Application of the Fluorous-Biphase Concept to Palladium-Catalyzed *Sonogashira* Couplings

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Dedicated to Professor *Wolfgang Pfleiderer* on the occasion of his 75th birthday

Sonogashira C,C couplings in a fluorous biphasic system by application of three differently perfluoro-tagged Pd complexes are reported. All three complexes were probed in the coupling of four bromoarenes to three alkynes. The parallel workup procedure allowed for straightforward product isolation and catalyst recovery by simple extraction steps. In particular, the coupling of electron-deficient bromoarenes proceeded with good yields and allowed for the catalyst to be used up to three times.

1. Introduction. – According to the alchemists rule *similia similibus solvuntur*, highly fluorinated compounds show greatly enhanced solubility in perfluorinated alkanes even in the presence of a second organic phase. This principle can be applied in catalytic processes as well as in combinatorial strategies. *Horváth* and *Rábai* [1] were the first to point out that this allows for a perfluoro-tagged catalyst to remain in the fluorous phase, while other reactants dissolve in the organic phase. Furthermore, the temperature-dependent miscibility of such fluorous biphasic systems (FBS) [2] provides an option to homogenize the phases at elevated temperatures. Workup is essentially straightforward, as the two phases reform after lowering the temperature again. Simple phase-separation suffices to recover the perfluoro-tagged catalyst. At the same time, product isolation can be reduced to an extraction protocol.

Syntheses in the nonpolar reaction medium *sc*CO_2 represent a further application of perfluoro-tags where they can be used to mediate sufficient solubility [3]. Hence, there is currently a great deal of interest in perfluoro-tagged catalysts.

So far, a number of reactions have been successfully evaluated under FBS conditions, including hydroformylation [4], hydroboration [5], hydrosilylation [6], epoxidation [7][8], and the Rh-catalyzed cyclopropanation of alkenes [9], oxidations of aldehydes [7], thioesters [7], and alkanes [10], as well as *Wacker* oxidations [11], Pd-catalyzed allylic substitutions [12], and *Negishi* [13] and *Heck* reactions [14].

Among the transition-metal catalyzed reactions, C,C couplings are of particular importance, as they allow construction of molecule skeletons. We have previously reported on highly efficient protocols for *Stille* [15] and *Suzuki* [16] cross-coupling

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reactions and introduced the use of some new perfluoro-tagged bis(triphenylphosphine)palladium complexes for this purpose[2]).

In alkyne chemistry, the *Sonogashira* reaction is probably the most widely used coupling reaction for enyne syntheses [17]. Here, we report the application of the FBS concept to the *Sonogashira* cross-coupling reaction, with the goal of straightforward isolation of products and catalysts by extraction procedures and the possibility to re-use the active catalyst for subsequent runs.

2. Results and Discussion. – Motivated by our results with perfluoro-tagged Pd complexes **1a** and **1b** (*Fig.*) as catalysts in *Stille* [15] and *Suzuki* [16] reactions, we were interested in developing a protocol for *Sonogashira* couplings.

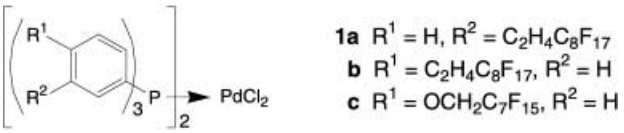

Figure. *Perfluoro-tagged Pd Complexes* **1a**–**c**

To the best of our knowledge, *Sonogashira* reactions employing FBS conditions have not been reported yet. These C,C couplings are complicated by the need for CuI as co-catalyst. As Pd precatalysts, we have applied complexes **1a**–**c**. In complexes **1a** and **1b**, the perfluoro entity and the phenyl rings are interspaced by a CH_2-CH_2 group to reduce the electron-withdrawing effect of the perfluoro tag. Preliminary experiments on *Sonogashira* couplings showed mainly formation of black Pd when analogous Pd complexes without such spacer groups were applied. Hence, we decided also to probe complex **1c** bearing a CH_2O spacer group, of which we expected to reduce the electron-withdrawing effect even more [18]. Both types of complexes (**1a** and **1b** *vs.* **1c**) should differ in the coordination properties of their phosphine ligands, and this might have also an influence on their catalytic properties and stabilities. Complex **1c** (*Fig.*) was prepared from the corresponding phosphine [19] as described for **1a** and **1b** [15][16][18].

The Pd-catalyzed *Sonogashira* couplings of bromoarenes **2a**–**2d** with alkynes **3a**–**3c** were carried out in a mixture of DMF and 1,2,2,3,4,4,5,5,6,6-decafluoro-1,3-bis(trifluoromethyl)cyclohexane at 100° for 4 h with 2 mol-% of **1a**–**1c** as precatalyst and 5 mol-% CuI as co-catalyst in the presence of 2 equiv. Bu_2NH (*Scheme*). This FBS remained biphasic at 100°, although the mutual miscibility of the phases was certainly increased. After the reaction, to separate the phases, the temperature was lowered to 0°. The products **4a**–**4l** were isolated and identified. The yields were based either on the isolated material or on ^{1}H-NMR spectra against an internal standard. The fluorous phase containing the active catalyst was washed several times with DMF and was re-used as such for the next run.

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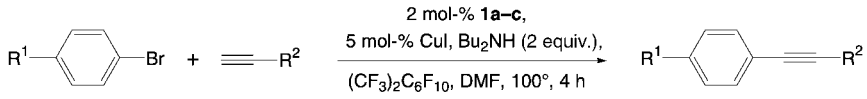
[2]) Compounds **1a** and **1b** are meanwhile commercially available (*Fluka*).

Scheme. *Reactions of Different Bromoarenes with Alkynes*



2a $R^1 = NO_2$ **3a** R^2 = TIPS
b R^1 = COMe **b** R^2 = Ph
c $R^1 = CO_2Et$ **c** $R^2 = CMe_2OH$
d R^1 = OMe

The scope of the reaction was investigated with electron-deficient and electron-rich bromoarenes, **2a**–**2c** and **2d**, respectively. Furthermore, three different types of alkynes were investigated bearing a silyl (**3a**), an aromatic (**3b**), or an aliphatic substituent (**3c**) (*Table*). The general trends in reactivity reported for *Sonogashira* couplings were confirmed by our experiments [20]. Electron-deficient bromoarenes and nonaliphatic alkynes proved to be reactive substrates. Hence, all three complexes **1a**–**1c** mediated the coupling of the strongly electron-deficient 1-bromo-4-nitrobenzene (**2a**) to alkynes **3a** and **3b** with virtually quantitative yield in up to three consecutive runs (*Entries 1* and *2*). However, the aliphatic alkyne **3c** tended to give lower yields (*Entry 3*). The reaction of the other two electron-deficient bromoarenes **2b** and **2c** also gave good results in two runs before yields decreased in a third run (*Entries 4–9*). Electron-rich bromoarenes are known to be the least reactive ones. For 1-bromo-4-methoxybenzene (**2d**), complexes **1b** and **1c** gave good results only with alkyne **2a** (*Entries 10–12*), but no consecutive runs were possible.

Table. Sonogashira *Cross-Couplings of Various Bromo-arenes* **2a**–**d** *with Alkynes* **3a**–**c** *in the Presence of Catalysts* **1a**–**c**

Entry	Substrates		Prod.	Yield[a]) [%]		
				Catalyst **1a**	Catalyst **1b**	Catalyst **1c**
1	**2a**	**3a**	**4a**	> 98, > 98, > 98	> 98, > 98, 96	> 98, > 98, 98
2	**2a**	**3b**	**4b**	> 98, > 98, 97	> 98, > 98, 96	> 98, > 98, 97
3	**2a**	**3c**	**4c**	73, 66, 69	74, 73, 68	71, 81, 73
4	**2b**	**3a**	**4d**	> 98, > 98, 89	> 98, 95, 82	> 98, 97, 81
5	**2b**	**3b**	**4e**	80, 76, 84	97, > 98, 90	95, 85, 18
6	**2b**	**3c**	**4f**	94, 92, 75	90, 95, 5	> 98, 91, 3
7	**2c**	**3a**	**4g**	> 98, 98, 69	98, 98, 95	95, 95, 65
8	**2c**	**3b**	**4h**	74, 85, 80	95, 95, 88	91, 82, 4
9	**2c**	**3c**	**4i**	68, 50, 3	85, 86, 38	99, 83, 5
10	**2d**	**3a**	**4j**	47, 8, 10	80, 16, 5	95, 10, 6
11	**2d**	**3b**	**4k**	22, 18, 0	20, 20, 0	25, 17, 0
12	**2d**	**3c**	**4l**	10, 0, 0	30, 0, 0	40, 0, 0

[a]) Yields based on isolated product or on NMR from run 1 to run 3.

The data summarized in the *Table* show similar activity for all three Pd complexes **1a**–**1c** under investigation. Apparently, both the position and the nature of the spacer group allows for variations.

Conclusions. – In summary, we were able to demonstrate that *Sonogashira* couplings can be performed with perfluoro-tagged precatalysts **1a**–**1c** under FBS conditions. Furthermore, we could show that, in most cases, the active Pd catalysts can be recycled and re-used after phase separation. All three catalysts generated from the precatalysts **1a**–**1c** showed similar activity. Neither the position of the perfluoro tag nor the nature of the spacer group exerted a crucial influence.

The outcome of the coupling reactions catalyzed by complexes **1a**–**1c** shows the known trends for *Sonogashira* couplings. Electron-deficient bromoarenes (**2a**–**2c**) proved to be good substrates, whereas the coupling of a donor-substituted bromoarene **2d** gave lower yields. This held particularly true for consecutive runs.

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Experimental Part

1. *General*. All reagents were obtained from either *Fluka* or *Aldrich*, and were used as received. The Pd complexes **1b**–**1c** were prepared according to literature procedures [15][16][21]. Pd Complex **1a** was a generous gift from *Fluka*. Anal. data for **1c**: ^{1}H-NMR (200 MHz, Hexafluorobenzene/$CDCl_3$): 4.63 (*t*, *J* = 12.6, CH_2); 7.13 (*d*, *J* = 8.7, H–C(3), H–C(5)); 7.83 (*m*, H–C(2), H–C(4)). ^{31}P-NMR (Hexafluorobenzene/$CDCl_3$): 20.6. Anal. calc. for $C_{84}H_{38}Cl_2F_{90}O_6P_2Pd$: C 32.63, H 1.24, Cl 2.29; found: C 32.40, H 1.27, Cl 1.83.

All reactions were carried out in parallel fashion in degassed solvents under Ar. Parallel evaporation of solvent was performed with an *IR-Dancer* vortex evaporator from *Labsource*. M.p. were measured with the electrothermal digital melting device *IA 9200* and are uncorrected. Column chromatography (CC): SiO_2 from *Baker* and alox (act. II–III) from *ICN Biomedicals*, D-Eschwege. NMR Spectra: 250, 300, or 400 MHz (^{1}H), 100 MHz (^{13}C); $CDCl_3$ solns.; chemical shifts δ in ppm rel. to Me_4Si (= 0 ppm) for ^{1}H-NMR and rel. to $CHCl_3$ (= 77.00 ppm) for ^{13}C-NMR; *J* in Hz. MS: *Finnigan MAT 8200* (EI) mass spectrometer.

2. *General Procedure for the Coupling of Bromoarenes* **2a**–**2d** *with Alkynes* **3a**–**3c**. To a suspension of precatalyst **1a**–**1c** (0.006 mmol) in 1,2,2,3,4,4,5,5,6,6-decafluoro-1,3-bis(trifluoromethyl)cyclohexane (0.7 ml) under Ar, bromoarene **2a**–**2d** (0.300 mmol), alkyne **3a**–**3c** (0.360 mmol), and CuI (0.015 mmol) in anh. DMF (0.5 ml; 0.03M stock soln. containing 20% (v/v) Bu_2NH (0.600 mmol)) were added. The mixture was heated at 100° for 4 h. After cooling to 0°, the org. phase was separated from the fluorous phase. The fluorous phase containing the active Pd catalyst was washed with anh. DMF (3 × 2 ml) and used as such for the next run. For the isolation of the product, brine (40 ml) and aq. HCl (0.5M, 10 ml) were added to the combined DMF layers, which were extracted with $CHCl_3$ (3 × 2 ml). After washing with sat. $NaHCO_3$ soln. (4 ml) and back-extraction of the $NaCO_3$ soln. with $CHCl_3$ (5 ml), the combined $CHCl_3$ phases were evaporated. For complete removal of DMF, the residue was taken up in Et_2O (5 ml) again, washed with brine (4 ml) and passed through a plug of silica (2 cm^3) and alox (neutral, act II–III; 2 cm^3) (in the case of 2-methylbut-3-yn-2-ol (**3c**), Na_2SO_4 was used instead of alox). The filtrate was evaporated, yielding the desired products **3a**–**3l** and remainders of the alkyne. All products were quantified by isolation or by comparing the intensities of their arom. H-atom signals in the ^{1}H-NMR spectra against 1,2-dibromoethane as an internal standard in $CDCl_3$ (100 µl, 1.50M stock soln. (= 3.65 ppm)).

1-Triisopropyl-4-(2-nitroethynyl)benzene (**4a**). Dark yellow oil. ^{1}H-NMR: 1.13–1.15 (*m*, 3 ^{i}Pr); 7.61 (*d*, *J* = 8.8, 2 arom. H); 8.17 (*d*, *J* = 8.8, 2 arom. H). ^{13}C-NMR: 11.3; 18.6; 97.6; 104.9; 123.6; 130.4; 132.8; 147.2. MS: 303 (14, M^+), 260 (100), 218 (27). Anal. calc. for $C_{17}H_{25}NO_2Si$: C 67.28, H 8.30, N 4.62; found: C 67.30, H 8.13, N 4.32.

1-Nitro-(4-phenylethynyl)benzene (**4b**). Yellow solid. M.p. 113° (cyclohexane/AcOEt) ([22]: m.p. 113–115°). ^{1}H-NMR: 7.32–7.41 (*m*, 3 arom. H); 7.55 (*d*, *J* = 7.6, 2 arom. H); 7.64 (*m*, 2 arom. H); 8.19 (*m*, 2 arom. H). ^{13}C-NMR: 87.6; 94.8; 122.2; 123.7; 128.6; 129.4; 130.4; 131.9; 132.4; 147.1. MS: 223 (100, M^+), 176 (39). Anal. calc. for $C_{14}H_9NO_2$: C 75.33, H 4.06, N 6.27; found: C 75.13, H 4.35, N 6.22.

2-Methyl-4-(4-nitrophenyl)but-3-yn-2-ol (**4c**). Yellow solid. M.p. 58° (cyclohexane/AcOEt). ^{1}H-NMR: 1.65 (*s*, 2 Me); 2.40 (br. *s*, OH); 7.55 (*d*, *J* = 8.8, 2 arom. H); 8.17 (*d*, *J* = 10.7, 2 arom. H). ^{13}C-NMR: 31.3; 65.7; 80.5;

99.2; 123.5; 129.8; 132.42; 147.2. MS: 205 (10, M^+), 190 (100). Anal. calc. for $C_{11}H_{11}NO_3$: C 64.38, H 5.40, N 6.83; found: C 64.16, H 5.55, N 6.67.

4-[(Triisopropylsilyl)ethynyl]acetophenone (**4d**). Yellow oil. ^{1}H-NMR: 1.13 – 1.14 (m, 3 ^{i}Pr); 2.59 (s, COMe); 7.54 (d, J = 8.5, 2 arom. H); 7.89 (d, J = 8.6, 2 arom. H). ^{13}C-NMR: 11.4; 18.7; 26.6; 94.8; 106.2; 128.2; 128.4; 132.2; 136.4; 197.2. MS: 300 (13, M^+), 257 (100), 215 (35). Anal. calc. for $C_{19}H_{28}OSi$: C 75.94, H 9.39; found: C 75.98, H 9.51.

4-(Phenylethynyl)acetophenone (**4e**) [23]. Pale yellow solid. M.p. 93° (cyclohexane) ([24]: m.p. 94 – 96°). ^{1}H-NMR: 2.60 (s, Me); 7.34 – 7.38 (m, 3 arom. H); 7.52 – 7.56 (m, 2 arom. H); 7.60 (d, J = 8.5, 2 arom. H); 7.93 (d, J = 8.5, 2 arom. H). ^{13}C-NMR: 26.6; 88.6; 92.7; 122.7; 128.2; 128.3; 128.5; 128.8; 131.7; 131.8; 136.2; 197.3. MS: 220 (70, M^+), 205 (100), 177 (21).

4-(3-Hydroxy-3-methylbut-1-ynyl)acetophenone (**4f**) [25]. Yellow oil. ^{1}H-NMR: 1.64 (s, 2 Me); 2.10 (s, OH); 2.58 (s, Me); 7.45 (m, 2 arom. H); 7.86 (m, 2 arom. H). ^{13}C-NMR: 26.8; 31.6; 65.9; 81.7; 97.3; 127.9; 128.4; 132.0; 136.5; 197.5. MS: 202 (27, M^+), 187 (100), 159 (16).

Ethyl 4-[(triisopropylsilyl)ethynyl]benzoate (**4g**). Yellow oil. ^{1}H-NMR: 1.14 (m, 3^{i}Pr); 1.39 (t, J = 7.2, *Me*CH$_2$); 4.37 (q, J = 7.2, MeC*H*$_2$); 7.52 (d, J = 8.5, 2 arom. H); 7.98 (d, J = 8.5, 2 arom. H). ^{13}C-NMR: 11.3; 14.3; 18.6; 61.1; 94.1; 106.3; 128.0; 129.3; 129.9; 131.9; 165.9. MS: 330 (11, M^+), 287 (100), 245 (34). Anal. calc. for $C_{20}H_{30}O_2Si$: C 72.67, H 9.15; found: C 72.38, H 9.12.

Ethyl 4-(phenylethynyl)benzoate (**4h**) [26]. Yellow solid. M.p. 65° (cyclohexane/AcOEt). ^{1}H-NMR: 1.40 (t, J = 7.3, *Me*CH$_2$); 4.39 (q, J = 7.2, MeC*H*$_2$); 7.34 – 7.39 (m, 3 arom. H); 7.52 – 7.57 (m, 2 arom. H); 7.59 (d, J = 8.3, 2 arom. H); 8.03 (d, J = 8.3, 2 arom. H). ^{13}C-NMR: 14.5; 61.3; 88.9; 92.5; 123.0; 128.1; 128.6; 129.0; 129.7; 130.1; 131.7; 132.6; 166.3. MS: 250 (93, M^+), 177 (23).

Ethyl 4-(3-hydroxy-3-methylbut-1-ynyl)benzoate (**4i**). Orange oil. ^{1}H-NMR: 1.38 (t, J = 7.2, *Me*CH$_2$); 1.63 (s, 2 Me); 2.20 (br. s, OH); 4.36 (q, J = 7.1, MeC*H*$_2$); 7.43 (d, J = 8.7, 2 arom. H); 7.95 (d, J = 8.7, 2 arom. H). ^{13}C-NMR: 14.2; 31.3; 61.1; 65.5; 81.4; 97.0; 127.5; 129.4; 129.8; 131.5; 166.1. MS: 232 (17, M^+), 217 (100), 187 (16), 159 (15). Anal. calc. for $C_{14}H_{16}O_3$: C 72.39, H 6.94; found: C 72.25, H 7.15.

1-Methoxy-4-[(triisopropylsilyl)ethynyl]benzene (**4j**). Yellow oil. ^{1}H-NMR: 1.13 (m, 3 ^{i}Pr); 3.75 (s, MeO); 6.79 (d, J = 8.9, 2 arom. H); 7.40 (d, J = 8.9, 2 arom. H). ^{13}C-NMR: 11.5; 18.8; 55.2; 88.6; 107.3; 113.9; 115.9; 133.5; 159.8. MS: 288 (27, M^+), 245 (100), 203 (48). Anal. calc. for $C_{18}H_{28}OSi$: C 74.94, H 9.78; found: C 75.18, H 10.02.

1-Methoxy-4-(phenylethynyl)benzene (**4k**) [23]. Orange solid. M.p. 46° (cyclohexane/AcOEt) ([24]: m.p. 50 – 51°). ^{1}H-NMR: 3.83 (s, MeO); 6.88 (d, J = 8.9, 2 arom. H); 7.30 – 7.35 (m, 3 arom. H); 7.47 (d, J = 9.0, 2 arom. H); 7.51 (d, J = 8.2, 2 arom. H). ^{13}C-NMR: 55.5; 88.3; 89.9; 114.2; 115.6; 123.8; 128.1; 128.5; 131.7; 133.3; 161.4. MS: 208 (100, M^+), 193 (49).

1-(3-Hydroxy-3-methylbut-1-ynyl-4-methoxybenzene (**4l**). Dark yellow oil. ^{1}H-NMR: 1.61 (s, 2 Me); 2.02 (br. s, OH); 3.80 (s, MeO); 6.82 (d, J = 8.9, 2 arom. H); 7.34 (d, J = 8.9, 2 arom. H). ^{13}C-NMR: 31.8; 55.5; 65.9; 82.2; 92.6; 114.1; 115.1; 133.3; 159.8. MS: 190 (29, M^+), 175 (51), 43 (100). Anal. calc. for $C_{12}H_{14}O_2$: C 75.76, H 7.42; found: C 75.73, H 7.42.

REFERENCES

[1] I. T. Horváth, J. Rábai, *Science* **1994**, *266*, 72.

[2] D. W. Zhu, *Synthesis* **1993**, 953; J. A. Gladysz, *Science* **1994**, *266*, 55; B. Cornils, *Angew. Chem.* **1997**, *109*, 2147; *Angew. Chem., Int. Ed.* **1997**, *36*, 2057; I. T. Horváth, *Acc. Chem. Res.* **1998**, *31*, 641; D. P. Curran, Z. R. Lee, *Green Chem.* **2001**, G3.

[3] P. G. Jessop, W. Leitner, 'Chemical Synthesis Using Supercritical Fluids', Wiley-VCH, Weinheim, 1999; J. M. DeSimone, E. E. Murray, Y. Z. Menceloglu, J. B. McClain, R. J. Romack, J. R. Combes, *Science* **1994**, *265*, 356; T. Osswald, S. Schneider, S. Wang, W. Bannwarth, *Tetrahedron Lett.* **2001**, *42*, 2965.

[4] I. T. Horváth, G. Kiss, A. Cook, J. E. Bond, P. A. Stevens, J. Rábai, *J. Am. Chem. Soc.* **1998**, *120*, 3133.

[5] J. J. J. Juliette, I. T. Horváth, J. A. Gladysz, *Angew. Chem.* **1997**, *109*, 1682; *Angew. Chem., Int. Ed.* **1997**, *36*, 1610; J. J. J. Juliette, D. Rutherford, I. T. Horváth, J. A. Gladysz, *J. Am. Chem. Soc.* **1999**, *121*, 2696.

[6] J. A. Gladysz, L. V. Dinh, *Tetrahedron Lett.* **1999**, *40*, 8995; E. de Wolf, E. A. Speets, B.-J. Deelman, G. van Koten, *Organometallics* **2001**, *20*, 3686.

[7] I. Klement, H. Lütjens, P. Knochel, *Angew. Chem.* **1997**, *109*, 1605; *Angew. Chem., Int. Ed.* **1997**, *36*, 1454.

[8] G. Pozzi, F. Cinato, S. Montanari, *Chem. Commun.* **1998**, 877; S. Quici, M. Cavazzini, S. Montanari, G. Pozzi, *Tetrahedron Lett.* **1999**, *40*, 3647; G. Pozzi, M. Cavazzini, F. Ciuato, S. Montanari, S. Quici, *Eur. J. Org. Chem.* **1999**, *12*, 1947; B. Betzemeier, F. Lhermitte, P. Knochel, *Synlett* **1999**, 489.

[9] A. Endres, G. Maas, *Tetrahedron Lett*. **1999**, *40*, 6365.
[10] J. M. Vincent, A. Rabion, V. K. Yachandra, R. H. Fish, *Angew. Chem*. **1997**, *109*, 2438; *Angew. Chem., Int. Ed.* **1997**, *36*, 2346 – 2349; G. Pozzi, M. Cavazzini, S. Quici, S. Fontana, *Tetrahedron Lett*. **1998**, *39*, 9439.
[11] B. Betzemeier, F. Lhermitte, P. Knochel, *Tetrahedron Lett*. **1998**, *39*, 6667.
[12] R. Kling, D. Sinou, G. Pozzi, A. Choplin, F. Quignard, S. Busch, S. Kainz, D. Koch, W. Leitner, *Tetrahedron Lett*. **1998**, *39*, 9439.
[13] B. Betzemeier, P. Knochel, *Angew. Chem*. **1997**, *109*, 2736; *Angew. Chem., Int. Ed*. **1997**, *36*, 2623.
[14] J. Moineau, G. Pozzi, S. Quici, D. Sinou, *Tetrahedron Lett*. **1999**, *40*, 7683.
[15] S. Schneider, W. Bannwarth, *Angew. Chem*. **2000**, *112*, 4293; *Angew. Chem., Int. Ed*. **2000**, *39*, 4142.
[16] S. Schneider, W. Bannwarth, *Helv. Chim. Acta* **2001**, *84*, 735.
[17] K. Sonogashira, Y. Tohda, N. Hagihara, *Tetrahedron Lett*. **1975**, *16*, 4467; S. Takahashi, Y. Kuroyama, K. Sonogashira, N. Hagihara, *Synthesis* **1980**, 627.
[18] S. Schneider, Ph. D. Thesis, Albert-Ludwigs-Universität, Freiburg, 2001.
[19] D. Sinou, G. Pozzi, E. G. Hope, A. M. Stuart, *Tetrahedron Lett*. **1999**, *40*, 849.
[20] R. Rossi, A. Carpita, F. Bellina, *Org. Prep. Proced. Int*. **1995**, *27*, 129; K. Sonogashira, in 'Metal-catalyzed Cross-coupling Reactions', Eds. F. Diederich, P. J. Stang, Wiley-VCH, Weinheim, 1998, p. 203; 'Transition Metals for Organic Synthesis', Vol. 1, Eds. M. Beller, C. Bolm, Wiley-VCH, Weinheim, 1998, p. 170 K. Sonogashira, in 'Comprehensive Organic Synthesis', Vol. 3, Eds. B. M. Trost, I. Fleming, Pergamon, Oxford, 1991, p. 521.
[21] S. Kainz, D. Koch, W. Baumann, W. Leitner, *Angew. Chem*. **1997**, *109*, 1699; *Angew. Chem., Int. Ed*. **1997**, *36*, 1628; S. Kainz, Z. Luo, D. P. Curran, W. Leitner, *Synthesis* **1998**, 1425.
[22] S. Akiyama, K. Tajima, S. Nakatsuji, K. Nakashima, K. Abiru, M. Watanabe, *Bull. Chem. Soc. Jpn*. **1995**, *68*, 2043.
[23] R. K. Gujadhur, C. G. Bates, D. Venkataraman, *Org. Lett*. **2001**, *3*, 4315.
[24] A. Arcadi, S. Cacchi, G. Fabrizi, F. Marinelli, P. Pace, *Eur. J. Org. Chem.* **1999**, *2*, 3305.
[25] T. Hundertmark, A. F. Littke, S. L. Buchwald, G. C. Fu, *Org. Lett*. **2000**, *2*, 1729; S. J. Havens, *J. Org. Chem*. **1985**, *50*, 1763.
[26] S.-W. Zhang, T. Sugioka, S. Takahashi, *J. Mol. Catal. A*. **1999**, *143*, 211.

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