction did not lead to any progress, modifications of the

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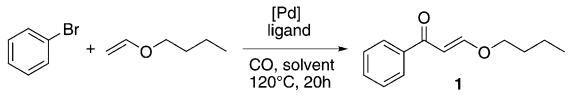
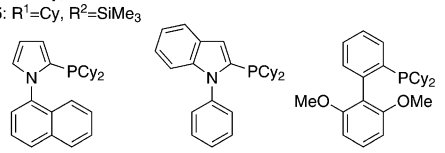
Table 1. Palladium-catalyzed coupling of bromobenzene with butyl vinyl ether: Variation of ligands.[a]



L1: R^1=*t*Bu, R^2=H
L2: R^1=Cy, R^2=H
L3: R^1=Ad, R^2=H
L4: R^1=Cy, R^2=OMe
L5: R^1=Cy, R^2=$SiMe_3$

L6: R^1=*t*Bu, R^2=R^3=*i*Pr
L7: R^1=Ad, R^2=R^3=*i*Pr
L8: R^1=Ad, R^2=H, R^3=OMe



L9 **L10** **L11**

Entry	Ligand	Conv. [%][b]	Yield **1** [%][b]
1	PPh_3	72	13
2	nBuP(Ad)$_2$	100	14
3	P(tBu)$_3$·HBF_4	95	15
4	PCy_3	42	6[c]
5	**L1**	75	9
6	**L2**	27	11
7	**L3**	67	1
8	**L9**	100	24
9	**L6**	46	7
10	**L7**	91	17
11	**L8**	99	24
12	**L11**	40	10[c]
13	Xantphos	100	6

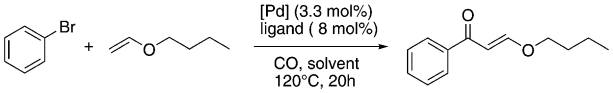
[a] General reaction conditions: bromobenzene (1 mmol), *n*-butyl vinyl ether (6 mmol), [{(cinnamyl)PdCl}$_2$] (0.017 mmol), ligand (0.08 mmol), NEt_3 (2 mmol), DMF (0.5 mL), CO (10 bar), 120 °C, 20 h; Ad = adamantyl; Cy = cyclohexyl. [b] Conversion and yield were determined by GC based on bromobenzene using hexadecane as the internal standard. [c] $PdBr_2$ (0.033 mmol), acetonitrile (0.5 mL), CO (5 bar), N_2 (75 bar).

palladium source showed that less-expensive palladium bromide gave a slightly increased yield (Table 2, entries 7 and 8). Variations of the CO pressure hardly affected the activity of the system (Table 2, entries 4, 7, and 9).

For further investigations, the lowest CO pressure (5 bar) was chosen. To maximize the concentration of the low-boiling vinyl ether in solution, additional nitrogen was pressurized to increase the total pressure. When the total pressure was slightly raised, the product yield was improved to 60% (Table 2, entries 10–12).

With the best conditions in hand, we finally tested some more commercially available ligands. To our delight, several 2-dicyclohexylphosphinopyrroles turned out to be capable ligands for our model system (Table 2, entries 13–15). While cataCXium POMeCy (**L4**) gave the best result,[12] the structurally similar SPhos ligand (**L11**) showed only low activity under the same conditions (Table 2, entry 14 vs. Table 1, entry 12). Therefore, the electronic properties of dicyclohexylphosphine-substituted pyrrole ligands, as well as the steric demand caused by substitution (**L10**) of the pyrrole part, *N*-

Table 2. Optimization of the model system: Variation of temperature, pressure, and solvent.[a]



Entry	Ligand	Solvent	CO [bar]	Conv. [%][b]	Yield [%][b]
1	**L9**	DMF	10	100	24
2	**L9**	toluene	10	70	24
3	**L9**	acetonitrile	10	99	46
4	**L9**	1,4-dioxane	10	100	44
5	**L9**	1,4-dioxane	10	70	24[c]
6	**L9**	1,4-dioxane	20	100	43[d]
7	**L9**	1,4-dioxane	5	99	46
8	**L9**	1,4-dioxane	5	100	48[e]
9	**L9**	1,4-dioxane	20	100	45
10	**L9**	acetonitrile	5	100	53[f]
11	**L9**	acetonitrile	5	100	56[g]
12	**L9**	acetonitrile	5	100	60[h]
13	**L10**	acetonitrile	5	96	58[h]
14	**L4**	acetonitrile	5	97	76[h]
15	**L5**	acetonitrile	5	100	52[h]

[a] General reaction conditions: bromobenzene (1 mmol), *n*-butyl vinyl ether (6 mmol), [{(cinnamyl)PdCl}$_2$] (0.017 mmol), ligand (0.08 mmol), NEt_3 (2 mmol), solvent (0.5 mL), 120 °C, 20 h. [b] Conversion and yield were determined by GC based on bromobenzene using hexadecane as the internal standard. [c] 100 °C. [d] 130 °C. [e] $PdBr_2$ (0.033 mmol). [f] $PdBr_2$ (0.033 mmol), CO (5 bar), N_2 (45 bar). [g] $PdBr_2$ (0.033 mmol), CO (5 bar), N_2 (55 bar). [h] $PdBr_2$ (0.033 mmol), CO (5 bar), N_2 (75 bar).

naphthyl (**L9**) or *ortho*-substituted *N*-aryl-moieties (**L4**, **L5**), seem to be crucial.

The generality of the protocol was demonstrated in the carbonylative coupling of sixteen different aryl bromides with *n*-butyl vinyl ether. Notably, in all cases only the *trans* coupling product was detected and less than 5% of the Heck coupling product was observed. The reaction proceeded in a highly regioselective manner and no products incorporating external double bonds were detected. *Para*-, *meta*-, and even *ortho*-substituted aryl bromides gave the desired products in moderate to good yields (Table 3, entries 1–12). Electron-rich and slightly electron-deficient aryl bromides led to the corresponding 1-aryl-3-butoxy-2-(*E*)-propen-1-ones in 50–70% yield (Table 3, entries 2–9). Surprisingly, stronger electron-poor aryl bromides, such as 4-bromobenzonitrile, -acetophenone, and -benzaldehyde, gave lower yields (Table 3, entries 10–12). Nevertheless, 2-bromonaphthalene and some heteroaromatic substrates were coupled smoothly in moderate to good yields (Table 3, entries 13–16).

In the following experiments, we turned our attention to the carbonylative vinylation with other vinyl ethers. As shown in Scheme 2, several different vinyl ethers could be applied successfully. Notably, using styrene under our optimized conditions led to the corresponding chalcone in 99% yield (Scheme 2). Hence, this system should lead to improved yields for other chalcones as well.

Finally, we proved the possibility to transform the obtained 1-aryl-3-butoxy-2-(*E*)-propen-1-ones in a novel one-pot synthesis to give aryl-substituted pyrazoles, which are

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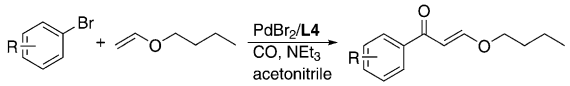
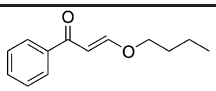
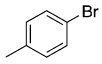
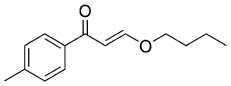
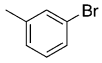
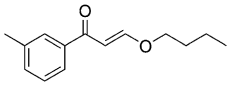
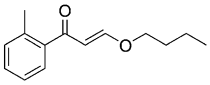
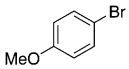
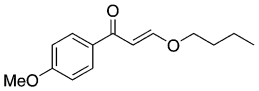
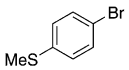
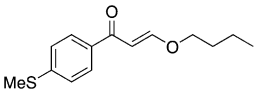
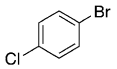
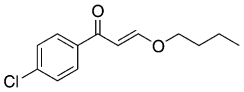
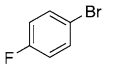
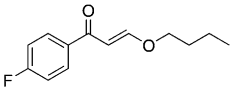
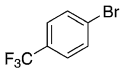
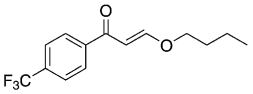
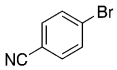
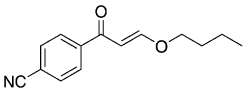
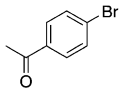
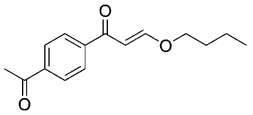
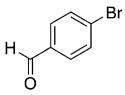
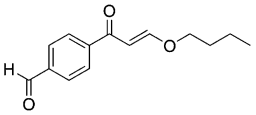
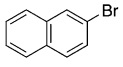
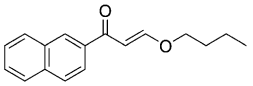
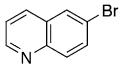
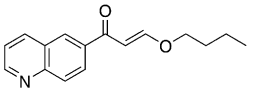
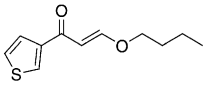
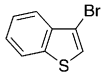
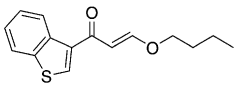
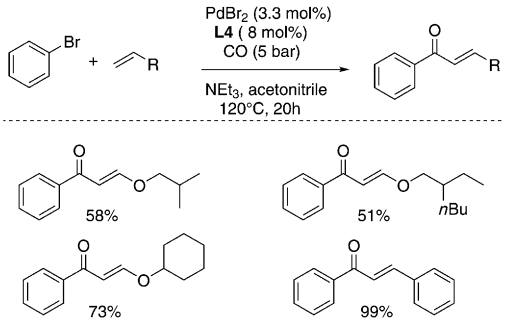
Table 3. Palladium-catalyzed coupling of aryl bromides with *n*-butyl vinyl ether.[a]



Entry	Aryl bromide	Product	Yield [%][b]
1			75
2			54
3			70
4			50
5			51
6			53
7			62
8			57
9			66
10			26
11			35
12			30
13			68
14			70
15			56
16			59

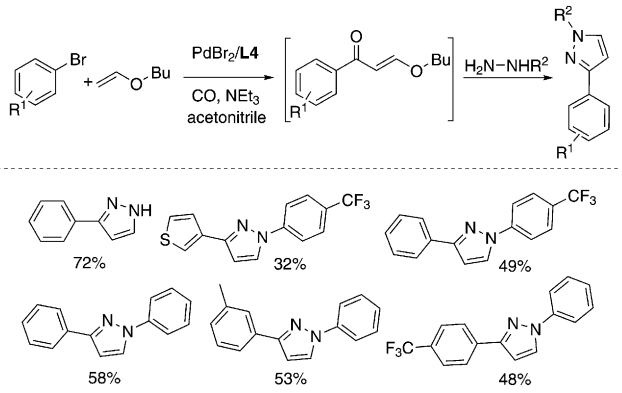
[a] General reaction conditions: aryl bromide (1 mmol), *n*-butyl vinyl ether (6 mmol), $PdBr_2$ (0.033 mmol), **L4** (0.08 mmol), NEt_3 (2 mmol), acetonitrile (0.5 mL), CO (5 bar), N_2 (75 bar), 120 °C, 20 h. [b] Isolated yield.



Scheme 2. Palladium-catalyzed coupling of aryl bromides with *n*-butyl vinyl ether (isolated yields are given).

known to have a broad spectrum of biological activities.[13] In the past, the synthesis of 1,3-substituted pyrazoles, particularly by cyclocondensation of *N*-arylhydrazines with 1,3-dicarbonyl compounds[14] or ethynyl ketones,[15] has been reported. The reaction of 3-alkoxy-1-phenyl propenones with phenylhydrazine to give pyrazoles had already been discovered by Panizzi et al. in 1943.[16]

Hence, after the palladium-catalyzed coupling process was finished, substituted hydrazines and molecular sieves were added and the reaction mixture was heated at 80 °C for another 3 h. In general, the corresponding 1,3-substituted pyrazoles were synthesized in moderate to good overall yields (Scheme 3). In most cases, less than 10 % of the regioisomeric 1,5-disubstituted pyrazoles were detected. Simply by using an aqueous hydrazine solution, 1-phenylpyrazole was isolated in 72 % yield.



Scheme 3. One-pot synthesis of pyrazoles.

In conclusion, we have established the first carbonylative Heck coupling reaction of aryl bromides and vinyl ethers. 19 different 1-aryl-3-alkoxy-2-propen-1-ones were synthesized in 30–75 % yield in a straightforward manner. Our novel protocol is a valuable extension of the recently published coupling of aryl halides with styrenes. Furthermore, it is exemplarily shown that the $PdBr_2$/**L4** catalyst system also gave improved yields for the carbonylative coupling of bromobenzene with styrene (99 % yield). Based on the coupling process, a one-pot synthesis of 1,3-diarylpyrazoles has been

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developed, demonstrating the usefulness of the synthesized products as building blocks. Six different pyrazole derivatives were prepared in an effective manner from simple bromobenzene, CO, vinyl ether, and phenylhydrazine. This also represents a new and easy access to various pyrazoles.

Experimental Section

General information: All reactions were performed by using standard Schlenk techniques (argon). Gas chromatography was performed on a Hewlett Packard HP 6890N chromatograph with an HP5 column. Chemicals were purchased from Fluka, Aldrich, and Strem and used as received. DMF, acetonitrile, dioxane, toluene, and triethylamine were distilled from sodium ketyl, CaH_2, or P_2O_5 and stored in Aldrich Sure/store flasks under argon.

Synthesis of 3-butoxy-1-phenyl-2(*E*)-propen-1-one: Six 4 mL glass vials were charged with $PdBr_2$ (3.3 mol%, 8.8 mg), **L4** (8 mol%, 30 mg), and a stirring bar. All vials were put into an alloy plate, equipped with a septum and an inlet needle, and then flushed with argon. Acetonitrile (0.5 mL), NEt_3 (2 mmol, 277 μL), bromobenzene (1 mmol, 105 μL), and butyl vinyl ether (6 mmol, 770 μL) were injected into each vial. The alloy plate with six vials was then placed in a 300 mL autoclave (Parr Instruments 4560 series). At room temperature, the autoclave was flushed with CO, pressurized with CO to 5 bar, and finally the pressure was increased to 80 bar by adding nitrogen. Afterwards, the autoclave was heated to 120°C for 20 h, then cooled to room temperature, and the remaining CO and nitrogen were released slowly. After discharging, water (2 mL) was added to each vial and the product was extracted with ethyl acetate. The aqueous phase was extracted three times. After drying the combined organic phases over sodium sulfate and evaporating the solvent, the crude product was purified by column chromatography (heptane/ethyl acetate 6:1) to give 3-butoxy-1-phenyl-2(*E*)-propen-1-one as a yellow oil.

Synthesis of 1,3-diphenylpyrazole: The synthesis of 3-butoxy-1-phenyl-2-(*E*)-propen-1-one was carried out as described above. After discharging the vials from the autoclave, molecular sieves (0.3 nm, 300 mg) and phenylhydrazine (6 mmol, 590 μL) were added to the reaction mixture. The vials were heated to 80°C in the alloy plate on a heating plate for 2 h. Finally, the reaction mixture was cooled to room temperature and purification was performed by column chromatography (heptane/ethyl acetate 15:1) to obtain 1,3-diphenyl-pyrazole as a white solid.

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[1] For selected reviews on palladium-catalyzed C–C coupling reactions since 2004, see: a) F. Alonso, I. P. Beletskaya, M. Yus, *Tetrahedron* **2008**, *64*, 3047–3101; b) D. S. Surry, S. L. Buchwald, *Angew. Chem.* **2008**, *120*, 6438–6461; *Angew. Chem. Int. Ed.* **2008**, *47*, 6338–6361; c) H. Doucet, J.-C. Hierso, *Angew. Chem.* **2007**, *119*, 850–888; *Angew. Chem. Int. Ed.* **2007**, *46*, 834–871; d) A. Roglans, A. Pla-Quintana, M. Moreno-Manas, *Chem. Rev.* **2006**, *106*, 4622–4643; e) P. Rollet, W. Kleist, V. Dufaud, L. Djakovitch, *J. Mol. Catal. A Chem.* **2005**, *241*, 39–51; f) A. Zapf, M. Beller, *Chem. Commun.* **2005**, 431–440; g) A. Frisch, M. Beller, *Angew. Chem.* **2005**, *117*, 680–695; *Angew. Chem. Int. Ed.* **2005**, *44*, 674–688; h) K. C. Nicolaou, P. G. Bulger, D. Sarlah, *Angew. Chem.* **2005**, *117*, 4516–4563; *Angew. Chem. Int. Ed.* **2005**, *44*, 4442–4489; i) I. P. Beletskaya, A. V. Cheprakov, *Coord. Chem. Rev.* **2004**, 2337–2364; j) R. B. Bedford, C. S. J. Cazin, D, Holder, *Coord. Chem. Rev.* **2004**, *248*, 2283- 2321.

[2] For some reviews on industrial applications, see: a) C. Torborg, M. Beller, *Adv. Synth. Catal.* **2009**, *351*, 3027–3043; b) A. Zapf, M. Beller, *Top. Catal.* **2002**, *19*, 101–109; c) C. E. Tucker, J. G. de Vries, *Top. Catal.* **2002**, *19*, 111–118.

[3] For books and reviews on palladium-catalyzed carbonylation reactions, see: a) A. Brennführer, H. Neumann, M. Beller, *Angew. Chem.* **2009**, *121*, 4176–4196; *Angew. Chem. Int. Ed.* **2009**, *48*, 4114–4133; b) C. F. J. Barnard, *Organometallics* **2008**, *27*, 5402–5422; c) M. Beller, in *Applied Homogeneous Catalysis with Organometallic Compounds*, 2nd ed. (Eds.: B. Cornils, W. A. Herrmann), Wiley-VCH, Weinheim, **2002**, pp. 145–156; d) R. Skoda-Földes, L. Kollár, *Curr. Org. Chem.* **2002**, *6*, 1097–1119; e) J. Tsuji, *Palladium Reagents and Catalysts: Innovations in Organic Synthesis*, Wiley, Chichester, **1995**; f) M. Beller, B. Cornils, C. D. Frohning, W. C. Kohlpaintner, *J. Mol. Catal. A Chem.* **1995**, *104*, 17–85; g) H. M. Colquhoun, D. J. Thomson, M. V. Twigg, *Carbonylation, Direct Synthesis of Carbonyl Compounds*, Plenum, New York, **1991**.

[4] For selected examples on palladium-catalyzed carbonylations of aryl halides, see: a) A. Schoenberg, I. Bartoletti, R. F. Heck, *J. Org. Chem.* **1974**, *39*, 3318–3326; b) A. Schoenberg, R. F. Heck, *J. Org. Chem.* **1974**, *39*, 3327–3331; c) A. Schoenberg, I. Bartoletti, R. F. Heck, *J. Am. Chem. Soc.* **1974**, *96*, 7761–7764; d) H. Neumann, A. Brennführer, P. Gross, T. Riermeier, J. Almena, M. Beller, *Adv. Synth. Catal.* **2006**, *348*, 1255–1261; e) S. Klaus, H. Neumann, A. Zapf, D. Strübing, S. Hübner, J. Almena, T. Riermeier, P. Gross, M. Sarich, W.-R. Krahnert, K. Rossen, M. Beller, *Angew. Chem.* **2006**, *118*, 161–165; *Angew. Chem. Int. Ed.* **2006**, *45*, 154–158; f) A. Brennführer, H. Neumann, S. Klaus, T. Riermeier, J. Almena, M. Beller, *Tetrahedron* **2007**, *63*, 6252–6258; g) H. Neumann, A. Brennführer, M. Beller, *Chem. Eur. J.* **2008**, *14*, 3645–3652.

[5] For carbonylative Suzuki reactions, see: a) H. Neumann, A. Brennführer, M. Beller, *Chem. Eur. J.* **2008**, *14*, 3645–3652; b) H. Neumann, A. Brennführer, M. Beller, *Adv. Synth. Catal.* **2008**, *350*, 2437–2442; c) N. A. Bumagin, A. B. Ponomaryov, I. P. Beletskaya, *Tetrahedron Lett.* **1985**, *26*, 4819–4822; d) Y. Hatanaka, S. Fukushima, T. Hiyama, *Tetrahedron* **1992**, *48*, 2113–2126; e) Y. Hatanaka, T. Hiyama, *Synlett* **1991**, 845–853; f) Y. Hatanaka, T. Hiyama, *Chem. Lett.* **1989**, 2049–2052; g) T. Ishiyama, H. Kizaki, N. Miyaura, A. Suzuki, *Tetrahedron Lett.* **1993**, *34*, 7595–7598; h) T. Ishiyama, H. Kizaki, T. Hayashi, A. Suzuki, N. Miyaura, *J. Org. Chem.* **1998**, *63*, 4726–4731; i) S. Zheng, L. Xu, C. Xia, *Appl. Organomet. Chem.* **2007**, *21*, 772–776; j) J.-J. Brunet, R. Chauvin, *Chem. Soc. Rev.* **1995**, *24*, 89–95.

[6] For carbonylative Sonogashira reactions, see: a) T. Kobayashi, M. Tanaka, *J. Chem. Soc., Chem. Commun.* **1981**, 333–334; b) L. Delaude, A. M. Masdeu, H. Alper, *Synthesis* **1994**, 1149–1151; c) A. Arcadi, S. Cacchi, F. Marinelli, P. Pace, G. Sanzi, *Synlett* **1995**, 823–824; d) B. Liang, M. Huang, Z. You, Z. Xiong, K. Lu, R. Fathi, J. Chen, Z. Yang, *J. Org. Chem.* **2005**, *70*, 6097–6100; e) M. S. M. Ahmed, A. Mori, *Org. Lett.* **2003**, *5*, 3057–3060; f) M. T. Rahman, T. Fukuyama, N. Kamata, M. Sato, I. Ryu, *Chem. Commun.* **2006**, 2236–2238; g) J. Liu, X. Peng, W. Sun, Y. Zhao, C. Xia, *Org Lett.* **2008**, *10*, 3933–3936; h) J. Liu, J. Chen, C. Xia, *J. Catal.* **2008**, *253*, 50–56; i) A. S. Karpov, E. Merkul, F. Rominger, T. J. J. Müller, *Angew. Chem.* **2005**, *117*, 7112–7117; *Angew. Chem. Int. Ed.* **2005**, *44*, 6951–6956.

[7] a) X.-F. Wu, H. Neumann, M. Beller, *Angew. Chem.* **2010**, *122*, 5412–5416; *Angew. Chem. Int. Ed.* **2010**, *49*, 5284–5287; b) X.-F. Wu, H. Neumann, A. Spannenberg, T. Schulz, H. Jiao, M. Beller, *J. Am. Chem. Soc.* **2010**, *132*, 14596–14602; c) X.-F. Wu, H. Jiao, H. Neumann, M. Beller, *ChemCatChem* **2011**, *3*, 726–733.

[8] P. Hermange, T. M. Gøgsig, A. T. Lindhardt, R. H. Taaning, T. Skrydstrup, *Org. Lett.* **2011**, *13*, 2444–2447.

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[9] For examples using 3-alkoxy alkenones as building blocks, see: a) T. Hudlicky, H. F. Olivo, M. G. Natchus, *J. Org. Chem.* **1990**, *55*, 4767–4770; b) F. Villar, T. Kolly-Kovac, O. Equey, P. Renaud, *Chem. Eur. J.* **2003**, *9*, 1566–1577; c) Y. Tominaga, Y. Ichihara, T. Mori, C. Kamio, A. Hosomi, *J. Heterocycl. Chem.* **1990**, *27*, 263–268; d) U. Lienhard, *Helv. Chim. Acta* **1978**, *61*, 1609–1621; e) C. D. Ritchie, A. Kawasaki, *J. Org. Chem.* **1981**, *46*, 4704; f) E. Stern, R. Millet, P. Depreux, J.-P. Henichart, *Tetrahedron Lett.* **2004**, *45*, 9257–9259; g) E. Stern, G. G. Muccioli, B. Bosier, L. Hamtiaux, R. Millet, J. H. Poupaert, J.-P. Henichart, P. Depreux, J.-F. Goossens, D. M. Lambert, *J. Med. Chem.* **2007**, *50*, 5471–5484; h) G. Mross, H. Reinke, P. Langer, *Synlett* **2008**, 963–966; i) G. Mross, S. Ladzik, H. Reinke, P. Langer, A. Spannenberg, C. Fischer, *Synthesis* **2009**, 2236–2248; j) E. Coutouli-Argyropoulou, E. Thessalonikeos, *J. Heterocycl. Chem.* **1991**, *28*, 429–432.

[10] C.-M. Andersson, A. Hallberg, *J. Org. Chem.* **1988**, *53*, 4257–4263.

[11] a) W. Mägerlein, A. Indolese, M. Beller, *J. Mol. Cat. A Chem.* **2000**, *156*, 213–221; b) K. Kumar, A. Zapf, D. Michalik, A. Tillack, M. Arlt, M. Beller, *Org. Lett.* **2004**, *6*, 7; c) A. Brennführer, H. Neumann, A. Pews-Davtyan, M. Beller, *Eur. J. Org. Chem.* **2009**, *1*, 38–42; d) A. Brennführer, H. Neumann, M. Beller, *ChemCatChem* **2009**, *1*, 28–41; e) A. Dumrath, X.-F. Wu, H. Neumann, A. Spannenberg, M. Beller, *Angew. Chem.* **2010**, *122*, 9172–9176; *Angew. Chem. Int. Ed.* **2010**, *49*, 8988–8992; f) S. Gowrisankar, A. G. Sergeev, P. Anbarasan, A. Spannenberg, H. Neumann, M. Beller, *J. Am. Chem. Soc.* **2010**, *132*, 11592–11598; g) X.-F. Wu, H. Neumann, M. Beller, *ChemCatChem* **2010**, *2*, 509–513; h) X.-F. Wu, P. Anbarasan, H. Neumann, M. Beller, *Angew. Chem.* **2010**, *122*, 7474–7477; *Angew. Chem. Int. Ed.* **2010**, *49*, 7316–7319; i) X.-F. Wu, H. Neumann, M. Beller, *Chem. Eur. J.* **2010**, *16*, 12104–12107; j) X.-F. Wu, H. Neumann, M. Beller, *Tetrahedron Lett.* **2010**, *51*, 6146–6149; k) X.-F. Wu, B. Sundararaju, H. Neumann, P. H. Dixneuf, M. Beller, *Chem. Eur. J.* **2011**, *17*, 106–110.

[12] For some other applications of this catalyst system, see: a) F. Ratabou, A. Zapf, R. Jackstell, S. Harkal, T. Riermeier, A. Monsees, U. Dingerdissen, M. Beller, *Chem. Eur. J.* **2004**, *10*, 2983–2990; b) A. Zapf, M. Beller, *Chem. Commun.* **2005**, *4*, 431–440; c) S. Harkal, F. Rataboul, A. Zapf, C. Fuhrmann, T. Riermeier, A. Monsees, M. Beller, *Adv. Synth. Catal.* **2004**, *346*, 1742–1748; d) N. Schwarz, A. Tillack, K. Alex, I. A. Sayyed, R. Jackstell, M. Beller, *Tetrahedron Lett.* **2007**, *48*, 2897; f) C. Torborg, A. Zapf, M. Beller, *ChemSusChem* **2008**, *1*, 91.

[13] a) Y. Shiga, I. Okada, Y. Ikeda, E. Takizawa, T. J. Fukuchi, *Pestic. Sci.* **2003**, *28*, 313–314; b) S. D. Lindell, B. A. Moloney, B. D. Hewitt, C. G. Earnhaw, P. J. Philip, J. E. Dancer, *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1985–1990; c) S. Fustero, R. Román, J. F. Sanz-Cervera, A. Simón-Fuentes, J. Bueno, S. Villanova, *J. Org. Chem.* **2008**, *73*, 8545–8552; d) N.-T. Ha-Duong, S. Dijols, C. Marques-Soares, C. Minoletti, P. M. Dansette, D. J. Mansuy, *J. Med. Chem.* **2001**, *44*, 3622–3631; e) T. de Paulis, K. Hemstapat, Y. Chen, Y. Zhang, S. Saleh, D. Alagille, R. M. Baldwin, G. D. Tamagnan, P. J. Conn, *J. Med. Chem.* **2006**, *49*, 3332–3344.

[14] a) A. N. Kost, I. Grandberg, in *Advances in Heterocyclic Chemistry* (Eds.: A. R. Katrizky, A. J. Boulton), Academic Press, New York, **1966**, pp. 347–429; b) Y. Luo, P. G. Potvin, *J. Org. Chem.* **1994**, *59*, 1761–1765; c) F. Gosselin, P. D. O'Shea, R. A. Webster, R. A. Reamer, R. D. Tillyer, E. J. J. Grabowski, *Synlett* **2006**, 3267–3270.

[15] M. Bagley, M. C. Lubinu, C. Mason, *Synlett* **2007**, *5*, 0704–0708.

[16] Panizzi, S. Siena, *Gazz. Chim. Ital.* **1943**, *73*, 355.

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