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$Pd(OAc)_2$/*p*-Benzoquinone-Catalyzed Anaerobic Electrooxidative Homocoupling of Arylboronic Acids, Arylboronates and Aryltrifluoroborates in DMF and/or Water

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A new anaerobic electrooxidative homocoupling of arylboronic acids, arylboronates and aryltrifluoroborates was developed in the presence of catalytic amounts of $Pd(OAc)_2$ and *p*-benzoquinone, which serves as a redox mediator for the oxidation of transient Pd^0 to the active Pd^{II} species. The homocoupling was performed in DMF, DMF/water or in pure water. This electrochemical process avoids the use of a stoichiometric amount of chemical oxidants and subsequent formation of co- and by-products.

Introduction

The problem in most Pd^{II}-catalyzed reactions arises from the formation of a Pd^0 moiety that must be oxidized back to the active Pd^{II} species involved in the first step of the catalytic cycle. This problem may be solved by using a chemical oxidant in *stoichiometric* amount. This strategy was successfully developed in the Wacker process,[1] acetoxylation of dienes,[2] Heck-type reactions from arenes,[3] oxidation of alcohols,[4] arylation of arenes by arylboronic acids[5] and homocoupling of arylboronic acids and arylboronates (Scheme 1).[6]

$$2\ \text{Ar-B(OZ)}_2 + \text{oxidant} \xrightarrow{\text{PdX}_2,\ \text{L}} \text{Ar–Ar}$$

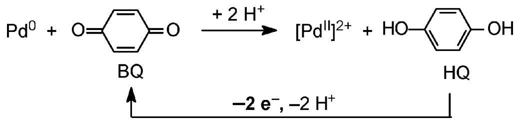
$$\text{Z = H, R; X = OAc, Cl}$$

Scheme 1. Pd-catalyzed homocoupling of arylboronic acids or arylboronates.

The homocoupling of arylboronic acids or arylboronates requires either expensive ligands such as phosphanes (PPh_3,[6a,6b,6d,6f,6i] dppp[6f]), a base,[6c–6e,6g] or a cocatalyst: Cu^{II}.[6c,6f] Some reactions are performed in pure water (but a phase-transfer catalyst is required)[6g] or in organic solvent/water mixtures (where H_2O is minor or in equal volume).[6e,6i] O_2 (or air) is often used as the oxidant.[6a–6d,6f–6j] The mechanism of the Pd-catalyzed homocoupling of arylboronic acids $ArB(OH)_2$ performed in the presence of O_2 with PPh_3 as the ligand has been established.[7] The reaction proceeds by the formation of the peroxo O_2PdL_2 complex, which undergoes transmetallation by $ArB(OH)_2$ leading to subsequent formation of perborate $(HO)_2B–OOH$ as a coproduct. Its hydrolysis releases H_2O_2, whose reaction with $ArB(OH)_2$ gives ArOH as a by-product.[7,6a–6c,6h] Protonolysis of palladium peroxo can also generate H_2O_2.[8a] Molecular sieves have been used to decompose H_2O_2 formed in the catalytic process.[6j]

The use of O_2 as an oxidant may also be problematic, as the rate of homocoupling may be limited by the slow dissolution[8b] and low solubility of O_2 in most solvents, which limits scale up of the reaction (e.g., $[O_2]$ = 5.4 mM at 20 °C,[9] 4.5 mM at 25 °C[8b] in DMF; $[O_2]$ = 1.3 mM at 25 °C in water[8b]).

We have developed an alternative anaerobic procedure for Pd^{II}-catalyzed reactions, such as Heck-type reactions performed from arenes[10a] or oxidation of alcohols to aldehydes or ketones.[10b] $Pd(OAc)_2$ is used as a catalyst in association with a *catalytic* amount of *p*-benzoquinone (BQ), which serves both as a ligand (cheaper than phosphane) for Pd^0 and as an oxidant, as pioneered by Bäckvall.[2,11] The latter reaction generates *p*-hydroquinone (HQ), which is oxidized back to *p*-benzoquinone at an anode (Scheme 2). *p*-Benzoquinone serves as a redox catalyst for the oxidation of Pd^0 to Pd^{II}.[10,11]



Scheme 2. *p*-Benzoquinone-mediated oxidation of Pd^0 to Pd^{II}.

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The same strategy is now used for the homocoupling of arylboronic acids or arylboronates, performed under anaerobic conditions, in DMF, pure H_2O or H_2O/DMF (4:1). The homocoupling was also extended to the unreported homocoupling of aryltrifluoroborates (Scheme 3).

$$2\ \text{Ar-}B \xrightarrow[\text{DMF, H}_2\text{O, 80 °C}]{\text{Pd(OAc)}_2\text{ (10 mol-\%)}\quad p\text{-benzoquinone (10 mol-\%)}} \text{Ar–Ar} + 2\,e^-$$

$$B = \text{B(OH)}_2,\ \text{B(OR)}_2,\ \text{BF}_3^-$$

Scheme 3. Electrooxidative homocoupling of nucleophilic boron derivatives.

Results and Discussion

For all Ar–*B* reagents, the electrolyses were carried out at the same potential of +0.75 V vs. SCE (the oxidation potential of *p*-hydroquinone). The electrolyses were interrupted when the current dropped to background levels.

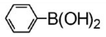
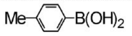
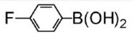
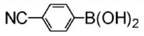
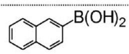
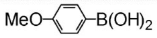
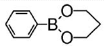
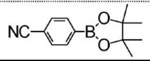
The homocoupling of arylboronic acids was first performed in DMF at 80 °C affording the biaryls in good yields under anaerobic conditions (Table 1). When performed in the absence of *p*-benzoquinone, the current dropped to background levels after 1 h (Table 1, entry 1) due to the formation of nonelectroactive palladium black. Consequently, the remaining $PhB(OH)_2$ could not be further converted into biphenyl and the reaction could not go to completion. In contrast, the reaction went to completion and was quantitative when performed in the presence of 10 mol-% of *p*-benzoquinone (Table 1, entry 2). This emphasizes the crucial role of *p*-benzoquinone, which may serve as a ligand for the transient Pd^0[11] species and oxidize it in a faster reaction than its decomposition to Pd black. Some reactions afforded quantitative yields after passage of 1 Faraday per mol of Ar–$B(OH)_2$ through the cell (Table 1, entries 2,11,13).

Interestingly, the homocoupling of arylboronic acids was also performed in pure water or in H_2O/DMF (4:1) with Na_2SO_4 as supporting electrolyte. Some DMF was added to avoid precipitation of the hydrophobic biaryl at the carbon anode. The reaction was scaled up to 5 mmol (Table 1, entry 5) with a yield even better than on a 1-mmol scale (Table 1, entry 4). The reaction was relatively fast, as 3.7 mmol were converted within 1 h (Table 1, entry 5). All homocouplings were regiospecific and compatible with functional groups.[12] A mechanism for the oxidative homocoupling of arylboronic acids is proposed in Scheme 4.

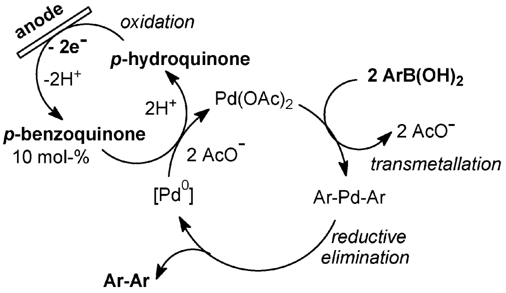
The heterocoupling of $PhB(OH)_2$ (1 mmol) with 4-$CNC_6H_4B(OH)_2$ (2 mmol) was tested under the experimental conditions of Table 1 in DMF. A nonoptimized reaction delivered a mixture of isolated PhPh (0.22 mmol), PhC_6H_4CN (0.39 mmol) and 4-CNC_6H_4–C_6H_4CN (0.51 mmol). 4-$CNC_6H_4B(OH)_2$ was expected to be less reactive than $PhB(OH)_2$ in the transmetallation of $Pd(OAc)_2$ and was consequently added in a larger amount to compensate its lower reactivity. Nevertheless, 4-CNC_6H_4–C_6H_4CN-4 was formed in the largest amount. This suggests that the transmetallation on $Pd(OAc)_2$ by $ArB(OH)_2$ is not so sensitive to the nucleophilicity of arylboronic acids (Scheme 4). This is in agreement with the fact that the rate of the homocoupling of arylboronic acids reported in Table 1 is not significantly affected by the electron-donating or -withdrawing properties of the substituent on the Ar group.

Table 1. $Pd(OAc)_2$/*p*-benzoquinone-catalyzed oxidative homocoupling of arylboronic acids and arylboronates in DMF and/or water.

$$\underset{Z\,=\,\text{H, R}}{2\ \text{Ar-B(OZ)}_2} \xrightarrow[\text{DMF, H}_2\text{O, 80 °C}]{\text{Pd(OAc)}_2\text{ (10 mol-\%)}\quad p\text{-benzoquinone (10 mol-\%)}} \text{Ar–Ar} + 2\,e^-$$

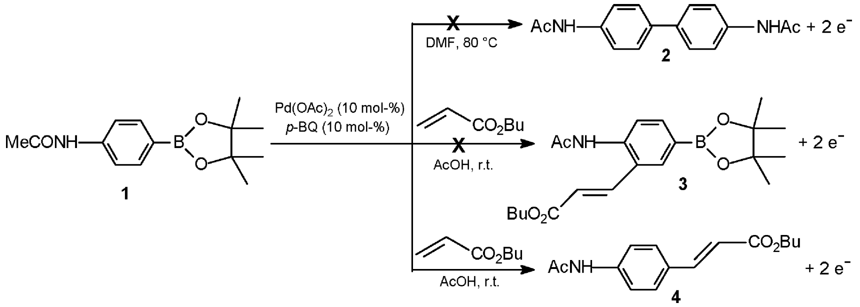
	Ar-B(OZ)$_2$[a]	Solvent	Time [h]	Ar–Ar [%][b,c]	Ar–*B* Rec. [%][b]
1		DMF[d]	1:00	54	46
2		DMF	2:10	99	0
3		H_2O	2:00	66	23
4		H_2O/DMF (4:1)	0:50	62	0
5		H_2O/DMF (4:1)[e]	0:48	75 (61)	24
6		DMF	0.35	(81)	0
7		H_2O	1:15	55	21
8		H_2O/DMF (4:1)	0:48	93	7
9		DMF	0:35	75	0
10		H_2O/DMF (4:1)	0:37	52	12
11		DMF	1:10	99	0
12		H_2O	2:30	65	5
13		DMF	1:10	99	0
14		H_2O/DMF (4:1)	2:30	82	0
15		DMF	0:20	32	–
16		DMF	1:10	67	0
17		H_2O/DMF (4:1)	0:30	68	0
18		DMF	1:20	68	30
19		H_2O/DMF (4:1)	0:45	29	18

[a] 1 mmol in 10 mL of solvent, either DMF (containing nBu_4NBF_4, 0.3 M), H_2O (containing Na_2SO_4, 0.3 M) or H_2O/DMF (4:1) (containing Na_2SO_4, 0.3 M). [b] Yields related to the initial $ArB(OR)_2$ were determined after work up by ^1H NMR spectroscopy by using $Cl_2CHCHCl_2$ as an internal standard. [c] Isolated yield in parentheses. [d] Without *p*-benzoquinone. [e] 5 mmol in 50 mL of H_2O/DMF (4:1) (containing Na_2SO_4, 0.3 M).



Scheme 4.

The homocoupling of arylboronates was performed in DMF or H_2O/DMF (4:1) (Table 1, entries 16–19) although they are less water soluble than arylboronic acids. The homocoupling of aryboronate **1** did not afford expected biaryl **2** (Scheme 5). First of all, a faster C–H activation by $Pd(OAc)_2$ than transmetallation was postulated, as ob-



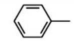
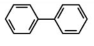
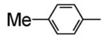
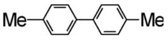
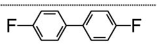
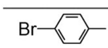
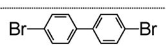
Scheme 5. Tentative Pd(OAc)$_2$/*p*-benzoquinone-catalyzed electrooxidative reactions from **1**.

served in Heck-type reactions performed with arenes substituted by the *ortho*-directing acetamido group.[10a] Such a reaction could have served as a quencher for the Pd^{II} catalyst, but when **1** was treated with $CH_2=CHCO_2nBu$ under the experimental conditions developed by us for the vinylation of arenes,[10a] expected alkene **3** was not produced (Scheme 5). Instead, the reaction gave compound **4** formed in an unprecedented electrooxidative Heck reaction,[13] which involves monotransmetallation of Pd(OAc)$_2$ by the arylboronate. The reason why **2** was not formed must arise from the unfavourable second transmetallation from Pd(OAc)$_2$ (Scheme 4).

To the best of our knowledge, the Pd^{II}-catalyzed homocoupling of aryltrifluoroborates in the presence of a stoichiometric oxidant (as O_2 or air) has never been reported.[14] It was first checked that the aryltrifluoroborates investigated herein were not oxidized in DMF in the range 0 to +1.6 V vs. SCE (gold disk electrode, d = 1 mm, scan rate = 0.5 V s^{-1}). In the presence of Pd(OAc)$_2$ (10 mol-%) and *p*-benzoquinone (10 mol-%), the oxidative homocoupling proceeded with good yields under anaerobic conditions in DMF (Table 2). The electrooxidative homocoupling of ionic $PhBF_3^-K^+$, which could serve as supporting electrolyte, was tested in DMF in the absence of the usual supporting electrolyte nBu_4NBF_4. The reaction was slower and 32% of Ph–Ph was formed (Table 2). Because aryltrifluoroborates are water soluble, the homocoupling was performed in pure water. However, the reactions were more efficient when conducted in H$_2$O/DMF (4:1) (Table 2). The homocoupling was regiospecific and good compatibility was observed in the *para*-bromo derivative, which indicates that the Pd^0 species formed in the catalytic cycle was oxidized to Pd^{II} before undergoing oxidative addition at the C–Br bond.

Table 2. Pd(OAc)$_2$/*p*-benzoquinone-catalyzed oxidative homocoupling of aryltrifluoroborates (K$^+$ salts) in DMF and/or water.

$$2\ \text{Ar-BF}_3^- \xrightarrow[\text{DMF, H}_2\text{O, 80 °C}]{\text{Pd(OAc)}_2\text{ (10 mol-\%)},\ p\text{-benzoquinone (10 mol-\%)}} \text{Ar–Ar} + 2\,e^- + 2\ \text{BF}_3$$

Ar–BF$_3^-$ [a]	Solvent	Time [h]	Ar–Ar yield [%][b]	
	DMF	0:24	76	
	DMF[c]	0:28	32	
	H$_2$O	1:00	68	
	DMF	0:30	41	
	H$_2$O	1:15	55	
	H$_2$O/DMF (4:1)	0:23	94	
	DMF	0:35	87	
	H$_2$O/DMF (4:1)	0:30	89	
	DMF	0:40	99	
	H$_2$O	2:30	65	
	H$_2$O/DMF (4:1)	0:50	74	

[a] 1 mmol of ArBF$_3$K in 10 mL of solvent, DMF (containing nBu_4NBF_4, 0.3 M), H$_2$O (containing Na$_2$SO$_4$, 0.3 M) or H$_2$O/DMF (4:1) (containing Na$_2$SO$_4$, 0.3 M). [b] Yields related to the initial ArBF$_3^-$ were determined after work up by ^{1}H NMR spectroscopy by using Cl$_2$CHCHCl$_2$ as an internal standard. The amount of recovered ArBF$_3^-$ (remaining in the aqueous phase) was not determined. [c] Without nBu_4NBF_4.

Conclusions

We developed a simple anaerobic, quite fast electrooxidative homocoupling of aryl boronic acids, arylboronates and aryltrifluoroborates catalyzed by ligandless Pd(OAc)$_2$ and *p*-benzoquinone. This procedure avoids the use of stoichiometric chemical oxidants (as O$_2$), the formation of peroxo moieties and subsequent by-products. The homocoupling can be performed in pure water. The reaction involves cheap and water-soluble supporting electrolyte (Na$_2$SO$_4$) as well as cheap and water-soluble *p*-benzoquinone as a redox mediator. Work is in progress on the heterocoupling of arylboron derivatives and on the homocoupling of aryl and vinylstannanes.

Experimental Section

General Procedure for Preparative Electrolysis Performed from Potassium Aryltrifluoroborates: The electrosynthesis of 4,4′-dimethylbiphenyl (Table 2) was performed under an atmosphere of argon at 80 °C in a two-compartment cell. The two compartments were separated by a sintered glass disk. The cathode was a nickel foam (ca. 1 cm^2 surface area). The anode was a carbon cloth (ca. 4 cm^2 surface area). The reference was a saturated calomel electrode separated from the solution by a bridge filled with a solution of Na$_2$SO$_4$ (0.3 M) in H$_2$O/DMF (4:1). The anodic and cathodic compartments were respectively filled with 10 and 2 mL of H$_2$O/DMF (4:1) containing Na$_2$SO$_4$ (0.3 M). Potassium 4-methylphenyltrifluoroborate (198 mg, 1 mmol) was added into the anodic compartment followed by sublimed *p*-benzoquinone (11 mg, 0.1 mmol) and Pd(OAc)$_2$ (22 mg, 0.1 mmol). Acetic acid (150 µL, 2.6 mmol) was introduced into the cathodic compartment (reduction of protons during the electrolysis). The electrolysis was carried out at a controlled potential of +0.75 V by using a Tacussel PJT 35-2 potentiostat. The electrolysis was stopped when the current dropped to background levels, after 23 min. A charge of 110 C was passed through the cell (theoretical charge: 106 C). After cooling to room temperature, the anodic compartment was hydrolyzed with water (40 mL). After extraction with diethyl ether, the organic phase was dried with $MgSO_4$, and the solvents were evaporated. The yield of 4,4′-dimethylbiphenyl (94%) was determined on the crude product by ^{1}H NMR (250 MHz) spectroscopy by using $Cl_2CHCHCl_2$ (0.5 mmol) as an internal standard. 4,4′-Dimethylbiphenyl was isolated as a pure compound (white powder) by flash chromatography (petroleum ether/ethyl acetate, 95:5). M.p. 119 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.31 (s, 6 H, CH_3), 7.16 (d, J = 7.6 Hz, 4 H, *o-H* relative to CH_3), 7.41 (d, J = 7.6 Hz, 4 H, *m-H* relative to CH_3) ppm. ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 20.03, 125.76, 128.39, 135.63, 137.25 ppm. MS (EI): *m/z* = 182 $[M]^+$, 167 (100), 152. Data are similar to those of an authentic sample.[15]

The electrosyntheses of the biaryls reported in Tables 1 and 2 are depicted in the Supporting Information

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra and MS of the biaryl products.

Acknowledgments

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[12] The fate of the $B(OH)_2$ moiety released in the reaction was not investigated. $B(OH)_3$ must be formed after work up.

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