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C–C Coupling

Single-Electron-Transfer-Induced Coupling of Arylzinc Reagents with Aryl and Alkenyl Halides**

Eiji Shirakawa, Fumiko Tamakuni, Eugene Kusano, Nanase Uchiyama, Wataru Konagaya, Ryo Watabe, and Tamio Hayashi*

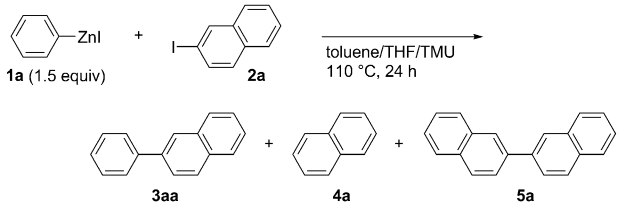
Abstract: *Arylzinc reagents, prepared from aryl halides/zinc powder or aryl Grignard reagents/zinc chloride, were found to undergo coupling with aryl and alkenyl halides without the aid of transition-metal catalysis to give biaryls and styrene derivatives, respectively. In this context, we have already reported the corresponding reaction using aryl Grignard reagents instead of arylzinc reagents. Compared with the Grignard cross-coupling, the present reaction features high functional-group tolerance, whereby electrophilic groups such as alkoxycarbonyl and cyano groups are compatible as substituents on both the arylzinc reagents and the aryl halides. Aryl halides receive a single electron and thereby become activated as the corresponding anion radicals, which react with arylzinc reagents, thus leading to the cross-coupling products.*

The cross-coupling reaction of arylmetals with aryl and alkenyl halides under transition-metal catalysis is widely used for the synthesis of biaryls and styrene derivatives.[1] The Negishi coupling utilizes palladium complexes as catalysts and arylzinc reagents as arylmetals that are compatible with various electrophilic functional groups.[2] On the other hand, we have recently reported the transition-metal-free coupling of aryl Grignard reagents with aryl and alkenyl halides.[3–5] Single-electron transfer (SET) from aryl Grignard reagents to aryl and alkenyl halides makes the cross-coupling possible without the aid of transition-metal catalysis. However, the use of aryl Grignard reagents limits the scope of substrates to those without electrophilic substituents that would react with aryl Grignard reagents. Herein, we report that the coupling reaction of arylzinc reagents with aryl and alkenyl halides proceeds through a single-electron-transfer mechanism to give biaryls and styrene derivatives with electrophilic substituents such as alkoxycarbonyl and cyano groups without using any costly additives.

Phenylzinc iodide (**1a**) was prepared by mixing iodobenzene and zinc powder (2 equiv) in *N*,*N*,*N*′,*N*′-tetramethylurea (TMU) at 110 °C for 16 h followed by five-fold dilution with THF and filtration to remove the unreacted zinc.[6] The reaction of 2-iodonaphthalene (**2a**) with the THF/TMU solution of **1a** (1.5 equiv) in toluene (toluene/THF/TMU = 5:4:1) at 110 °C was not completed (70 % conv.) in 24 h, giving 2-phenylnaphthalene (**3aa**) in 52 % yield in addition to considerable amounts (10 %) of naphthalene (**4a**) and 2,2′-binaphthyl (**5a**; Table 1, entry 1).[7] A longer reaction time (48 h) was required for full conversion of **2a** (Table 1, entry 2). The addition of LiCl accelerated the reaction, thereby allowing it to be completed in 24 h (Table 1, entries 3–5). Considering the intensive investigation into this issue by Koszinowski[8], LiCl likely enhances the reactivity of PhZnI by forming more nucleophilic lithium zincates such as $\mathrm{Li^+[PhZnICl]^-}$. A higher selectivity for **3aa** was observed when using a larger amount of LiCl, where 4 equiv was found to be sufficient.[9]

The coupling reaction in the presence of 4 equiv of LiCl is applicable to various arylzinc iodides and aryl halides

Table 1: Coupling of phenylzinc iodide with 2-iodonaphthalene.[a]



Entry	Amount of LiCl (equiv)	Conv. of **2a** [%][b]	Yield [%][b]		
			3aa	**4a**	**5a**
1	0	70	52	7	3
2[c]	0	>99	82	9	8
3	1.5	>99	81	4	7
4	4	>99	95 (92)[d]	1	2
5	8	>99	91	2	2

[a] The reaction was carried out under a nitrogen atmosphere at 110 °C for 24 h using a THF/TMU (4:1) solution of phenylzinc iodide (**1a**: 0.35 M, 0.86 mL, 0.30 mmol) and 2-iodonaphthalene (**2a**: 0.20 mmol) in the presence or absence of LiCl in toluene (0.86 mL). [b] Determined by GC. [c] Reaction time = 48 h. [d] The yield of isolated product is given in parentheses.

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[*] Prof. E. Shirakawa, F. Tamakuni, E. Kusano, N. Uchiyama, W. Konagaya, R. Watabe
Department of Chemistry, Graduate School of Science
Kyoto University, Sakyo, Kyoto, 606-8502 (Japan)
E-mail: shirakawa@kuchem.kyoto-u.ac.jp
Prof. T. Hayashi
Institute of Materials Research and Engineering
3 Research Link, 117602 (Singapore)
and
Department of Chemistry, National University of Singapore
3 Science Drive 3, 117543 (Singapore)

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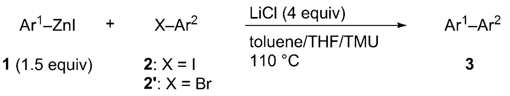
Table 2: Coupling of arylzinc iodides with aryl halides.[a]



$$\underset{\mathbf{1}\ (1.5\ \text{equiv})}{\mathrm{Ar^1{-}ZnI}} + \underset{\mathbf{2}:\ X = I;\ \mathbf{2'}:\ X = Br}{\mathrm{X{-}Ar^2}} \xrightarrow[\text{toluene/THF/TMU, 110 °C}]{\text{LiCl (4 equiv)}} \underset{\mathbf{3}}{\mathrm{Ar^1{-}Ar^2}}$$

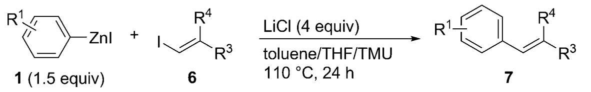
Entry	Ar^1 in Ar^1–ZnI (**1**)	Ar^2–X (**2**)	*t* [h]	Yield [%][b]	Product
1	Ph (**1a**)	2-naphthyl–I (**2a**)	24	92	**3aa**
2	Ph (**1a**)	*p*-$EtOCOC_6H_4$–I (**2b**)	24	88	**3ab**
3	Ph (**1a**)	*p*-NCC_6H_4–I (**2c**)	24	91	**3ac**
4	Ph (**1a**)	*p*-$CF_3C_6H_4$–I (**2d**)	24	85	**3ad**
5	Ph (**1a**)	*p*-ClC_6H_4–I (**2e**)	24	78	**3ae**
6	Ph (**1a**)	*p*-$MeOC_6H_4$–I (**2f**)	24	91	**3af**
7	Ph (**1a**)	*p*-MeC_6H_4–I (**2g**)	48	71[c]	**3ag**
8	Ph (**1a**)	*o*-PhC_6H_4–I (**2h**)	24	90	**3ah**
9	Ph (**1a**)	*o*-homoallyl-C_6H_4–I (**2i**)	24	92	**3ai**
10	Ph (**1a**)	1-$PhSO_2$-5-indolyl–I (**2j**)	48	90	**3aj**
11	Ph (**1a**)	1-Me-5-indolyl–I (**2k**)	48	71[d]	**3ak**
12	Ph (**1a**)	6-quinolyl–I (**2l**)	48	78	**3al**
13	Ph (**1a**)	3-quinolyl–I (**2m**)	48	72	**3am**
14	Ph (**1a**)	2-naphthyl–Br (**2′a**)	48	92	**3aa**
15	Ph (**1a**)	*p*-$EtOCOC_6H_4$–Br (**2′b**)	48	83	**3ab**
16	Ph (**1a**)	*p*-NCC_6H_4–Br (**2′c**)	48	94	**3ac**
17	*p*-$EtOCOC_6H_4$ (**1b**)	2-naphthyl–I (**2a**)	48	84	**3ba**
18	*p*-$EtOCOC_6H_4$ (**1b**)	*p*-$CF_3C_6H_4$–I (**2d**)	48	80	**3bd**
19	*p*-$EtOCOC_6H_4$ (**1b**)	Ph–I (**2n**)	48	92	**3bn**
20	*p*-$CF_3C_6H_4$ (**1c**)	2-naphthyl–I (**2a**)	48	89	**3ca**
21	*p*-$CF_3C_6H_4$ (**1c**)	*p*-$EtOCOC_6H_4$–I (**2b**)	48	80	**3cb**
22	*p*-$MeOC_6H_4$ (**1d**)	2-naphthyl–I (**2a**)	48	89	**3da**
23	*p*-$MeOC_6H_4$ (**1d**)	*p*-$EtOCOC_6H_4$–I (**2b**)	24	88	**3db**
24	*p*-$MeOC_6H_4$ (**1d**)	*p*-$CF_3C_6H_4$–I (**2d**)	24	88	**3dd**
25	2-thienyl (**1e**)	2-naphthyl–I (**2a**)	24	98	**3ea**
26	2-thienyl (**1e**)	1-$PhSO_2$-5-indolyl–I (**2j**)	24	97	**3ej**

[a] The reaction was carried out under a nitrogen atmosphere at 110 °C using a THF/TMU (4:1) solution (0.8 mL on average) of an arylzinc iodide (**1**: 0.30 mmol), an aryl halide (**2** or **2′**: 0.20 mmol), and LiCl (0.80 mmol) in toluene (0.8 mL on average). Unless otherwise noted, the conversion of **2** or **2′** was $>90\%$. [b] The yield of isolated product based on **2** or **2′**. [c] Conversion of **2g** was 85 %. 87 % yield/$>99\%$ conversion was achieved with a reaction time of 96 h. [d] Conversion of **2k** was 82 %.

(Table 2). Besides 2-iodonaphthalene (**2a**), diverse aryl iodides underwent the coupling reaction with phenylzinc iodide (**1a**; Table 2, entries 1–13).[10] The reaction of aryl iodides with a substituent that would react with aryl Grignard reagents gave the corresponding biphenyls (Table 2, entries 2 and 3). *p*-(Trifluoromethyl)phenyl iodide (**2d**) did not undergo halogen–metal exchange with PhZnI (**1a**) in contrast to the case with PhMgBr,[3a]but rather gave the coupling product in a high yield (Table 2, entry 4). Chloro substitution was also compatible (Table 2, entry 5). A methoxy-substituted phenyl iodide was more reactive than a methyl-substituted one, the conversion of which was only 85 % even after 48 h to give **1a** in 71 % yield (Table 2, entries 6 and 7). *Ortho* substitution was tolerated (Table 2, entries 8 and 9). Heteroaryl iodides also participated in the coupling (Table 2, entries 10–13). The reaction of aryl bromides gave the coupling products in comparable yields (Table 2, entries 14–16).[11] Ester functionality is also compatible on the phenylzinc moiety (Table 2, entries 17–19). Phenylzinc reagents with an electron-withdrawing or -donating group underwent coupling with aryl iodides (Table 2, entries 20–24). Finally, the coupling is applicable to heteroarylzinc reagents (Table 2, entries 25 and 26).

In addition to aryl halides, alkenyl iodides can be used as sp^2-carbon electrophiles to give styrene derivatives upon reaction with arylzinc reagents (Table 3).[4] (*E*)- and (*Z*)-1-octenyl iodides (**6a**) underwent coupling with phenylzinc iodide (**1a**), thereby giving the corresponding coupling products with retention of stereochemsitry (Table 3, entries 1 and 2). (*E*)-Styryl iodide (**6b**) also participated in the coupling (Table 3, entry 3). β-Iodoacrylate **6c**, which has a low-lying LUMO, showed high reactivity and underwent coupling with **1a** even at 80 °C to give cinnamate **7ac** (Table 3, entry 4). Ethoxycarbonyl and methoxy groups were compatible as substituents on the arylzinc reagents (Table 3, entries 5 and 6).

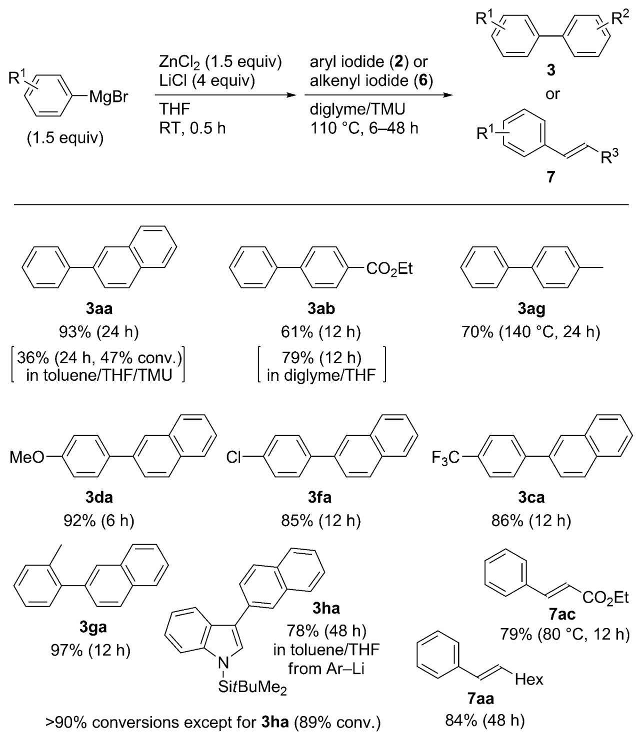
Table 3: Coupling of arylzinc iodides with alkenyl iodides.[a]



Entry	Ar^1 in Ar^1–ZnI (**1**)	Alkenyl halide (**6**) R^3	R^4		Yield [%][b]	Product
1	Ph (**1a**)	hexyl	H	(*E*)-**6a**	84	(*E*)-**7aa**
2	Ph (**1a**)	H	hexyl	(*Z*)-**6a**	76	(*Z*)-**7aa**
3	Ph (**1a**)	Ph	H	(*E*)-**6b**	90	(*E*)-**7ab**
4[c]	Ph (**1a**)	CO_2Et	H	(*E*)-**6c**	80	(*E*)-**7ac**
5[d]	*p*-$EtOCOC_6H_4$ (**1b**)	hexyl	H	(*E*)-**6a**	81	(*E*)-**7ba**
6	*p*-$MeOC_6H_4$ (**1d**)	hexyl	H	(*E*)-**6a**	91	(*E*)-**7da**

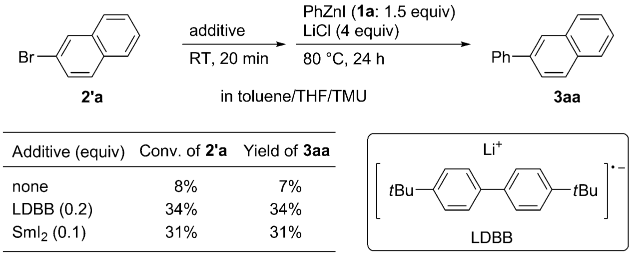
[a] The reaction was carried out under a nitrogen atmosphere at 110 °C for 24 h using a THF/TMU (4:1) solution (0.7 mL on average) of an arylzinc iodide (**1**: 0.30 mmol), an alkenyl halide (**6**: 0.20 mmol), and LiCl (0.80 mmol) in toluene (0.7 mL on average). Full conversion of **6** was observed for all entries. [b] The yield of isolated product based on **6**. [c] At 80 °C. [d] Reaction time = 48 h.

Arylzinc reagents are also readily available through transmetalation of aryl Grignard reagents with zinc salts. As shown in Scheme 1, a phenylzinc reagent prepared from PhMgBr and $ZnCl_2$[12] underwent coupling with 2-iodonaphthalene (**2a**) under the conditions employed in Table 2 (toluene/THF/TMU = 5:4:1, 110 °C, 24 h) but the reaction did not reach completion (36 % yield/47 % conv.).[13] The use of diglyme as a cosolvent instead of toluene enhanced the reaction rate, thus resulting in the production of **3aa** in 93 % yield ($>99\%$ conv. of **2a**).[14] Other aryl iodides including those with an ester moiety underwent coupling to give **3ab** and **3ag**.[15] Phenylzinc reagents with an electron-donating or -withdrawing group at the *para* position and an *o*-tolylzinc reagent participated in the coupling. An indolylzinc reagent prepared from the corresponding organolithium underwent coupling. Styrene derivatives **7aa** and **7ac** were obtained through coupling with alkenyl iodides.



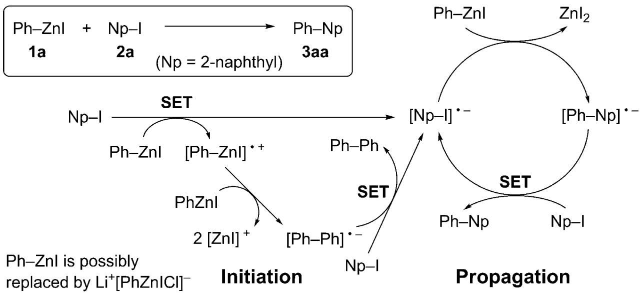
Scheme 1. Coupling of arylzinc reagents prepared from aryl Grignard reagents.

In our report,[3a] the occurrence of SET initiation in the coupling of aryl Grignard reagents with aryl halides was confirmed by the observation that the addition of lithium 4,4′-di-*tert*-butylbiphenylide (LDBB) drastically accelerated the coupling. This result may be rationally understood by inferring that LDBB works as a much more efficient single-electron donor than Grignard reagents in the slow initiation step and thus the overall reaction rate is increased. We conducted similar experiments for the arylzinc coupling using LDBB or SmI_2 as a single-electron donor. The reactivity of 2-bromonaphthalene (**2′a**) toward PhZnI (**1a**) is quite low at 80 °C, giving only 7% yield of coupling product **3aa** (Scheme 2). By contrast, the treatment of **2′a** with LDBB (0.2 equiv)[16] or SmI_2 (0.1 equiv),[17] 20 min before the addition of **1a**, gave **3aa** in 34% or 31% yield, respectively.[18] The observed acceleration is compatible with SET initiation, and it is likely that $[Np{-}Br]^{\bullet-}$, generated by SET, has a lifetime long enough to react with **1a** before undergoing decomposition to $Np^{\bullet}$.[19]



Additive (equiv)	Conv. of **2′a**	Yield of **3aa**
none	8%	7%
LDBB (0.2)	34%	34%
SmI_2 (0.1)	31%	31%

Scheme 2. Effect of addition of single-electron donors.



Scheme 3. A plausible mechanism.

Considering the above result in conjunction with similarities in intrinsic character between arylzinc and arylmagnesium reagents, the present coupling reaction is likely to follow the mechanism of the Grignard cross-coupling[3b] as shown in Scheme 3, exemplified by the reaction of Ph–ZnI (**1a**) with 2-iodonaphthalene (Np–I: **2a**). The reaction is initiated by SET from Ph–ZnI to Np–I to give the anion radical $[Np{-}I]^{\bullet-}$, which reacts with Ph–ZnI. SET from the resulting anion radical, $[Ph{-}Np]^{\bullet-}$, to Np–I gives the coupling product Ph–Np and regenerates $[Np{-}I]^{\bullet-}$, thereby beginning another propagation cycle. The cation radical $[Ph{-}ZnI]^{\bullet+}$, generated upon SET in the initiation step, reacts with Ph–ZnI to give the anion radical $[Ph{-}Ph]^{\bullet-}$, which acts as another single-electron donor toward Np–I to give $[Np{-}I]^{\bullet-}$ and Ph–Ph. A small amount of $Ar^1{-}Ar^1$ derived from $Ar^1{-}ZnI$ is always observed.[20] Lack of involvement by aryl radical intermediates is confirmed by the fact that no cyclization products were detected in the reaction of *o*-homoallylphenyl iodide (**2i**; Table 2, entry 9).[21] The conservation of stereochemistry in the reaction of alkenyl halides (Table 3) also supports there being no involvement of σ-radical species.[4,22]

In conclusion, we have developed a coupling reaction of arylzinc reagents with aryl and alkenyl halides. The cross-coupling reaction, mediated by single-electron transfer, features a wide substrate scope that includes substrates with an electrophilic substituent such as an alkoxycarbonyl or cyano group.

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[1] For reviews, see: a) J. Hassan, M. Sévignon, C. Gozzi, E. Schulz, M. Lemaire, *Chem. Rev.* **2002**, *102*, 1359–1469; b) *Metal-Catalyzed Cross-Coupling Reactions*, *Vol. 1–2*, 2nd ed. (Eds.: A. de Meijere, F. Diederich), Wiley-VCH, Weinheim, **2004**.

[2] a) E. Negishi, A. O. King, N. Okukado, *J. Org. Chem.* **1977**, *42*, 1821–1823; For reviews, see: b) E. Negishi, *Acc. Chem. Res.* **1982**, *15*, 340–348; c) E. Negishi in *Handbook of Organopalladium Chemistry for Organic Synthesis*, *Vol. 1* (Eds.: E. Negishi, A. de Meijere), Wiley-Interscience, New York, **2002**, chap. III.2.1, pp. 229–247.

[3] For the coupling with aryl halides: 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; for the mechanistic aspects, see: b) N. Uchiyama, E. Shirakawa, T. Hayashi, *Chem. Commun.* **2013**, *49*, 364–366.

[4] For the coupling with alkenyl halides: E. Shirakawa, R. Watabe, T. Murakami, T. Hayashi, *Chem. Commun.* **2013**, *49*, 5219–5221.

[5] The transition-metal-free cross-coupling reaction of allyl halides with aryl- and alkenylboronic acids has been reported, for which a nonradical mechanism is proposed; 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**, 1085–1089.

[6] a) K. Takagi, *Chem. Lett.* **1993**, 469–472; b) M. Amano, A. Saiga, R. Ikegami, T. Ogata, K. Takagi, *Tetrahedron Lett.* **1998**, *39*, 8667–8668.

[7] The coupling of PhMgBr (1.5 equiv) with **2a** in toluene in the presence of THF (6 equiv) at 110 °C for 24 h gave **3aa** in 96 % yield. See Ref. [3a].

[8] Formation of lithium organozincates such as $Li^+[RZnXCl]^-$ upon mixing RZnX (R = alkyl or aryl) with LiCl has been confirmed; a) J. E. Fleckenstein, K. Koszinowski, *Organometallics* **2011**, *30*, 5018–5026; for examples reported by others of enhancement of the reactivities of organozinc reagents by addition of LiCl, see: b) A. Krasovskiy, V. Malakhov, A. Gavryushin, P. Knochel, *Angew. Chem.* **2006**, *118*, 6186–6190; *Angew. Chem. Int. Ed.* **2006**, *45*, 6040–6044; c) H. Ren, G. Dunet, P. Mayer, P. Knochel, *J. Am. Chem. Soc.* **2007**, *129*, 5376–5377; d) N. Boudet, S. Sase, P. Sinha, C.-Y. Liu, A. Krasovskiy, P. Knochel, *J. Am. Chem. Soc.* **2007**, *129*, 12358–12359; e) A. Metzger, M. A. Schade, P. Knochel, *Org. Lett.* **2008**, *10*, 1107–1110; f) H. Ochiai, M. Jang, K. Hirano, H. Yorimitsu, K. Oshima, *Org. Lett.* **2008**, *10*, 2681–2683; g) G. T. Achonduh, N. Hadei, C. Valente, S. Avola, C. J. O'Brien, M. G. Organ, *Chem. Commun.* **2010**, *46*, 4109–4111; h) D. R. Armstrong, W. Clegg, P. García-Álvarez, A. R. Kennedy, M. D. McCall, L. Russo, E. Hevia, *Chem. Eur. J.* **2011**, *17*, 8333–8341.

[9] Zinc powder (99.995 % trace metals basis, Aldrich Co., product number 324930) was used for the preparation of arylzinc reagents. Inductively coupled plasma atomic emission spectroscopy (ICP-AES) analysis of the zinc powder showed that the content of Fe, Co, Ni, Cu, Ru, Rh, Pd, Ag, Ir, Pt, and Au are less than 5 ppm (under the detection limit). For details of the ICP-AES analysis, see the Supporting Information. LiCl (≥ 99.99 % trace metals basis, Aldrich Co., product number 203637) was used as an additive. The reaction of **1a** with **2a** under the conditions of entry 4 in Table 1 using a different lot of zinc powder (99.9 % purity, Wako Pure Chemical Industries, product number 262-01581) or LiCl (99 % purity, Wako Pure Chemical Industries, product number 123-01162) gave essentially the same result: Zn (Aldrich) and LiCl (Wako), > 99 % conv. of **2a**, 91 % yield of **3aa**, 2 % yield of **4**, 3 % yield of **5**; Zn (Wako) and LiCl (Aldrich), > 99 % conv. of **2a**, 91 % yield of **3aa**, 1 % yield of **4**, 2 % yield of **5**. It is impossible to completely eliminate the possibility that small amounts of transition-metal impurities show some positive effect. But even in that case, they are considered to be involved in the SET mechanism described below.

[10] We asked Dr. Yoshiaki Nakao (Graduate School of Engineering, Kyoto University) to repeat the reaction and he confirmed that the reaction of PhZnI (**1a**: prepared by him from Ph–I and Zn) with ethyl *p*-iodobenzoate (**2b**) under the conditions of entry 2 of Table 2 gave **3ab** in 85 % yield. This result, in conjunction with the result that the coupling is insensitive to the lot of the reagents used (Zn and LiCl) as shown in Ref. [9], shows that this method is reproducible. In addition, **3aa** and **3ab** were obtained in similar yields (92 % and 88 %, respectively) under the conditions of entries 1 and 2 in Table 2 by using pippeters equipped with a polypropylene chip and Teflon-coated spatulas instead of the glass syringes with a metallic needle and metallic spatulas that we usually use. For details, see the Supporting Information.

[11] 2-Naphthyl triflate was much less reactive than the corresponding bromide (**2′a**) and gave **3aa** in only 4 % yield (4 % conv.) in the reaction with **1a** under the conditions of entry 14 in Table 2. Aryl triflates are usually more reactive than aryl bromides under transition-metal catalysis.

[12] $ZnCl_2$ (anhydrous powder, ≥ 99.995 % trace metals basis, Aldrich Co., product number 429430) was used. Magnesium turning (99.95 % purity trace metals basis, Aldrich Co., product number 403148) was used for the preparation of the Grignard reagents in Scheme 1. For analysis of the magnesium turning, see footnote 9 of Ref. [3a].

[13] MgX_2 (X = halogen) generated upon transmetalation might alter the structure of the zincate derived from PhZnX and LiCl and thus affect its reactivity. For a report on the effect of the method used to prepare the arylzinc halides on the efficiency of the reaction, see: L. Jin, C. Liu, J. Liu, F. Hu, Y. Lan, A. S. Batsanov, J. A. K. Howard, T. B. Marder, A. Lei, *J. Am. Chem. Soc.* **2009**, *131*, 16656–16657.

[14] Although it is unclear how diglyme affects the reaction, a possible explanation is that the magnesium halides produced upon transmetalation have a negative effect that is negated by complexation of the salt with diglyme. For complexation of magnesium halides with diglyme, see: a) Y. Saheki, K. Sasada, N. Satoh, K. Kawaichi, K. Negoro, *Chem. Lett.* **1987**, 2299–2300; b) N. Metzler, H. Noeth, M. Schmidt, A. Z. Treitl, *Z. Naturforsch. B* **1994**, *49*, 1448–1451.

[15] Diglyme/THF/TMU (5:4:1) was a better solvent system than diglyme/THF (3:2) in the reactions shown in Scheme 1 except for that of **1a** with **2b**.

[16] For an example of utilization of a radical anion of an arene, sodium naphthalenide, as a single-electron donor in the $S_{RN}1$ reaction, see: G. A. Russell, R. K. Norris, E. J. Panek, *J. Am. Chem. Soc.* **1971**, *93*, 5839–5845.

[17] For examples of utilization of SmI_2 as a single-electron donor in the $S_{RN}1$ reaction, see: a) M. A. Nazareno, R. A. Rossi, *Tetrahedron Lett.* **1994**, *35*, 5185–5188; b) Y. Zhang, H. Guo, *Heteroat. Chem.* **2001**, *12*, 539–541.

[18] In our previous report (Ref. [3a]), the addition of LDBB to a mixture of PhMgBr and **2′a** accelerated the reaction. In contrast, addition in this sequence for **1a** and **2′a** gave no acceleration; only 3 % or < 1 % yield of **3aa** was obtained with LDBB and SmI_2, respectively. It is unclear why the addition of these single-electron donors in the presence of **1a** did not work. In the latter case, SmI_2 could be converted into organometallic species such as Ph_2Sm, which may negatively affect the reaction system.

[19] The lifetime of $[Ar{-}X]^{\bullet-}$ is reported to be too short to react with some substrates owing to fast fragmentation into $Ar^\bullet$ and X^-. However, only data for the reaction in polar solvents such as *N*-methylpyrrolidone and *N*,*N*-dimethylformamide are available. For recent examples, see: a) C. Costentin, M. Robert, J.-M. Savéant, *J. Am. Chem. Soc.* **2004**, *126*, 16051–16057; b) N. Takeda, P. V. Poliakov, A. R. Cook, J. R. Miller, *J. Am. Chem. Soc.* **2004**, *126*, 4301–4309.

[20] For example, 0.008 mmol of Ph–Ph was detected by GC in the reaction of PhZnI (**1a**: 0.30 mmol) with Np–I (**2a**: 0.20 mmol; Table 1, entry 4).

[21] The *o*-homoallylphenyl radical is known to readily cyclize ($k_c = 5 \times 10^8\,s^{-1}$ at 50 °C): a) A. N. Abeywickrema, A. L. J. Beckwith, *J. Chem. Soc. Chem. Commun.* **1986**, 464–465; b) H. Yasuda, Y. Uenoyama, O. Nobuta, S. Kobayashi, I. Ryu, *Tetrahedron Lett.* **2008**, *49*, 367–370; consequently, if the aryl radical is involved as an intermediate, it must undergo cyclization at least in part. For a detailed discussion, see Equation (4) of Ref. [3b] and its explanatory sentences.

[22] We reported competition between different aryl bromides in the reaction with PhMgBr to show operation of the SET mechanism in the Grignard cross-coupling (Ref. [3a], Scheme 3). A similar outcome was obtained in the competition reaction between the aryl bromides or iodides when using PhZnI instead of PhMgBr (Scheme S1 and S2 in the Supporting Information). In addition, the effect of the addition of a catalytic amount of a Fe, Cu, Ni, Co, or Pd complex on the selectivity of the cross-coupling reaction was examined (Schemes S1–S4 in the Supporting Information), to show that these transition-metal complexes are not involved as small amounts of impurities that catalyze the present cross-coupling reaction. For details, see the Supporting Information.