Electrochemical generation of silver acetylides from terminal alkynes with a Ag anode and integration into sequential Pd-catalysed coupling with arylboronic acids[†]

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An electro-oxidative method for generating silver acetylides from acetylenes with a Ag anode was developed. The reaction could be integrated into a Pd-catalysed electrochemical Sonogashira-type reaction. In the presence of the catalytic amount of $Pd(OAc)_2$ and 4-BZO-TEMPO, electro-generated silver acetylides reacted immediately with arylboronic acids to afford the corresponding coupling adducts in high yields.

Silver acetylides are among the oldest organometallics and several applications to organic syntheses have been reported.^{1,2} The most common methods for preparing silver acetylides are (i) the reaction of terminal alkynes with silver salts such as silver nitrate and silver triflate, and (ii) the reaction of alkynylsilanes with silver salts.

$$\mathsf{R} \xrightarrow{} \begin{array}{c} \mathsf{AgNO}_3 \text{ or } \mathsf{AgOTf} \\ \hline \mathsf{base} \end{array} \xrightarrow{} \begin{array}{c} \mathsf{R} \xrightarrow{} \begin{array}{c} \mathsf{Ag} \end{array} \xrightarrow{} (i)$$

$$\mathsf{R} \xrightarrow{} \mathsf{SiR}_3 \xrightarrow{} \mathsf{AgNO}_3 \text{ or AgOTf} \xrightarrow{} \mathsf{R} \xrightarrow{} \mathsf{Ag}$$
(ii)

We have been interested in the electrochemical transformation of organometallics and in reactions which involve thus-generated organometallic species.³ During the course of our study, we found that terminal alkynes were transformed easily to silver acetylides under the electro-oxidative conditions with a Ag anode (Scheme 1). This electrochemical system for the generation of silver acetylides could be readily integrated into an electro-oxidative reaction. The advantage of the reaction is that the synthesis and reaction of silver acetylide proceeded simultaneously in one reactor. We report here a facile electrochemical method for the synthesis of silver acetylides and integration of this method to the Pd-catalysed electro-oxidative coupling of arylboronic acids and terminal alkynes.⁴



Scheme 1 Strategy for the electro-oxidative synthesis of silver acetylides.

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 Table 1
 Electro-oxidative synthesis of several silver acetylides^a

 DBU (2 equiv)

	R-=== 1 Ag electro	anode R——Ag poxidation 2	
Entry	1	2	$\operatorname{Yield}^{b}(\%)$
1	() la	Ag 2a	88
2	-<		65
3 ^{<i>c</i>}	Br - lc	Br- Ag ₂ c	70

^a Reaction conditions: 1 (0.2 mmol), DBU (2 equiv.), CH₃CN (10 mL),
 ⁵ mA, 1 F mol⁻¹. ^b Isolated yield. ^c 1.5 F mol⁻¹.

 Table
 2
 Pd/TEMPO-catalysed
 electro-oxidative
 coupling
 of

 phenylacetylene and phenylboronic acid with several bases^a

Pd(OAc)₂/TEMPO base CH₃CN/H₂O (7/1) Ag anode electrooxidation Entry Base Yield^b (%) Et₃N 51 1 2 DBU 81 3 DABCO 42 K₂CO₃ 4 24 None 5

^{*a*} Reaction conditions: **1a** (0.5 mmol), **3a** (0.5 mmol), Pd(OAc)₂ (10 mol%), TEMPO (30 mol%), base (2 equiv.), NaClO₄ (0.2 M), CH₃CN/H₂O (7/1), 50 mA, 4 F mol⁻¹. ^{*b*} Isolated yield.

Table 3 Pd/TEMPO-catalysed electro-oxidative coupling ofphenylacetylene and phenylboronic acid with several anodes^a

	1a	+	3а	Pd(OAc) ₂ /TEMPO additive/DBU	4aa
				CH ₃ CN/H ₂ O (7/1) Ag anode electrooxidation	
Entry	Anode		ode	Additive	Yield ^b (%)

1	Ag	None	81
2	Cu	None	56
3	Pt	None	5
4	Pt	Ag wire	36
5	Pt	Cu wire	2

^{*a*} Reaction conditions: **1a** (0.5 mmol), **3a** (0.5 mmol), $Pd(OAc)_2$ (10 mol%), TEMPO (30 mol%), DBU (2 equiv.), $NaClO_4$ (0.2 M), CH_3CN/H_2O (7/1), 50 mA, 4 F mol⁻¹. ^{*b*} Isolated yield.

We first chose silver phenylacetylide (2a) as a target compound (Table 1). Electro-oxidation was performed in a two-compartment cell divided by a glass filter. To the anodic chamber was added a solution of terminal alkyne 1a (0.2 mmol) and DBU (1,8-diazabicyclo[5.4.0]undec-7-ene, 2.0 equiv.) in 0.05 M Et₄NOTs/CH₃CN (10 mL), and to the cathodic chamber was added a solution of 0.05 M Et₄NOTs/ CH₃CN (10 mL). Constant-current electrolysis of the solution afforded silver acetylide 2a in 88% yield (entry 1). Similarly, silver acetylides 2b and 2c could be obtained in respective yields of 65% and 70% (entries 2 and 3).

We next investigated the integration of this electrochemical synthesis of silver acetylides to Pd-catalysed coupling with arylboronic acids. First, the electro-oxidative coupling of phenylacetylene (**1a**) and phenylboronic acid (**3a**) was carried out in the presence of several bases (Table 2). In the presence of Pd(OAc)₂ (10 mol%), TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl, 30 mol%), and Et₃N (2 equiv.), the electrooxidative coupling reaction proceeded smoothly to afford product **4aa** in 51% yield (entry 1). Further screening revealed that the addition of DBU was highly advantageous for the reaction, and the yield of **4aa** increased drastically up to 81% (entry 2). The addition of DABCO (1,4-diazabicyclo[2.2.2]octane) or potassium carbonate did not promote the reaction efficiently

(entries 3 and 4). The addition of base was indispensable for the reaction. Without base, the yield of **4aa** decreased to 5% (entry 5).

To evaluate the utility of the obtained silver acetylide, several different anodes were used in the reaction (Table 3). With a Cu anode, the reaction also proceeded to afford internal alkyne **4aa** in 56% yield (entry 2). In contrast, only a trace amount of **4aa** was obtained with a Pt anode, which could not act as a sacrificial anode (entry 3). These results suggest that the generation of a metal acetylide, such as silver acetylide or copper acetylide, might be essential for the reaction. We next examined the reaction with a Pt anode in the presence of Ag wire in the reaction mixture. The reaction proceeded, and **4aa** was obtained in 36% yield (entry 4). The lower yield compared to that of entry 1 might be due to the lower efficiency of the generation of silver acetylide.

To exploit the utility of this reaction, the scope of the reaction was investigated (Table 4). During the course of the optimization of the conditions, we found that the amount of $Pd(OAc)_2$ could be reduced to 5 mol%, and 4-BzO-TEMPO was a better mediator than TEMPO. The electro-oxidative coupling of 1a and 3a afforded 4aa in 93% yield under the optimized conditions (entry 1). Unexpectedly, the reaction also proceeded without a mediator to afford 4aa in a similar yield.

 Table 4
 Pd-catalysed electro-oxidative coupling of terminal alkynes and arylboronic acids^a

$R^{1} \longrightarrow + (HO)_{2}B - R^{2} \xrightarrow{Pd(OAc)_{2}/mediator} R^{1} \longrightarrow R^{2}$ $1 \qquad 3 \qquad electrooxidation \qquad 4$							
Entry	1	3	4	$\mathrm{Yield}^{b}\left(\%\right)$			
1	((HO) ₂ B	√→→→→→→→→→→→→→→→→→→→→→→→→→→→→→→→→→→→→	93 (91) ^c			
2 ^{<i>d</i>}	() — 1a	(HO) ₂ B-OPh 3b	⟨_>-=-⟨_>-oph _{4ab}	91			
3 ^{<i>d</i>}	() — 1a	(HO) ₂ B	()-=-()-'Bu 4ac	99 (42) ^c			
4	() — 1a	(HO) ₂ B-CI 3d	CCl _{4ad}	91 (84) ^c			
5 ^{<i>d</i>}	→	(HO) ₂ B-Ac 3e	Ac 4ae	76 (77) ^c			
6	-<->-=1b	(HO) ₂ B3f		99			
7	-<->-=_1b	(HO) ₂ B-Ac 3e	- Ac 4be	95 ^c			
8	-<->-=1b	(HO) ₂ B		96 ^c			
9^d	0 ₂ N-	(HO) ₂ B	0 ₂ N-{	80^c			
10 ^{<i>d</i>}	0 ₂ N-{	$(HO)_2B \longrightarrow Ac_3e$	O ₂ N- Ac 4de	76			

^{*a*} Reaction conditions: 1 (0.5 mmol), 3 (0.5 mmol), Pd(OAc)₂ (5 mol%), 4-BzO-TEMPO (15 mol%), DBU (2 equiv.), NaClO₄ (0.2 M), CH₃CN/ H₂O (7/1), 50 mA, 4 F mol⁻¹. ^{*b*} Isolated yield. ^{*c*} Without mediator. ^{*d*} 10 mA of electricity was passed.



Fig. 1 A plausible mechanism for the electro-oxidative coupling of terminal alkynes and arylboronic acids.

For arylboronic acids bearing an electron-donating group, the addition of mediator was essential. In the reaction of **1a** with **3b** or **3c**, the reactions proceeded smoothly to afford **4ab** and **4ac** in respective yields of 91% and 99% (entries 2 and 3). In contrast, in the reaction of electron-deficient arylboronic acids, the electro-oxidative reaction was not affected by the mediator (entries 4 and 5). *p*-Tolylacetylene (**1b**) exhibited high reactivity in the reaction, and the corresponding alkynes **4** were obtained in excellent yields (entries 6–8). In contrast, when *p*-nitrophenylacetylene (**1d**) was used, the yields of **4** were slightly lower than those of **1a** and **1b** (entries 9 and 10). We assumed that this difference is due to the efficiency of the generation of silver acetylide. Electron-rich alkynes would interact efficiently with Ag⁺, and silver acetylide would be generated faster than electron-deficient alkynes.

A plausible mechanism for the coupling reaction is illustrated in Fig. 1. First, $R^{1}Pd(\Pi)L_{n}$ (L = ligand) would be generated from Pd(Π) and arylboronic acid. Following transmetallation with silver acetylide would give an alkynylpalladium intermediate, and subsequent reductive elimination would afford the coupling product and Pd(0) species.⁵ Pd(II) complex would be regenerated through the oxidation by *N*-oxoammonium cation, which would be generated by the electro-oxidation of 4-BzO-TEMPO. In the absence of 4-BzO-TEMPO, silver species would act as a mediator.

In summary, we have developed an electro-oxidative method for preparing silver acetylides. The *in situ* integration of the synthetic procedure of silver acetylides and the Pd-mediatory electro-oxidative cross-coupling with arylboronic acids were also successful. The further application of this strategy is being studied in our laboratory.

Notes and references

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- 5 Another plausible mechanism is that transmetallation with a silver acetylide would be the first step, and following transmetallation with arylboronic acid and reductive elimination would afford the coupling product. The details of the mechanism is currently under investigation.