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Electron-Catalyzed Cross-Coupling Reaction of Arylboron Compounds with Aryl Iodides**

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Abstract: Arylboroxines in combination with zinc chloride and potassium tert-butoxide were found to undergo the electron-catalyzed cross-coupling reaction with aryl iodides to give the corresponding biaryls with no aid of transition metal catalysis.

The transition metal-catalyzed cross-coupling reaction of arylmetals with aryl halides is one of the most useful and powerful methods for biaryl synthesis.^[1] Among these, the Suzuki–Miyaura coupling reaction, employing arylboron compounds as arylmetals, is one of the most widely used ones due to the high stability and high availability of the reagents and the high functional group tolerance of the reaction.^[2] On the other hand, since the finding by our group on the first electron-catalyzed cross-coupling reaction, where aryl Grignard reagents are employed and an electron derived from them instead of a transition metal acts as a catalyst,^[3] we and other groups have reported the transition metal-free cross-coupling reaction of arylmetals (Zn^[4]/Al^[5]/Sn^[6]) as well as alkyl-^[7] and alkynylzinc^[8] reagents.^[9,10] Here we report that arylboron compounds are utilized as aryl nucleophiles, for the first time, in the electron-catalyzed cross-coupling reaction with the aid of a zinc reagent such as diethylzinc and zinc chloride/potassium *tert*-butoxide.^[11]

Many reports are available on preparation of arylzinc reagents from arylboronic acids by treating with an excess amount of diethylzinc.^[12,13] Then we anticipated that thus prepared arylzinc reagents undergo the electron-catalyzed cross-coupling reaction. However, treatment of phenylboronic acid (**1a**: 2 equiv) with Et₂Zn (6 equiv) in THF at 23 °C for 1 h followed by the reaction with 4iodoanisole (**2a**) in toluene/THF (1:3) at 110 °C for 24 h did not give the corresponding coupling product, 4-methoxybiphenyl (**3aa**), at all with a low conversion of **2a** (Table 1, entry 1). In contrast, rather surprisingly, use of a much decreased amount (1.5 equiv) of Et₂Zn promoted the coupling to some extent (19% yield of **3aa** with 22% conv. of **2a**) (Table 1, entry 2). Addition of LiCl (1.5 equiv), an effective accelerator in the previous electron-catalyzed crosscoupling reactions,^[3c,4b,6] led to a full conversion of **2a** to give **3aa** in a high yield (Table 1, entry 3). No reaction took place in the absence of diethylzinc (Table 1, entry 4).

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Table 1: Effect of the amounts of diethylzinc and lithium chloride in the coupling of phenylboronic acid (1a) with 4-iodoanisole (2a).^[a]

PhB(OH) ₂ 1a (2.0 equiv)	+	Et ₂ Zn	LiCI THF 23 °C, 1	I tolu h 110	OMe 2a ene/THF (1:3) °C, 24 h))	Ph — — — — 3aa	-ON
Entry		Et₂Zn	Li	CI	Conv. of		Yield of	
		(equiv)	(e	quiv)	2a (%) ^[b]		3aa (%) ^[b]	
1		6	0		9		<1	
2		1.5	0		22		19	
3		1.5	1.8	5	>99		95 (93) ^[c]	
4		0	1.	5	3		<1	

[a] A toluene solution of diethylzinc (1.2 mmol for entry 1; 0.30 mmol for entries 2 and 3) was added to phenylboronic acid (**1a**: 0.40 mmol) in THF in the presence or absence of lithium chloride (0.30 mmol) under a nitrogen atmosphere. After stirring the resulting mixture at 23 °C for 1 h, addition of 4-iodoanisole (**2a**: 0.20 mmol, 0.22 M) was followed by stirring at 110 °C for 24 h. [b] Determined by GC based on **2a**. [c] Yield of the isolated product based on **2a**.

The electron-catalyzed cross-coupling reaction of phenylboronic acid (1a) by use of Et₂Zn (1.5 equiv) was found to be applicable to iodobenzene having an alkyl or ester substituent (Scheme 1, top). However, the coupling reaction was found to show a low reproducibility, depending on arylboronic acids used. For example, the reaction of 4-methoxyphenylboronic acid (1b) with ethyl 4-iodobenzoate (2c) resulted in a low yield with a low conversion (Scheme 1, top). Analysis of the purity of 1b used here showed that it contains a certain amount of the corresponding boroxine (boronic acid/boroxine = 63/37),^[14] prompting us to consider that arylboroxines are unreactive in this coupling. Actually, the boronic acid/boroxine ratio with a phenylboron system was found to affect the conversion and the yield, where genuine phenylboroxine have an extremely low reactivity (Scheme 1, bottom). The property of arylboronic acids to be transformed into the corresponding arylboroxines by spontaneous dehydoration potentially damages the reproducibility of this method.



Scheme 1. Coupling of arylboronic acids with aryl iodides using diethylzinc as an activator.

In order to develop a more reliable cross-coupling system using arylboron compounds, we investigated what kind of species is generated at the starting point of the cross-coupling reaction by analyzing the mixture (A in Scheme 2) after treatment of phenylboronic acid (1a) with Et₂Zn (0.75 equiv) in the presence of lithium chloride (0.75 equiv) in toluene- d_8 -THF- d_8 (1:2) at 23 °C for 1 h (cf. Table 1, entry 3). In the ¹H NMR spectrum of mixture A, no peaks of Et-B and Et-Zn but Et-H were observed as those derived from the ethyl group of Et₂Zn (Scheme 2, top), showing that no Zn-B transmetalation takes place at this point, where each Et-Zn unit of Et₂Zn works as a base to abstract protons from the hydroxyl groups of PhB(OH)2 to give arylboron species I having a Ph-B-O-Zn sequence (Scheme 2, top right). The observation that the C-B bond of 1a is not cleaved at this stage was further confirmed by the outcome that the phenylboron unit was trapped as the corresponding boronate in 84% yield upon treatment of a mixture, prepared in the same way as above (mixture A) but in nondeuterated solvents, with 2,2-dimethyl-1,3-propanediol (3 equiv) and ammonium chloride (1.5 equiv) followed by MgSO₄ (Scheme 2, bottom). However, after treatment of 1a with Et₂Zn and LiCl for 1 h at 110 °C instead of 23 °C, the phenylboron unit remained only in 20%, showing that, under the cross-coupling conditions at a high temperature, the phenylboron species is converted to some others, which are likely to be the real active species for the cross-coupling reaction. We anticipated that, if we prepare a species of type I having a Ph-B-O-Zn sequence in whatever way, it should be converted at a high temperature into some active species that can undergo the coupling with aryl iodides. We expected that treatment of arylboroxines with ZnCl₂ and KOt-Bu as shown in Scheme 3 gives species II that is suitable for this purpose. This method will be advantageous over the previous one because no organometallic reagents such as Et₂Zn are required and the boronic acid/boroxine equilibrium does not matter under anhydrous conditions.



Scheme 2. Elucidation of the species generated by mixing an arylboronic acid and diethylzinc.



Scheme 3. Working hypothesis to generate arylboron species ready for the cross-coupling.

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As we expected, arylboroxine-derived species underwent the coupling reaction, though some modification was required. After stirring a mixture of phenylboroxine (4a: 1.5 equiv), ZnCl₂ (1.5 equiv) and KOt-Bu (3.0 equiv) in THF at 23 °C for 1 h, the resulting mixture was treated with 4-iodoanisole (2a) at 110 °C for 24 h to give 4-methoxybiphenyl (3aa) in 15% yield with 19% conversion of 2a (Table 2, entry 1). An increased amount (2.4 equiv) of ZnCl₂ enhanced the reactivity, where reduction of the amount (1.8 equiv) of KOt-Bu did not affect the yield (Table 2, entries 2 and 3). Use of N-methylpyrrolidone (NMP) as a solvent instead of THF drastically improved the conversion and the yield (Table 2, entry 4), where reduction of the amounts of the reagents keeping the ratio among these $(4a/ZnCl_2/KOt-Bu = 1.2/2.1/1.5)$ also worked (Table 2, entry 5). Use of a weaker base was ineffective (Table 2, entries 6 and 7).^[15] No coupling product was obtained in the absence of ZnCl₂, where anisole was the major product (60% yield) (Table 2, entry 8).^[16]

Table 2: Effect of the amounts of zinc chloride and potassium *tert*butoxide in the coupling of phenylboroxine with 4-iodoanisole.^[a]

(F	hBO) ₃ 4a	+ ZnCl ₂ ·	+ KO <i>t</i> -Bu	solvent 11 23 °C, 1 h	OMe 2a 0 °C, 24 h	Ne → Ph → OMe 3aa		
	Entry	4a (equiv)	ZnCl₂ (equiv)	Base (equiv)	Solvent	Conv. of 2a (%) ^[b]	Yield of 3aa (%) ^[b]	
	1	1.5	1.5	KO <i>t</i> -Bu (3.0)	THF	19	15	
	2	1.5	2.4	KO <i>t</i> -Bu (3.0)	THF	46	38	
	3	1.5	2.4	KO <i>t</i> -Bu (1.8)	THF	42	40	
	4	1.5	2.4	KO <i>t</i> -Bu (1.8)	NMP	>99	99	
	5	1.2	2.1	KO <i>t</i> -Bu (1.5)	NMP	>99	98	
	6	1.2	2.1	K ₃ PO ₄ (1.5)	NMP	3	1	
	7	1.2	2.1	K ₂ CO ₃ (1.5)	NMP	8	2	
	8	1.2	0	KO <i>t</i> -Bu (1.5)	NMP	98	<1	
	· · ·		<i>.</i> .					

[a] To a mixture of phenylboroxine (**4a**), zinc chloride and potassium *tert*butoxide was added THF (1.0 mL for entries 1–3) or NMP (1.0 mL for entries 4–8). After stirring the resulting mixture at 23 °C for 1 h, addition of 4-iodoanisole (**2a**: 0.50 mmol, 0.50 M) was followed by stirring at 110 °C for 24 h. [b] Determined by GC.

The coupling of arylboroxines with aryl iodides using the combination of ZnCl₂ and KOt-Bu showed a wide scope (Table 3). Phenyl iodides having an electron-donating or -withdrawing group at the *para*- or *meta*-position underwent coupling with phenylboroxine (**4a**) in high yields (Table 3, entries 1–6). *ortho*-Substituted phenyl iodides also reacted with **4a** (Table 3, entries 7 and 8). The coupling is applicable also to heteroaryl iodides (Table 3, entries 9–11). As for arylboroxines, both electron-donating and - withdrawing substituents at *para*-position are tolerant (Table 3, entries 12–18). In addition to arylboroxines, heteroarylboroxines underwent coupling (Table 3, entries 19 and 20).

As described above, some active species are considered to be generated at a high temperature from $(Ar^1BO)_3/ZnCl_2/KOt$ -Bu via arylboron species having a Ar^1 -B-O-Zn sequence such as II. Such an active species, designated as Ar^1 -Y here, is likely to undergo coupling with an aryl iodide (I-Ar²) through the same mechanism as the previous electron-catalyzed cross-coupling reaction of aryl magnesium and -zinc reagents as shown in Scheme 4.^[3,4b] Namely, single electron transfer (SET) from Ar^1 -Y to I-Ar² gives [I-Ar²]^{•-}, which reacts with Ar^1 -Y to give $[Ar^1$ -Ar²]^{•-}. SET from $[Ar^1$ -Ar²]^{•-} to I-Ar² gives Ar^1 -Ar² and regenerates $[I-Ar^2]^{•-}$.^[17,18,19] The involvement of the anion radical intermediates is strongly supported

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Table 3: Coupling of arylboroxines with aryl iodides using zinc chloride and potassium *tert*-butoxide as activators.^[a]

(4-100)	+	ZnCl	+	KOt Bu		Ar1_Ar2	
(APBO) ₃ 4	т	211012	т	KOI-Bu	NMP, 23 °C, 1 h	110 °C, 24 h	3
(1.2 equiv)	(2	2.1 equiv	()	(1.5 equiv)			

Entry	Ar ¹ in 4	Ar ² in 2	Time (h)	Yield (%) ^[b]	Prod.
1	Ph (4a)	4-MeOC ₆ H ₄ (2a)	24	95	3aa
2	Ph (4a)	4-MeC ₆ H ₄ (2b)	48	87	3ab
3	Ph (4a)	4-EtO ₂ CC ₆ H ₄ (2c)	24	83	3ac
4	Ph (4a)	$4-CF_{3}C_{6}H_{4}(2d)$	24	91	3ad
5	Ph (4a)	4-CIC ₆ H ₄ (2e)	48	93	3ae
6	Ph (4a)	3-EtO ₂ CC ₆ H ₄ (2f)	24	92	3af
7 ^[c]	Ph (4a)	2-PhC ₆ H ₄ (2g)	48	92	3ag
8 ^[c]	Ph (4a)	2-(3-butenyl)C ₆ H ₄ (2h)	24	92	3ah
9 ^[c]	Ph (4a)	6-quinolyl (2i)	48	81	3ai
10 ^[c]	Ph (4a)	2-dibenzothiophenyl (2j)	24	93	3aj
11 ^[c]	Ph (4a)	3-(9-phenyl)carbazolyl (2k)	24	90	3ak
12	$4\text{-}\text{MeOC}_6\text{H}_4~(\textbf{4b})$	4-EtO ₂ CC ₆ H ₄ (2c)	24	87	3bc
13	$4\text{-}\text{MeOC}_6\text{H}_4~(\textbf{4b})$	$4-CF_{3}C_{6}H_{4}(2d)$	24	96	3bd
14	$4-CF_{3}C_{6}H_{4}$ (4c)	4-MeOC ₆ H ₄ (2a)	48	92	3ca
15	$4-CF_{3}C_{6}H_{4}$ (4c)	4-EtO ₂ CC ₆ H ₄ (2c)	24	88	3cc
16	4-CIC ₆ H ₄ (4d)	Ph (2I)	48	90	3dl
17 ^[c]	4-CIC ₆ H ₄ (4d)	4-MeOC ₆ H ₄ (2a)	48	95	3da
18 ^[c]	4-CIC ₆ H ₄ (4d)	4-EtO ₂ CC ₆ H ₄ (2c)	24	86	3dc
19 ^[d]	2-thiophenyl (4e)	4-EtO ₂ CC ₆ H ₄ (2c)	48	91	3ec
20	3-furyl (4f)	4-EtO ₂ CC ₆ H ₄ (2c)	24	97	3fc

[a] To a mixture of an arylboroxine (4: 1.2 equiv), zinc chloride (2.1 equiv) and potassium *tert*-butoxide (1.5 equiv) was added NMP (1.0 mL). After stirring the resulting mixture at 23 °C for 1 h, addition of an aryl iodide (2: 0.50 mmol, 0.50 M) was followed by stirring at 110 °C for 24 or 48 h. [b] Yield of the isolated product based on **2**. [c] An arylboroxine (4: 1.5 equiv), zinc chloride (2.4 equiv) and potassium *tert*-butoxide (1.8 equiv) were used. [d] At 140 °C.

by the experiments shown in Scheme 5. The reaction of phenylboroxine (4a) with 4-bromo(iodo)benzene (2m) using $ZnCl_2$ and KOt-Bu (4a/ZnCl₂/KOt-Bu = 1.2/2.1/1.5) in a short reaction period (30 min) gave *p*-terphenyl (3'am), the bisphenylation product of 2m, in preference to 4-bromobiphenyl (3am), a monophenylation product of 2m (Scheme 5, eq. 1). The result is rationally understood as follows: anion radical IV of 4-bromobiphenyl, generated from 2m through the usual pathway





Scheme 5. Verification of the involvement of anion radical intermediates.

consisting of SET to 2m and the reaction of the resulting anion radical (III) with Ph–Y, undergoes reaction with another Ph–Y, leading to $3^{\circ}am$, faster than passes an electron to another 2m, leading to 3am.^[20] The possibility that 4-bromobiphenyl (3am) possesses an extraordinary reactivity and thus production of $3^{\circ}am$ is predominated was excluded by the result that the coupling of 3am with 4a under the same conditions did not give $3^{\circ}am$ at all even after 24 h (Scheme 5, eq. 2).

In conclusion, we have developed the electron-catalyzed crosscoupling reaction of arylboroxines with aryl iodides by use of zinc chloride and potassium *tert*-butoxide as activators, where use of a transition metal and even an organometal is not required.

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- For reviews, see: a) Metal-Catalyzed Cross-Coupling Reactions and more, Vol. 1–2, 2nd ed. (Eds.: A. de Mijere, S. Bräse, M. Oestreich), Wiley-VCH, Weinheim, 2014; b) J.-P. Corbet, G. Mignani, Chem. Rev. 2006, 106, 2651–2710.
- For reviews, see: a) N. Miyaura, A. Suzuki, *Chem. Rev.* 1995, *95*, 2457–2483; b) F.-S. Han, *Chem. Soc. Rev.* 2013, *42*, 5270–5298.
- [3] a) E. Shirakawa, Y. Hayashi, K. Itoh, R. Watabe, N. Uchiyama, W. Konagaya, S. Masui, T. Hayashi, *Angew. Chem.* 2012, *124*, 222–225; *Angew. Chem. Int. Ed.* 2012, *51*, 218–221; b) N. Uchiyama, E. Shirakawa, T. Hayashi, *Chem. Commun.* 2013, *49*, 364–366; c) E. Shirakawa, K. Okura, N. Uchiyama, T. Murakami, T. Hayashi, *Chem. Lett.* 2014, *43*, 922–924. For the coupling with alkenyl halides, see: d) E. Shirakawa, R. Watabe, T. Murakami, T. Hayashi, *Chem. Commun.* 2013, *49*, 5219–5221.
- [4] a) H. Minami, X. Wang, C. Wang, M. Uchiyama, *Eur. J. Org. Chem.*2013, 7891–7894; b) E. Shirakawa, F. Tamakuni, E. Kusano, N. Uchiyama, W. Konagaya, R. Watabe, T. Hayashi, *Angew. Chem.*2014, *126*, 531–535; *Angew. Chem. Int. Ed.* 2014, *53*, 521–525.
- [5] H. Minami, T. Saito, C. Wang, M. Uchiyama, Angew. Chem. 2015, 127, 4748–4751; Angew. Chem. Int. Ed. 2015, 54, 4665–4668.
- [6] Q. He, L. Wang, Y. Liang, Z. Zhang, S. F. Wnuk, J. Org. Chem. 2016, 81, 9422–9427.

- [7] K. Okura, E. Shirakawa, Eur. J. Org. Chem. 2016, 3043–3046.
- [8] K. Okura, H. Kawashima, F. Tamakuni, N. Nishida, E. Shirakawa, *Chem. Commun.* 2016, 52, 14019–14022.
- [9] Borylation of aromatic compounds including aryl halides with diborons or silvlboranes is reported to proceed with no aid of transition metal catalysis. a) F. Mo, Y. Jiang, D. Qiu, Y. Zhang, J. Wang, Angew. Chem. 2010, 122, 1890-1893; Angew. Chem. Int. Ed. 2010, 49, 1846-1849; b) E. Yamamoto, K. Izumi, Y. Horita, H. Ito, J. Am. Chem. Soc. 2012, 134, 19997-20000; c) J. Yu, L. Zhang, G. Yan, Adv. Synth. Catal. 2012, 354, 2625-2628; d) D. Qiu, L. Jin, Z. Zheng, H. Meng, F. Mo, X. Wang, Y. Zhang, J. Wang, J. Org. Chem. 2013, 78, 1923-1933; e) J. Zhang, H.-H. Wu, J. Zhang, Eur. J. Org. Chem. 2013, 6263-6266; f) W. Erb, A. Hellal, M. Albini, J. Rouden, J. Blanchet, Chem. Eur. J. 2014, 20, 6608-6612; g) E. Yamamoto, S. Ukigai, H. Ito, Chem. Sci. 2015, 6, 2943-2951; h) R. Uematsu, E. Yamamoto, S. Maeda, H. Ito, T. Taketsugu, J. Am. Chem. Soc. 2015, 137, 4090-4099; i) K. Chan, M. S. Cheung, Z. Lin, P. Li, Org. Chem. Front. 2016, 3, 875-879; j) A. M. Mfuh, J. D. Doyle, B. Chhetri, H. D. Arman, O. V. Larionov, J. Am. Chem. Soc. 2016, 138, 2985-2988; k) K. Chen, S. Zhang, P. He, P. Li, Chem. Sci. 2016, 7, 3676-3680; l) M. Jiang, H. Yang, H. Fu, Org. Lett. 2016, 18, 5248-5251; m) A. M. Mfuh, V. T. Nguyen, B. Chhetri, J. E. Burch, J. D. Doyle, V. N. Nesterov, H. D. Arman, O. V. Larionov, J. Am. Chem. Soc. 2016, 138, 8408-8411; n) L. Zhang, L. Jiao, J. Am. Chem. Soc. 2017, 139, 607-610; o) L. Zhang, L. Jiao, Chem. Sci. 2018, 9, 2711-2722
- [10] For reviews on "electron catalysis", see: a) A. Studer, D. P. Curran, *Nat. Chem.* **2014**, *6*, 765–773; b) A. Studer, D. P. Curran, *Angew. Chem.* **2016**, *128*, 58–106; *Angew. Chem. Int. Ed.* **2016**, *55*, 58–102.
- [11] The transition metal-free coupling of arylboronic acids with allylic, propargylic and benzylic halides has been reported, where a non-radical mechanism is proposed, see: a) A. Scrivanti, V. Beghetto, M. Bertoldini, U. Matteoli, *Eur. J. Org. Chem.* 2012, 264–268; b) M. Ueda, K. Nishimura, R. Kashima, I. Ryu, *Synlett* 2012, 23, 1085–1089; c) M. Ueda, K. Nishimura, I. Ryu, *Synlett* 2013, 24, 1683–1686; d) M. Ueda, D. Nakakoji, Y. Kuwahara, K. Nishimura, I. Ryu, *Tetrahedron Lett.* 2016, 57, 4142–4144.
- [12] Aryl(ethyl)zinc reagents, prepared from arylboronic acids and diethylzinc, have often been used for the asymmetric arylation of aldehydes. For the first example, see: a) C. Bolm, J. Rudolph, J. Am. Chem. Soc. 2002, 124, 14850–14851. For reviews, see: b) F. Schmidt, R. T. Stemmler, J. Rudolph, C. Bolm, Chem. Soc. Rev. 2006, 35, 454–470; c) M. W. Paixão, A. L. Braga, D. S. Lüdtke, J. Braz. Chem. Soc. 2008, 19, 813–830.
- [13] For a mechanistic study on transmetalation between boron and zinc, see: a) C. Jimeno, S. Sayalero, T. Fjermestad, G. Colet, F. Maseras, M. A. Pericàs, Angew. Chem. 2008, 120, 1114–1117; Angew. Chem. Int. Ed. 2008, 47, 1098–1101. Transmetalation between arylboronic acids and diethylzinc is reported to give not only aryl(ethyl)zinc species but also aryln(ethyl)4-nborates (n = 0-4). b) R. B. Bedford, N. J. Gower, M. F. Haddow, J. N. Harvey, J. Nunn, R. A. Okopie, R. F. Sankey, Angew. Chem. 2012, 124, 5531–5534; Angew. Chem. Int. Ed. 2012, 51, 5435–5438.
- [14] Electron-rich arylboronic acids such as 1b are reported to have high tendency to form the corresponding boroxines. Y. Tokunaga, H. Ueno, Y. Shimomura, T. Seo, *Heterocycles* 2002, *57*, 787–790.
- [15] ZnCl₂ (99.999% trace metals basis, Sigma-Aldrich Co., product number 229997) and KOt-Bu (99.99% trace metals basis, Sigma-Aldrich Co., product number 659878) were used in all entries in Table 2. The reaction using ZnCl₂ and KOt-Bu purchased from a different supplier (Wako Pure Chemical Industries) under the conditions of entry 5 scored a comparable yield (96%) of **3aa** with a full conversion of **2a**. For the details, see Supporting Information. In addition to this result, the outcome that no coupling took place by use of K₃PO₄ or K₂CO₃ instead of KOt-Bu (entries 6 and 7 of Table 2) supports to exclude the possibility that the present cross-coupling is catalyzed by a trace amount of a transition metal such as palladium

contained in the reagents because K₃PO₄ and K₂CO₃ are known to be effective bases for the palladium-catalyzed Suzuki–Miyaura coupling reaction. For a recent example of the Suzuki–Miyaura coupling that was initially considered to be transition metal-free but later was revealed to be catalyzed by a trace amount of palladium contained in the reagents, see: a) K. Inamoto, C. Hasegawa, K. Hiroya, Y. Kondo, T. Osako, Y. Uozumi, T. Doi, *Chem. Commun.* **2012**, *48*, 2912–2914; b) K. Inamoto, L. D. Campbell, T. Doi, K. Koide, *Tetrahedron Lett.* **2012**, *53*, 3147–3148.

- [16] An enolate derived from NMP and KOt-Bu is known to work as a single electron donor toward aryl halides in the reduction of aryl halides into arenes. S. Zhou, E. Doni, G. M. Anderson, R. G. Kane, S. W. MacDougall, V. M. Ironmonger, T. Tuttle, J. A. Murphy, J. Am. Chem. Soc. 2014, 136, 17818–17826.
- [17] No involvement of aryl radical species is supported by a radical clock experiment using 2-(3-butenyl)phenyl iodide (2h), which is often used for a radical clock reaction and the radical derived from which is known to readily cyclize (k_c = 5 x 10⁻⁸ s⁻¹ at 50 °C). The coupling of 2h did not give any cyclization product but the coupling product in a high yield (Table 3, entry 8). For radical clock reactions using 2h, see: a) A. L. J. Beckwith, W. B. Gara, *J. Am. Chem. Soc.* 1969, *91*, 5691–5692; b) H.-X. Zheng, X.-H. Shan, J.-P. Qu, Y.-B. Kang, *Org. Lett.* 2017, *19*, 5114–5117. See also Refs. [3b] and [4b].
- [18] A DFT calculation study on the coupling of aryl Grignard reagents with aryl iodides (*cf.* Ref. [3a]) is reported to show that the coupling proceeds through an aryl radical intermediate derived from an aryl iodide in a unique situation, where the aryl radical does not behave as a usual σ-radical species. B. E. Haines, O. Wiest, *J. Org. Chem.* **2014**, *79*, 2771–2774.
- [19] Cation radical [Ar¹-Y]⁺, which is generated by SET in the initiation step, reacts with another Ar¹-Y to give [Ar¹-Ar¹]⁺, from which SET to I-Ar² takes place to give Ar¹-Ar¹ and [I-Ar²]⁺. Actually, a small amount of Ar¹-Ar¹ derived from an arylboroxine (4) is observed in each reaction. For example, the coupling reaction of phenylboroxine (4a) with 4-iodoanisole (2a) gave biphenyl in 1.1% yield based on 2a (Table 2, entry 5). See also Refs. [3b] and [4b].
- [20] Bromo- or chloro-substituted iodobenzenes are often used for the probe of the involvement of radical anion intermediates in $S_{RN}1$ reaction, where bissubstitution predominantly takes place. a) J. F. Bunnett, X. Creary, J. Org. Chem. **1974**, 39, 3611–3612. b) J. F. Bunnett, X. Creary, J. Org. Chem. **1974**, 39, 3612–3614. For an effective utilization of this system, see: c) B. Janhsen, C. G. Daniliuc, A. Studer, Chem. Sci. **2017**, 8, 3547–3553.

Entry for the Table of Contents

COMMUNICATION



An electron was found to catalyze the coupling of arylboron compounds with aryl iodides with the aid of zinc chloride and potassium *tert*-butoxide to give the corresponding biaryls. The transformation requires no transition metal catalysts.

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Page No. – Page No.

Electron-Catalyzed Cross-Coupling Reaction of Arylboron Compounds with Aryl Iodides

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