Supplementary Material (ESI) for Green Chemistry

Facile protocol for Palladium catalyzed Suzuki-Miyaura coupling in air and water at ambient temperature

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Supplementary Information

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1. Materials and Methods. All experiments were carried out under an atmosphere of argon using Schlenk and glove-box techniques. Toluene was dried over Na/benzophenone, distilled under argon and deoxygenated prior to use. Ethanol was dried over Na/Diethylphtalate, distilled under argon and deoxygenated prior to use. Pentane was dried and deoxygenized by passing through columns packed with activated alumina and Q5, respectively. Deuterated solvents were dried by distillation from CaH_2 (CD_2Cl_2 and $CDCl_3$) and deoxygenated by three *freeze-pump-thaw* cycles. NEt_3 was purchased from Merck and dried over CaH_2, distilled under argon and deoxygenated prior to use. $PdCl_2$ (ABCR), $Pd(OAc)_2$ and $AgSO_4$ (ABCR) were used as purchased. Compounds **1**, **2, 3, 4, 5** and **6** were prepared as reported inliterature.[1,2] $P(OH)^iPr_2$ was received from hydrolysis of chlorodiisopropyl phoshine in aqueous 1 M carbonate buffer (pH = 11)

2. Analytical Methods. Elemental analyses were obtained from the Microanalytical Laboratory of Technische Universität München. The IR spectra were recorded on a Jasco FT/IR-460 PLUS spectrometer as nujol mulls between KBr plates. NMR spectra were recorded on Jeol Lambda 400 spectrometer at room temperature and were calibrated to the residual proton resonance and the natural abundance ^{13}C resonance of the solvent (CD_2Cl_2, δ_H = 5.32 and δ_C = 53.8 ppm; $CDCl_3$, δ_H = 7.25 and δ_C = 77.0 ppm). ^{31}P NMR chemical shifts are reported relative to external phosphoric acid (δ_P = 0.0 ppm). Signal multiplicities are abbreviated as: s (singlet), d (dublet), t (triplet), vt (virtual triplet), sp (septet), m (multiplet), br (broad).

3. Procedures

Synthesis of $\mathbf{4^{ligand}}$ (*2-Phenylphenol Diisopropylphosphinite*)

In a Schlenk tube *2*-Phenylphenol (1.70 g, 10.0 mmol, 1.0 eq.) was dissolved in toluene and Triethylamine (1.51 g, 14.9 mmol, 1.5 eq.) was added. After stirring the solution for 15 min at r.t. chlorodiisopropylphosphine (1.51 g, 9.9 mmol, 0.95 eq.) was added. The reaction mixture was refluxed overnight. After cooling to room temperature pentane was (50 mL) added. A precipitated white solid was removed by filtration through a pad of Celite and washed with pentane (3 × 10 mL). The combined organic fractions were then evaporated to dryness *in vacuo* yielding the phosphinite ligand which was used without further purification.

Yield: 5.21 g (18.2 mmol, 92%).

Anal. calcd. for $C_{18}H_{23}OP$ (286.35): C, 75.50; H, 8.10. Found: 75.08; H, 8.70.

NMR δ_H (399.8 MHz, $CDCl_3$, r.t., [ppm]): 7.59 (2H, m, C$H_{aromat.}$), 7.51-7.43 (3H, m, C$H_{aromat.}$), 7.39-7.32 (3H, m, C$H_{aromat.}$), 7.10 (1H, t, $^3J_{(H,H)}$ = 7.5 Hz, C$H_{aromat.}$), 1.86 (2H, dvt, $^2J_{(P,H)}$ = 2.9 Hz, $^3J_{(H,H)}$ = 9.1 Hz, PC*H*), 1.06 (6H, dd, $^3J_{(P,H)}$ = 11.4 Hz, $^3J_{(H,H)}$ = 7.0 Hz, PCH(CH_3)$_2$), 1.05 (6H, dd, $^3J_{(P,H)}$ = 15.4 Hz, $^3J_{(H,H)}$ = 7.1 Hz, PCH(CH_3)$_2$).

δ_C (100.6 MHz, $CDCl_3$, r.t., [ppm]): 156.2 (d, $^2J_{(P,C)}$ = 8.5 Hz, $C_{aromat.}$), 138.9 (s, $C_{aromat.}$), 132.6 (s, $C_{aromat.}$), 130.8 (s, $C_{aromat.}$), 130.0 (s, $C_{aromat.}$), 128.6 (s, $C_{aromat.}$), 127.8 (s, $C_{aromat.}$), 126.9 (s, $C_{aromat.}$), 121.7 (s, $C_{aromat.}$), 118.2 (s, $C_{aromat.}$), 28.3 (d, $^2J_{(P,C)}$ = 17.7 Hz, PCH(CH$_3$)$_2$), 17.7 (d, $^2J_{(P,C)}$ = 19.2 Hz, PCH(CH$_3$)$_2$), 17.1 (d, $^2J_{(P,C)}$ = 8.5 Hz, PCH).

δ_P (161.8 MHz, $CDCl_3$, r.t., [ppm]): 151.4 (s, P^iPr_2).

CI-MS: m/z = 286.7 [M^+, 100%].

Synthesis of **4**, *[{Pd(μ-Cl){κ²-P,C-P(ⁱPr)₂(OC₆H₃-2-Ph)}}₂]*

In a Schlenk tube phosphinite ligand $\mathbf{4}^{\mathbf{ligand}}$ (401 mg, 1.40 mmol, 1.0 eq.) and palladium dichloride (250 mg, 1.40 mmol, 1.0 eq.) were placed in toluene (30 mL). The reaction mixture was refluxed overnight. After cooling to r.t. the solvent was removed *in vacuo*. The residue was extracted with dichloromethane (30 mL) and filtered through a pad of Celite. The product was precipitated from the organic solution by addition of ethanol, collected by filtration and recrystallised from CH_2Cl_2/EtOH.

Two isomers were obtained in a ratio of 1/1.49. Only the major isomer is interpreted. Yield: 0.51 g (0.60 mmol, 43%).

Anal. calcd. for $C_{36}H_{44}Cl_2O_2P_2Pd_2$ (854.43): C, 50.61; H, 5.19. Found: 50.20; H, 5.76.

NMR δ_H (399.8 MHz, CD_2Cl_2, r.t., [ppm]): 7.63 (1H, t, $^3J_{(H,H)}$ = 6.0 Hz , C$H_{aromat.}$), 7.56-7.48 (5H, m, C$H_{aromat.}$), 7.42-7.36 (4H, m, C$H_{aromat.}$), 7.31-7.29 (2H, m, C$H_{aromat.}$), 7.10-7.06 (2H, t, $^3J_{(H,H)}$ = 6.9 Hz, C$H_{aromat.}$), 6.93-6.83 (2H, m, C$H_{aromat.}$), 2.45 (4H, m, $^2J_{(P,H)}$ = 13.3 Hz, $^3J_{(H,H)}$ = 7.0 Hz, PCH(CH$_3$)$_2$), 1.28 (12H, dd, $^3J_{(P,H)}$ = 16.2 Hz, $^3J_{(H,H)}$ = 7.0 Hz, PCH(CH_3)$_2$).

δ_C (100.6 MHz, CD_2Cl_2, r.t., [ppm]): 161.8 (d, $^2J_{(P,C)}$ = 6.2 Hz, $C_{aromat.}$), 139.0 (s, $C_{aromat.}$), 136.3 (s, $C_{aromat.}$), 135.9 (s, $C_{aromat.}$), 135.8 (s, $C_{aromat.}$), 129.0 (s, $C_{aromat.}$), 128.1 (s, $C_{aromat.}$), 126.9 (s, $C_{aromat.}$), 125.6 (d, $^3J_{(P,C)}$ = 16.1 Hz, $C_{aromat.}$), 122.5 (d, $^3J_{(P,C)}$ = 10.8 Hz, $C_{aromat.}$), 29.7 (d, $^2J_{(P,C)}$ = 29.2 Hz, PCH(*C*H$_3$)$_2$), 17.4 (d, PCH(*C*H$_3$)$_2$), 16.4 (d, PCH(*C*H$_3$)$_2$).

δ_P (161.8 MHz, CD_2Cl_2, r.t., [ppm]): 202.8 (s, *P*CH(*C*H$_3$)$_2$, 100%), 201.71 (67%).

CI-MS: m/z = 391.04 [M^+/2-Cl^-, 52%]; 426.01 [M^+/2, 24%]; 817.1 [M^+-Cl^-, 20%]; 851.9 [M^+, 15%].

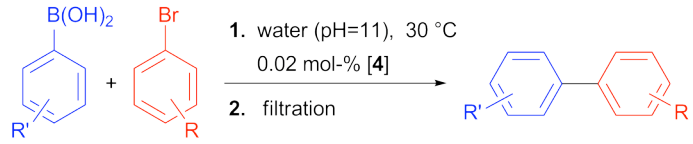
Synthesis of **7**, *$Pd_2Br_4(\mu\text{-}Br)_2(n\text{-}Bu_4N)_2$*

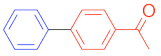
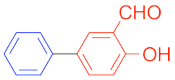
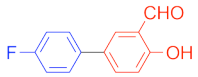
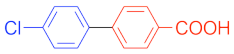
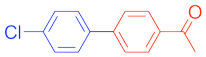
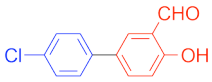
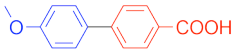
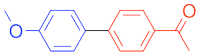
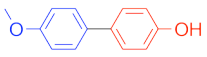
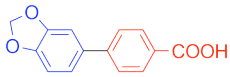
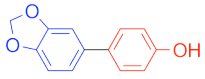
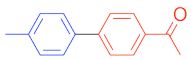
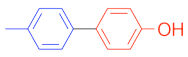
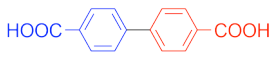
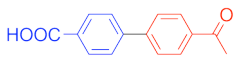
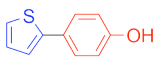
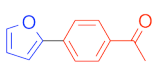
To a stirred suspension of $PdBr_2$ (53.3 mg, 0.20 mmol) in 2 mL of dichloromethane a solution of *n*Bu_4NBr (64.5 mg, 0.20 mmol) in 2 mL of dichloromethane was added. The reaction was stirred over night at r.t.. The solvent was removed *in vacuo* to give a red oil. A brown solid was precipitated by addition of diethylether. The solid was filtered off, washed twice with diethylether and dried in vacuo to give a brown solid. Yield: 0.23 g (0.196 mmol, 98%).

Anal. calcd. for $C_{32}H_{72}N_2Br_6Pd_2$ (1177.19): C, 32.65; H, 6.16; N, 2.38; Br, 40.73; Pd, 18.08. Found: C, 31.98; H 6.10, N, 2.34; Br, 40.48; Pd, 18.90.

4. Cross-Coupling products were analysed for purity by GC-MS, ^{1}H-NMR and elemental analysis. Analytical data correspond to the reported literature values. For respective literature, see table S1.

Table S1 Suzuki cross-coupling products



Entry	Product [a)]	Reference for analytical data
1		G. M. Scheuermann, L. Rumi, P. Steurer, W. Bannwarth, R. Mülhaupt, *J. Am. Chem. Soc.* **2009**, *131*, 8262–8270.
2		J. K. Cho, R. Najman, T. W. Dean, O. Ichihara, C. Müller, M. Bradley, *J. Am. Chem. Soc.* **2006**, *128*, 6276–6277.
3		G. A. Morris and S.B. T. Nguyen, *Tetrahedron Letters* **2001**, *42*, 2093-2096.
4		W. L. Fitch, P. W. Berry, Y. Tu, A. Tabatabaei, L. Lowrie, F. Lopez-Tapia, Y. Liu, D. Nitzan, M. R. Masjedizadeh, A. Varadarajan, *Drug Metabolism and Disposition*, **2004**, *32*, 1482-1490.
5		T. Kylmälä, N. Kuuloja, Y. Xu, K. Rissanen, R. Franzén, *Eur. J. Org. Chem.* **2008**, *23*, 4019-4024.
6		T. Kylmälä, N. Kuuloja, Y. Xu, K. Rissanen, R. Franzén, *Eur. J. Org. Chem.* **2008**, *23*, 4019-4024.
7		M. Braun, A. Hahn, M. Engelmann, R. Fleischer, W. Frank, C. Kryschi, S. Haremza, K. Kürschner, R. Parker, *Chem. Eur. J.* **2005**, *11*, 3405-3412.
8		G. M. Scheuermann, L. Rumi, P. Steurer, W. Bannwarth, R. Mülhaupt, *J. Am. Chem. Soc.* **2009**, *131*, 8262–8270
9		NMR[b)] δ_H (399.8 MHz, $CDCl_3$, r.t., [ppm]): 8.00 (2H, d, $^3J_{(H,H)}$ = 8.5 Hz), 7.65 (2H, d, $^3J_{(H,H)}$ = 8.5 Hz), 7.58 (2H, d, $^3J_{(H,H)}$ = 9.0 Hz), 7.00 (2H, d, $^3J_{(H,H)}$ = 8.5 Hz), 3.86 (3H, s), 2.61 (s, 3H).
10		G. M. Scheuermann, L. Rumi, P. Steurer, W. Bannwarth, R. Mülhaupt, *J. Am. Chem. Soc.* **2009**, *131*, 8262–8270
11		NMR[b)] δ_H (399.8 MHz, $CDCl_3$, r.t., [ppm]): 12.99 (1H, s(br)), 7.96 (2H, d, $^3J_{(H,H)}$ = 8.3 Hz), 7.73 (2H, $^3J_{(H,H)}$ = 8.3 Hz), 7.33 (1H, s), 7.23 (1H, d, $^3J_{(H,H)}$ = 7.9 Hz), 7.03 (1H, d, $^3J_{(H,H)}$ = 8.3 Hz), 6.11 (2H, s).
12		NMR[b)] δ_H (399.8 MHz, $CDCl_3$, r.t., [ppm]): 9.50 (1H, s(br)), 7.39 (2H, d, $^3J_{(H,H)}$ = 8.7 Hz), 7.13 (1H, s), 7.02 (1H, d, $^3J_{(H,H)}$ = 7.9 Hz), 6.92 (1H, d, $^3J_{(H,H)}$ = 8.3 Hz), 6.81 (2H, d, $^3J_{(H,H)}$ = 8.7 Hz), 6.02 (2H, s).
13		J. K. Cho, R. Najman, T. W. Dean, O. Ichihara, C. Müller, M. Bradley, *J. Am. Chem. Soc.* **2006**, *128*, 6276–6277.
14		Haga, N.; Takayanagi, H. *J. Org. Chem.* **1996**, *61*, 735.
15		NMR[b)] δ_H (399.8 MHz, $CDCl_3$, r.t., [ppm]): 13.03 (2H, s(br)), 8.05 (4H, d, $^3J_{(H,H)}$ = 8.7 Hz), 7.86 (4H, $^3J_{(H,H)}$ = 8.3 Hz).
16		M. E. Sigman, T. Autrey, G. B. Schuster *J. Am. Chem. Soc.* **1988**, *110*, 4297-4305.
17		M. P. Capparelli, R. E. DeSchepper, J. S. Swenton *J. Org. Chem.* **1987**, *52*, 4953-4961.
18		A. Ohta, Y. Akita, T. Ohkuwa, M. Chiba, R. Fukunaga, A. Miyafuji, T. Nakata, N. Tani, Y. Aoyagi, *Heterocycles* **1990**, *31* 1951.

Reaction conditions: 2 mmol (1 eq.) 4-bromophenol, 1.0 equiv. boronic acid, 20 ml buffer (1.0 M, NaOH/$NaHCO_3$, pH = 11), air, cat. (0.02 mol% palladacycle **4**). Reaction times not optimized. [a] Carboxylic acids isolated as corresponding sodium salts. [b] No analytical data available.

[1] Blancam, I.; San Martin, R.; Churruca, F.; Domínguez, E.; Urtiaga, M. K.; Arriortua, M. I. *Organometallics* **2008**, *27*, 2833-2839.

[2] Bedford, R. B.; Hazelwood, S. L.; Horton, P. N.; Hursthouse M. B. *Dalton Trans.* **2003**, 4164-4174.